2019-05-29

Psychosocial Reserve Capacity as Moderator of the Relationship Between Chronic Stress and Cardiovascular Health: Results from the Multi-Ethnic Study of Atherosclerosis

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PSYCHOSOCIAL RESERVE CAPACITY AS MODERATOR OF THE RELATIONSHIP BETWEEN CHRONIC STRESS AND CARDIOVASCULAR HEALTH: RESULTS FROM THE MULTI-ETHNIC STUDY OF ATHEROSCLEROSIS

By

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A DISSERTATION

Submitted to the Faculty
of the University of Miami
in partial fulfillment of the requirements for
the degree of Doctor of Philosophy

Coral Gables, Florida

August 2019

UNIVERSITY OF MIAMI

A dissertation submitted in partial fulfillment of
the requirements for the degree of
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FOTI, SAMANTHA A. (Ph. D., Psychology)
Psychosocial Reserve Capacity as Moderator of the Relationship Between Chronic Stress and Cardiovascular Health: Results from the Multi-Ethnic Study of Atherosclerosis (August 2019)

Abstract of a dissertation at the University of Miami.

Dissertation supervised by Professor Maria M. Llabre.
No. of pages in text. (82)

Chronic stress can result in long-term changes that influence susceptibility to disease, including cardiovascular disease (CVD). Perceptions of stressors such as relationship struggles, financial burden, and job strain, differ based on availability of both tangible and intangible resources, such as level of education, emotional support, and health insurance coverage. The availability of these resources, which comprise an individual's psychosocial reserve capacity, may moderate the relationship between chronic stress burden and cardiovascular health. Since chronic stress has been inconsistently operationalized in literature, the current study examined a latent variable model of chronic stress in relation to components of the metabolic syndrome (MetS) (waist circumference, HDL cholesterol, triglycerides, fasting glucose, systolic and diastolic blood pressure) and CVD. We then determined the extent to which certain resources in the psychosocial reserve capacity moderate the relationship between chronic stress and cardiovascular health. Exploratory analyses examined the moderating role of sex on health outcomes and the relationship between chronic stress and depressive symptoms.

Analyses were conducted on previously collected data from 6685 White, Black, Hispanic, and Chinese American men and women between the ages of 45 - 84 enrolled in 2000 - 2002 in the Multi-Ethnic Study of Atherosclerosis. CVD outcome was collected up until nine years post-baseline. A latent variable model, comprised of four indicators of

chronic stress (namely, money/financial, job/ability to work, relationship, and health problem (other) stress), fit the data (CFI = .988; RMSEA = .019 90% CI (.004 - .031); SRMR = .020). Additionally, measurement invariance was achieved across the four races/ethnicities, demonstrating that comparisons can be made on the same construct across groups. Results showed that latent chronic stress was positively associated with waist circumference (B = 1.00, 95% CI: 0.30 – 1.69, $p < .01$), and fasting glucose (B = 2.16, 95% CI: 0.75 – 3.56, $p < .01$) but not significantly related to HDL cholesterol, triglycerides, systolic, or diastolic blood pressure. Level of education moderated the relationship between chronic stress and HDL cholesterol, such that for less educated individuals, as chronic stress increases, HDL also increases by 1.62 mg/dL. Emotional support and health insurance coverage did not moderate the relationship between chronic stress and any MetS component. Surprisingly, chronic stress was not significantly related to CVD in any race/ethnicity, and none of the predicted moderators moderated the relationship between chronic stress and CVD.

Exploratory analyses examined the moderating role of sex on MetS components and CVD. Sex moderated the relationship between chronic stress and waist circumference (B = -1.70, 95% CI: -2.88 - -0.53, $p < .01$). In both women and men, stress was positively related to waist circumference. However, the relationship was stronger in women than in men. Sex was also a significant moderator of the relationship between chronic stress and CVD. For three races/ethnicities, men had higher odds of CVD than women. Sex did not significantly moderate the relationship between stress and CVD in Chinese Americans.

Additional exploratory analyses showed that chronic stress was positively related to depressive symptoms (B = 6.45, 95% CI: 5.61 - 7.29, $p < .001$). Higher levels of education and emotional support buffered the negative effects of chronic stress on depressive symptoms. For both levels of education, chronic stress was associated with an increase in depressive symptoms; however, this relationship was stronger in less educated individuals. Chronic stress was associated with more depressive symptoms at all levels of emotional support. However, this relationship was strongest for individuals at the lowest level of emotional support. Sex significantly moderated the relationship between chronic stress and depressive symptoms. Women started out with more depressive symptoms, than men; however, each additional increase in chronic stress was associated with a greater increase in depressive symptoms in men relative to women ($p < .001$).

These findings enhance our understanding of the concept of chronic stress in a multi-ethnic sample. Results from this study suggests that future research examining the role of chronic stress in multiple populations could utilize a latent variable over a sum score or assigning individuals to groups of stress (high, medium, low), since all indicators loaded reliably onto a latent factor in an invariant manner across races/ethnicities. Future studies should test a second-order or bi-factor latent model to enhance the definition of latent chronic stress by including more information on what contributes to the individual sources of stress. Additional research is needed to identify moderators in the chronic stress-cardiovascular health pathway.

TABLE OF CONTENTS

LIST OF FIGURES

LIST OF TABLES

Page

Chapter 1: Introduction

Chronic stress

Although there is no unified definition of stress, most scientific theorists agree that stress can be both adaptive and maladaptive; is associated with changing, threatening, or harmful events; and, over time, is characterized by disagreeable feelings and mood. Research shows that stress has significant effects on physical and mental health and pathophysiology of disease (Dougall & Baum, 2011). Generally speaking, stress results when individuals perceive that the demands of the environment exceed their adaptive capacity (Cohen, Janicki-Deverts, & Miller, 2007). Chronic stress, compared to acute stress, is considered especially toxic because it results in long-term changes to emotional, physiological, and behavioral responses that influence susceptibility to and course of diseases, such as metabolic syndrome (MetS) and cardiovascular disease (CVD) (Cohen et al., 2007).

Stress is considered a major contributing factor to the six leading causes of death in the United States: cancer, coronary heart disease, accidental injuries, respiratory disorders, cirrhosis of the liver, and suicide (Salleh, 2008). In fact, research suggests 60-90% of all doctor visits are stress-related (Perkins, 1994). Chronic stress may be triggered by a variety of social stressors, such as caregiving, social isolation, job strain, socioeconomic status, and/or marital problems. Regardless of how it is operationalized, research has consistently demonstrated that sustained stressful states are linked to negative mental and physical health outcomes (Johnson, Abbasi, & Master, 2013; Steptoe & Kivimaki, 2013).

Theories on stress and health

Stress can impact health at all stages of the disease process – etiology, progression, treatment, recovery, or recurrence. Stress has a direct impact on the body through physiological changes (e.g., damage to blood vessels, increases in heart rate, release of glucocorticoids) and through cognitive and behavioral changes (e.g., intrusive thoughts, drinking alcohol) (Dougall & Baum, 2011). Stress also affects mood and behavior and may make individuals more likely to engage in harmful behaviors (e.g. smoking or drug use) and less likely to engage in health-promoting behaviors (e.g. less exercise, higher fat food choices) (Ng & Jeffery, 2003; Zellner et al., 2006). Thus, not only is the body's biological response important to consider when evaluating theories of stress, but also the cognitive appraisals of the stressor. The biological stress response, psychological risk factors, and cognitive appraisals of a stressful situation may all influence development of later disease.

Transactional model of stress and coping

Outlined by Lazarus and Folkman (1984), the transactional model of stress and coping emphasizes the important role the individual has when interacting with a stressor. In other words, the stressor itself is not sufficient to produce stress; but rather, the stressor, in conjunction with a cognitive interpretation of the stressor as threatening, leads to the body's stress response. This transactional model of stress and coping features two stages of appraisals: primary and secondary. In the primary appraisal, an individual assesses the stressor as either harmful and threatening or benign. If a stressor is not considered threatening, no stress results. If a stressor is considered threatening, an

individual then enters the secondary stage of appraisal; in this stage, an individual assesses his/her ability to cope with the stressor based on internal (i.e. will-power, inner strength) and external (i.e. peers, professional help) resources. Differences in primary and secondary appraisals will lead to differences in stress responses.

Lifespan biopsychosocial model of cumulative vulnerability and minority health

The biopsychosocial model is a broad framework that outlines the dynamic interaction of biological factors (genetic, biochemical), psychological factors (personality, behavior, mood, cognitions), and social factors (cultural, socioeconomic) to explain health and illness, but does not account for health disparities among races/ethnicities. Research indicates a robust and persistent disparity in health status among minority groups. Black Americans experience higher rates of morbidity and mortality compared to White, Hispanic, and Asian Americans (American Heart Association, 2008; Centers for Disease & Prevention, 1998). Research also suggests that Black Americans may be more susceptible to cardiovascular consequences of stress, especially hypertension and stroke (Jonas & Lando, 2000). Furthermore, Hispanics experience higher rates of obesity, diabetes, and other CVD risk factors compared to Whites (American Heart Association, 2008).

Given the significance of minority health disparities, Myers (2009) proposed a multidimensional biopsychosocial model examining the way in which race/ethnicity interacts with a number of variables over the life course and shapes an individual's health status. This complex model, called the lifespan biopsychosocial model of cumulative vulnerability and minority health, outlines several pathways that predict health status.

This model emerged as a conceptual tool to integrate literature on minority health disparities, increase understanding of ethnic group differences, and evaluate health status based on several synergistic factors. The six primary pathways are as follows: (1) long-term chronic exposure to psychosocial adversities (namely, chronic stress burden); (2) psychosocial reserve capacity; (3) cognitive-emotional processing; (4) clustering of health injurious behaviors; (5) biological; and (6) health care pathways. The model depicts race/ethnicity interacting with socioeconomic history; which, in turn, shapes exposure to psychosocial adversities, including chronic life stressors, community stressors, and race-related stressors. Cognitive processing and emotional regulation (e.g., cognitions, mood), health behaviors (e.g. food choices, alcohol/drug use), biological vulnerabilities (e.g. family history), and stress processes are all interconnected pathways that lead to ultimate health status. This model also proposes that an individual's psychosocial reserve capacity, as adapted from Gallo and Matthews (2003), may act either as a key mediator or moderator of the relationship between chronic stress and health status. An individual's psychosocial reserve capacity refers to the availability of tangible, cultural, interpersonal, and intrapersonal resources that individuals utilize in order to buffer the negative effects of life stressors and ultimately prevent disease development (Gallo & Matthews, 2003).

The concept of the psychosocial reserve capacity aligns well with notion of secondary appraisal in the transactional model of stress and coping. Tying the two models together, an individual in the secondary stage of appraisal is likely mentally assessing and reviewing his/her reserve capacity to determine if sufficient resources are available. If an individual does not have adequate resources available in the reserve capacity and is

unable to alter, eliminate, adjust to, or minimize negative effects of a stressor, the stressor remains, perhaps chronically, and the body's adaptive stress response system will go awry (Dougall & Baum, 2011; Schneiderman, Ironson, & Siegel, 2005). Persistent activation of the stress response system, which occurs in the case of chronic stress, can lead to several diseases, including MetS and CVD.

The comprehensive nature of this model is both advantageous and disadvantageous. On one hand, its holistic and dynamic representation highlights the notion that chemical imbalances, viruses, and genetic predispositions are not the only causes of disease and illness. However, the breadth of this model also makes it difficult to empirically research the many pathways and elements. Therefore, the current study specifically focuses on the pathway linking chronic stress to cardiovascular health (namely, individual MetS components and CVD) and to what degree the psychosocial reserve capacity moderates this relationship.

Stress, MetS, and CVD

Individuals exposed to chronic stress are more likely to suffer from cardiovascular diseases such as coronary artery disease, hypertension, and coronary heart disease (CHD) (Janczura et al., 2015; Mujahid, Diez Roux, Cooper, Shea, & Williams, 2011; Troxel, Matthews, Bromberger, & Sutton-Tyrrell, 2003). A recent study conducted by Kershaw and colleagues (2015), which used data from the Multi-Ethnic Study of Atherosclerosis (MESA), found that individual-level sources of stress (i.e. health, job, relationship, and/or financial problems) were more strongly associated with incident CHD than neighborhood-level stressors (i.e., excessive trash/litter, crime, poor access to food shops,

etc.). In this study, CHD was defined as nonfatal myocardial infarction (MI), resuscitated cardiac arrest, or CHD death. Cox proportional hazard models showed that higher reported levels of individual stressors were associated with a 65% increased risk of incident CHD (95% CI:1.23 – 2.22) compared to those in the lowest category, after adjusting for age, race/ethnicity, sex, income, marital status, field site, and neighborhood poverty. In contrast, there was a non-linear relationship between neighborhood stressors and incident CHD, such that individuals in the medium category had 49% higher CHD risk compared to those in the low stress category; and those in the highest stress category had 27% higher incident CHD risk.

While this study highlighted the importance of presence and perceived stressfulness of individual level sources of chronic stress, there are certain measurement concerns. In this study, the definition of chronic stress arbitrarily assigns individuals to one of three categorical levels of stress (low, medium, high stress). More specifically, using the Chronic Burden Scale, participants endorse or deny ongoing, financial, job, relationship or health-related (both self and someone close to the participant) problems lasting at least six months. In addition, participants indicate how stressful the problems have been on a scale ranging from 1 (not very stressful) to 3 (very stressful). In the Kershaw (2015) paper, a chronic burden score was created by summing the number of domains in which moderate-to-severe stress was reported. Possible scores ranged from 0 to 5; a sum score of 0 was considered low stress, 1 was medium stress, and 2 or more was high stress. As outlined in the Measures section of the current study, the indicator of health-related stress (self), which asks the participant to what degree (s)he is stressed by his/her health status, was removed in our measure of stress. It was kept in the Kershaw

(2015) definition; in doing so, this effectively uses one's own health status to predict later health status.

Additionally, by creating a sum score in the aforementioned way, an assumption is made that responses to presence and perceived stressfulness of chronic stress is measured without any error, which is unrealistic. Latent variables are variables that are not directly observed, but rather inferred from information provided by observed variables. Latent variables are created by the shared variance of observed variables, or the degree to which variables move together. Variables that are uncorrelated cannot result in a latent variable. Examining the concept of chronic stress using a latent variable model may be a more precise and reliable approach. In a latent variable model, measurement error is explicitly examined by separating residual terms of the indicators, which includes variance that is unique to an indicator or random error. Moreover, interpretation of stressors may vary by race/ethnicity. Using a latent variable approach provides an opportunity to test for measurement invariance across races/ethnicities, to ensure that comparisons are made on the same construct across groups. Given these measurement concerns, the present study builds upon the important findings of the Kershaw et al. (2015) paper and examines a latent variable model of chronic stress burden and its relationship to CVD, defined as MI, resuscitated cardiac arrest, stroke (not transient ischemic attack), CHD death, and stroke death, using the same sample from MESA.

Furthermore, elucidating the relationship between chronic stress and MetS components may help identify individuals at risk of developing CVD (Qiao, Gao, Zhang, Nyamdorj, & Tuomilehto, 2007). Psychobiological studies have shown that increased stress reactivity directly affects blood pressure, inflammatory biomarkers, and alters

adrenocortical functioning. Increased secretion of cortisol is one marker of disrupted adrenocortical functioning. This, in turn, may lower HDL cholesterol concentration and impair glucose tolerance (Bonora et al., 2003; Krotkiewski, Bjomtorp, Sjostrom, & Smith, 1983). Furthermore, long-term stressors are associated with elevated blood pressure, lipids, and insulin levels (Innes, Vincent, & Taylor, 2007; Liu, Hanley, Young, Harris, & Zinman, 2006; Vrijkotte, van Doornen, & de Geus, 2000).

Moreover, a systematic review of prospective cohort studies supports the finding that increased psychological stress is positively related to MetS (Bergmann, Gyntelberg, & Faber, 2014). Data from the Whitehall II study also show that chronic job strain increases risk of having MetS (according to ATP III criteria); more specifically, men with chronic job strain were twice as likely to be diagnosed with MetS and women were nearly five times as likely to have MetS. Researchers found a dose-response relationship, such that greater exposure to job strain was associated with higher risk of MetS (Chandola, Brunner, & Marmot, 2006). Stress, defined by the Perceived Stress Scale (Cohen, Kamarck, & Mermelstein, 1983), was positively related to MetS diagnosis (defined via WHO, ATP III, and IDF clinical criteria) (Raikkonen, Matthews, & Kuller, 2007). The Perceived Stress Scale measures the degree to which situations in one's life are evaluated as stressful in the past month. Sample questions include, “How often have you been able to control irritations in your life”; “How often have you dealt successfully with irritating life hassles”; and, “How often have you felt nervous and ‘stressed’?” Answers are rated on a “0 = never” to “4 = very often” scale and summed for a total. Psychological distress, which is defined by the General Health Questionnaire (Goldberg & Williams, 1988) and measures the ability (or inability) to carry out normal functions

due to psychologically distressing experiences, was positively related to MetS diagnosis (Puustinen, Koponen, Kautiainen, Mantyselka, & Vanhala, 2011).

Additionally, marital stress, perceived stress, job stress, and psychological distress have been associated with weight gain (Allard et al., 2011; Block, He, Zaslavsky, Ding, & Ayanian, 2009; Kouvonen et al., 2011; Puustinen et al., 2011; Roos, Lallukka, Rahkonen, Lahelma, & Laaksonen, 2013). Some studies have found that psychological distress was positively related to diabetes, suggesting that greater distress increases levels of fasting glucose (Eriksson et al., 2008; Rod, Gronbaek, Schnohr, Prescott, & Kristensen, 2009). However, this finding has been disputed. A study on middle-aged Swedish men and women found that job stress was associated with decreased risk of diabetes after 10 years of follow-up (Eriksson, van den Donk, Hilding, & Ostenson, 2013). Another study found no association between job stress and diabetes after 8 years of follow up (Kawakami, Araki, Takatsuka, Shimizu, & Ishibashi, 1999). Using psychological distress as a predictor, Puustinen et al. (2011) found no significant association with fasting glucose after 6.5 years of follow up. Therefore, examining the relationship between chronic stress and fasting glucose is particularly important to help clarify this association.

These same researchers did find that psychological distress was associated with lower HDL cholesterol, but not significantly associated with triglycerides (Puustinen et al., 2011). Job stress was negatively associated with HDL cholesterol and positively associated with triglycerides in another study (Gimeno et al., 2010). Oksanen et al. (2011) examined job stress and found a positive relationship with hypertension, in men only. However, several other studies on job strain did not find a significant relationship

with blood pressure (Fauvel et al., 2003; Kivimaki et al., 2007). Psychological distress also was not a significant predictor of hypertension (Puustinen et al., 2011).

Overall, the operational definition of chronic stress differs across many of these studies. In some cases, specific domains of stress (job stress, marital stress) are examined and others draw conclusions about global psychological distress or perceived stress. Depending on the way in which stress is defined, outcomes differ, whether examining a diagnosis of MetS or the individual components. However, it is likely that stress leads to disrupted metabolic health, which may ultimately result in CVD. Clarifying the relationship between chronic stress and MetS components can help identify individuals in need of early intervention to prevent the development of later disease.

Stress and depression

Over the past 20 years, much research has been devoted to examining the relationship between chronic stress and depression (Hammen, 2005; Paykel, 2003; Tennant, 2002). In fact, McGonagle and Kessler (1990), found that chronic stress (defined as stress lasting more than 12 months) was a stronger predictor of depressive symptoms than acute life stressors, based on interviews with 1755 participants. Mazure (1998) noted that 80% of depressed cases were preceded by stress. Other research studies examining the role of chronically adverse conditions, including poverty, medical disabilities, and marital discord, have reported a strong positive association with depression (Brown & Harris, 1978; Bruce & Hoff, 1994; B. P. Dohrenwend et al., 1992; Swindle, Cronkite, & Moos, 1989).

Moreover, what moderates the relationship between stress and depression has been explored. The moderating role of sex has been particularly well researched, with the majority of studies showing that women are more susceptible to depression following a chronic stressor (Hammen, 2005). However, Kendler, Thornton, and Prescott (2001) found specific sex differences, such that for men, divorce, separation, or work problems were more strongly associated with depression risk; for women, problems in social relationships were more strongly associated with depression risk. The buffering hypothesis suggests that social support is also a key moderator in the stress-depression link; however, it remains unclear whether education or health insurance weakens the effects of stress on depression. Lastly, depression rates differ among races/ethnicities, such that Whites have the highest rates of depression, followed by Blacks, and then Hispanics (Riolo, Nguyen, Greden, & King, 2005). Nonetheless, it is unknown whether the relationship between chronic stress and depression is the same or different across races/ethnicities.

The role of race/ethnicity

Research shows mixed results regarding the role of race/ethnicity as a moderator of the relationship between chronic stress and cardiovascular health. In the study done by Kershaw and colleagues (2015), there was no significant interaction between race/ethnicity and the relationship between chronic stress and CHD outcome. Perhaps it is not simply race/ethnicity that moderates the relationship, but rather resources available (or unavailable) in the psychosocial reserve capacity that moderates the relationship. Examining both tangible and intangible resources in the psychosocial reserve capacity

may help elucidate the relationship between chronic stress and cardiovascular health outcomes.

In a study of middle-aged White and Black women, the relationship between chronic stress burden and subclinical carotid artery disease was significant only in Blacks, but not Whites, highlighting an important stress x race interaction (Troxel et al., 2003). However, these analyses did not control for socioeconomic status (SES) or education level, despite significant differences between Blacks and Whites. SES and education level are highly correlated with mental and physical health, perceived stress, and available resources (Baum, Garofalo, & Yali, 1999; Diez Roux et al., 2001). Given that education level may impact perceived stress and health status, it is important to determine if the relationship between chronic stress and disease is moderated by these variables or other resources in the psychosocial reserve capacity.

Psychosocial reserve capacity

As previously mentioned, the psychosocial reserve capacity is comprised of resources from several domains. Initially, Gallo and Matthews (2003) proposed the Reserve Capacity Model as emphasizing resilient personal and social factors related to SES and health status, which alter the body's stress response. Low SES increases risk for poor health outcomes by decreasing reserve capacity for coping with stress. Research that informed this model and provided indirect support, shows that resilient resources including emotional and social support, perceived control (mastery), optimism, and self-esteem may all affect health via converging biological and behavioral pathways. For purposes of the current study, a few resources highlighted by Myers (2009) will be

examined as resources in the psychosocial reserve capacity, and, therefore, as potential moderators of the relationship between chronic stress and both MetS and CVD. Those resources are: level of education, emotional support, and healthcare coverage status.

Education is a vital element of an individual's reserve capacity. Varying degrees of psychosocial and material resources are available based on a person's level of education. Low educational attainment is associated with worse health outcomes based on self-reported health, physical functioning, levels of morbidity, mortality, and disability (Feldman, Makuc, Kleinman, & Cornoni-Huntley, 1989; Guralnik, Land, Blazer, Fillenbaum, & Branch, 1993; Morris, 1990). Education level shapes a person's employment opportunities, earnings, and social-psychological resources, including a sense of personal control and social support (Ross & Wu, 1995). Individuals with more education make more money, have a better sense of mastery and personal control, and report greater social support than individuals with a lower education (Ross & Wu, 1995). Education helps form an individual's ability to communicate, gather and interpret information, and solve problems on many levels; therefore, it is likely that higher education can increase an individual's adaptive capacities and resources needed to successfully manage life stressors.

Social support is likely another important moderator in the stress-health relationship. People who perceive themselves to be socially and emotionally supported lead healthier, happier, and longer lives (Cohen & Wills, 1985). Moreover, social support has been consistently negatively associated with the development and progression of CVD (Angerer et al., 2000; Brummett et al., 2001; Knox et al., 2000; Kop et al., 2005; Wang, Mittleman, Leineweber, & Orth-Gomer, 2006; Wang, Mittleman, & Orth-Gomer,

2005). Research shows that social support both benefits well-being overall and also buffers the negative effects of stress (Cohen & Wills, 1985). In fact, several studies have replicated the finding that social support moderates or buffers the impact of psychosocial stress on mental and physical health (Cobb, 1976; Cohen & Hoberman, 1983; Cohen & Wills, 1985). Moreover, laboratory studies show that social support may reduce cardiovascular reactivity to stress, by reducing autonomic activation (i.e. smaller increases in systolic and diastolic blood pressure) (Bowen et al., 2014; Kamarck, Manuck, & Jennings, 1990; Lepore, Allen, & Evans, 1993). Perceived availability of social/emotional support is a key resource in the psychosocial reserve capacity. Consequently, it is likely a moderator in the relationship between chronic stress and both MetS and CVD.

Additionally, health insurance coverage is one of the most important factors contributing to health status disparities. Regardless of age, sex, or race/ethnicity, uninsured individuals are more likely to forgo or delay medical services compared to individuals with health insurance (Chen, Rizzo, & Rodriguez, 2011). Prior research also suggests that uninsured individuals are more likely to report unmet physical and mental healthcare needs (O'Hara & Caswell, 2013). Research conducted by Lee and colleagues (2012) found that health insurance coverage moderated the relationship between the stressful experience of acculturation and health status in Asian, Black, Hispanic, and multiracial U.S. immigrants. Thus, health insurance status is an important, tangible resource, especially for individuals experiencing chronic stress.

The present study

Previous research suggests that chronic stress increases risk of CVD, but has not examined the degree to which shared variance among social stressors may be implicated in the onset of disease. The current study expands the findings established by Kershaw and colleagues (2015). Specifically, a latent variable model of chronic stress was developed, and measurement invariance of this model across races/ethnicities was examined. Next, the relationship between latent chronic stress and MetS components was explored. Additional analyses examined potential moderation of this relationship by level of education, emotional support, and health insurance coverage. The relationship between chronic stress and CVD was also examined. Additional analyses explored potential moderation between chronic stress and CVD by level of education, emotional support, and health insurance coverage. Exploratory analyses examined the role of sex as a moderator and depressive symptoms as an outcome.

Study aims and hypothesis

(Aim 1) Create a latent variable of chronic stress burden and examine measurement invariance across the four races/ethnicities represented.

(Aim 2) Examine the relationship between chronic stress and MetS components.

(Aim 3) Determine to what degree level of education, emotional support, and health insurance coverage moderate the relationship between chronic stress and MetS components.

(Aim 4) Examine the relationship between chronic stress and CVD.

(Aim 5) Determine to what degree level of education, emotional support, and health insurance coverage moderate the relationship between chronic stress and CVD.

Exploratory Aims:

(Aim 6) Examine whether sex moderates the relationship between chronic stress and both MetS components and CVD.

(Aim 7) Examine the relationship between chronic stress and depressive symptoms.

(Aim 8) Determine to what degree level of education, emotional support, health insurance coverage, and sex moderate the relationship between chronic stress and depressive symptoms.

Chapter 2: Methods

Participants

The Multi-Ethnic Study of Atherosclerosis (MESA) is comprised of 6,814 men and women, between the ages of 45 – 84 enrolled between July 2000 and August 2002 from six field centers across the United States (Wake Forest University, Columbia University, Johns Hopkins University, University of Minnesota, Northwestern University, and University of California at Los Angeles). This multi-ethnic population included White, Black, Hispanic, and Chinese American participants. Individuals were excluded if they had prior diagnosis of a heart attack, stroke, transient ischemic attack, heart failure, angina, atrial fibrillation, or history of any cardiovascular procedure. Participants who had any existing medical condition that would prevent long-term participation, were pregnant, or weighed over 300 pounds were also excluded from the study. The MESA protocol has been approved by the Institutional Review Boards of all collaborating institutions. The specific protocol for the current study has been approved by the University of Miami Institutional Review Board. All participants gave informed consent prior to joining the study protocol.

Procedure

MESA was initiated to investigate the prevalence, correlates, and progression of subclinical CVD in a population-based sample of men and women. Random population samples were selected at each field site using lists of area residents, and eligibility for participation was initially determined by phone call. Final eligibility was determined in the clinic. Of those eligible for the study, 59.8% participated. At Visit 1, participants

arrived at the clinic fasting and completed the following measures: questionnaires, anthropometry, blood pressure, ankle/brachial blood pressure index, electrocardiogram, coronary calcium determination, carotid ultrasound, arterial wave forms, flow-dependent brachial artery vasodilation, cardiac magnetic resonance imaging, and laboratory measurements. At Visit 2 (beginning in July 2002), Visit 3 (beginning in January 2004), Visit 4 (beginning in July 2005), and Visit 5 (between April 2010 – January 2012) selected questionnaires, anthropometry, blood pressure, and laboratory tests were repeated. Baseline questionnaire results, demographic variables, and MetS components were used in analysis along with CVD outcome using nine years of follow-up data. For more information on the objectives and design of MESA see Bild et al. (2002).

Measures

Covariates

Relevant covariates that have a known relationship and influence on MetS or CVD were included. Covariates were age (45 – 84 years), sex (M/F), cigarette status, and income. Age, sex, cigarette status, and income were based on self-reported responses from questionnaires completed at baseline. Cigarette status was grouped in never smokers, former smokers, and current smokers.

Life stress

Participants completed the Chronic Burden Scale to assess presence and perceived stressfulness of ongoing stressors over the past six months (or more) in the following domains: health problems (own), health problems (someone close to you), job or ability

to work, relationships, and finances (Everson-Rose et al., 2014; Mujahid et al., 2011). The domain of health problems (self) was excluded from analyses so as not to use one's own health problems to predict later health outcomes. For the individual stressors, participants were coded as experiencing chronic stress if the stressor was present for at least six months and was marked as "moderately" or "very" stressful. Responses were recoded in the following way: a score of 0 indicated no chronic stress; a score of 1 indicated that the stressor was present for less than six months. A score of 2 indicated that the stressor was present for at least six months, but was not subjectively stressful. A score of 3 indicated that the chronic stressor was present for at least six months and was "moderately" stressful; a score of 4 indicated it was "very" stressful. These re-coded variables were entered as the indicators in the latent variable model of chronic stress.

Moderators

Education was reported via questionnaire. Level of education was grouped into less than HS and more than HS. Research supports significant differences in those who complete high school versus those who drop out of high school before graduation. For example, failure to complete high school has been associated with increased crime, increased demand for social services, lower levels of self-esteem, and poorer levels of health (Rumberger, 1987). **Health insurance coverage** (yes/no) was assessed via self-report questionnaire.

Emotional/social support was assessed via the Emotional Social Support Index (ESSI, range: 6–30, Cronbach's alpha: 0.88). Participants responded to a series of six

questions with responses ranging from “1 = none of the time” to “5 = all of the time” about perceived presence of social/emotional support, including having someone to talk to, get advice from, receive affection, provide emotional support, and confide in. For example, “Is there someone available to you who shows you love and affection? Can you count on anyone to provide you with emotional support (talking over problems or helping you make a difficult decision)? Do you have as much contact as you would like with someone you feel close to, someone in whom you can trust and confide?” Scores were summed; higher scores indicate more available support (Mitchell et al., 2003). This measure has modest correlations with other indices of social support, including the Perceived Social Support Scale (Mitchell et al., 2003).

Endpoints

MetS components, measured at Visit 1, were examined as individual outcomes, including: waist circumference, HDL cholesterol, triglycerides, fasting glucose, and systolic and diastolic blood pressure**.** Waist circumference (at the umbilicus) was measured to the nearest 0.1 cm. HDL-cholesterol, triglycerides, and glucose concentrations were measured directly with reagents from Roche Diagnostics (Indianapolis, IN) and analyzed at the Collaborative Studies Clinical Laboratory (Fairview-University Medical Center; Minneapolis, MN). Resting blood pressure was measured with participants in the seated position with the use of a Dinamap model Pro 100 automated oscillometric sphygmomanometer (Critikon, Tampa, FL). Three measurements were taken, and the average of the last two measurements was used in analyses.

CVD, examined up until nine years after baseline, was defined as myocardial infarction (MI), resuscitated cardiac arrest, CHD death, stroke (not transient ischemic attack), or stroke death. Events were adjudicated for better sensitivity and specificity.

Depressive symptoms were an exploratory outcome of interest and measured using the CES-D. The CES-D is a 20-item scale which assesses areas of depressive symptomatology such as depressed affect, interpersonal relations, and positive affect over the past week. The CES-D has very high internal consistency and adequate test-retest repeatability. The scale has been validated for population studies, showing a Cronbach's alpha of 0.85 (Radloff, 1977).

Chapter 3: Data Analysis Plan

Mplus Version 8.0 was used for statistical analyses. All variable distributions were examined for outliers, skewness, and kurtosis.

Covariate selection

Age, sex, and cigarette status are important covariates, given the well-established relationships these variables have with the outcomes of interest, MetS and CVD (Wilson et al., 1998). Since income may affect both stress levels and the outcomes of interest, it is considered to be a confounder variable, or common cause of both X (chronic stress) and Y (MetS and CVD), according to the literature on directed acyclic graphs (DAGs) (Shrier & Platt, 2008). Based on recommendations from the DAG literature, controlling for a confounder variable opens up the pathway and reduces bias in the results (Shrier & Platt, 2008). Given this information, and the fact that income level is an important aspect of the Myers (2009) lifespan psychosocial model of cumulative risk, income was included as a covariate.

Also, given the high correlation typically found between income and level of education, models examining level of education as a moderator were examined both with and without income as a covariate.

Latent variable analyses

A model that specified four domains of stress (job/ability to work, money/financial, relationship, and health problem (other)) loading on a single latent factor of chronic stress was tested. Correlations between the latent variable of chronic

stress and each of its indicators, also known as standardized factor loadings, were examined. Next, measurement invariance of this factor across all four races/ethnicities was tested. Establishing whether factor loadings, intercepts, and residual variances are equal across groups is necessary to ensure that comparisons made on the latent variable are valid across groups. This is also especially important, given that the lifespan biopsychosocial model of cumulative vulnerability and minority health emerged due to health disparities among races/ethnicities.

Primary analyses

(Aim 1) First, a latent variable of chronic stress was created, and measurement invariance across the four races/ethnicities was examined. To establish measurement invariance at various levels, a series of increasingly constrained models were run. Chi square tests determined whether or not the unconstrained model fit significantly better than the constrained model. If the unconstrained model did not fit significantly better, the constrained model was retained and additional constraints were added to the model. First, passing configural invariance confirms the model has the same structure across racial/ethnic groups. Next, metric invariance confirms the loadings for each of the factors may be held the same (constrained equal) across groups. This means that participants from all four races/ethnicities attribute the same meaning to the latent construct. Scalar invariance determines whether or not the item intercepts may be held the same (constrained equal) across groups. This assesses whether the meaning of the levels of the underlying items (intercepts) are equal across the races/ethnicities (van de Schoot, Lugtig, & Hox, 2012).

(Aim 2) Next, the relationship between latent chronic stress and MetS components was analyzed using linear regression. Each model was run with and without constraining paths equal across the grouping variable of race/ethnicity. Chi square difference tests were run to examine whether the unconstrained model fit significantly better than the constrained model, indicating group differences. If the two models were not significantly different, the constrained model was retained and the prediction was assumed to be equal across groups.

(Aim 3) Level of education, emotional support, and health insurance coverage were examined as potential moderators of the relationship between stress and MetS.

(Aim 4) Data were examined to determine if acceleration or deceleration of CVD events occurred to justify usage of pooled or regular logistic regression.

Regression analyses were used to explore the relationship between latent chronic stress and CVD. Race/ethnicity comparisons were made using chi square difference tests between constrained and unconstrained models. If the two models were not significantly different, the constrained model was retained and the prediction was assumed to be equal across groups.

(Aim 5) Level of education, emotional support, and health insurance coverage were examined as potential moderators of the relationship between stress and CVD.

Exploratory analyses

Sex as moderator

Although sex is not a resource in the psychosocial reserve capacity, stress may influence disease risk differently in men and women. Therefore, sex was also examined as a moderator of the relationship between chronic stress and MetS components and chronic stress and CVD.

Depressive symptoms as outcome

Chronic stress likely influences mental, as well as physical health; therefore, depressive symptoms were examined as an outcome variable in exploratory analyses. Analyses examined the relationship between chronic stress and depressive symptoms on a continuous scale. Resources in the psychosocial reserve capacity, namely level of education, emotional support, and health insurance coverage were entered as moderators of the relationship between chronic stress and depressive symptoms. Sex was also examined as a moderator of this relationship.

Chapter 4: Results

Sample characteristics

Sample descriptive statistics are listed in **Table 1** for both the full sample and for each race/ethnicity. A total of 129 participants had either partial or completely missing data on the Chronic Burden Scale, and they were removed from analysis. These individuals did not differ from individuals with complete data on any covariate or outcome variable, with the exception of triglycerides ($t(6789) = 2.43$, $p < .05$). Those removed from analysis had a lower level of triglycerides ($M = 112.9$, $SD = 64.4$) compared to those with complete data ($M = 131.6$, $SD = 89.1$).

In descriptive analyses, only participants with available data on the variables were used. Therefore, degrees of freedom differ across variables described below, due to some missing data on certain variables; however, it should be noted that missingness was minimal. For all linear and logistic regression analyses, full information maximum likelihood was employed, which uses all available information. The final N was 6685 for all linear and logistic regression models.

Mean age was 62 years ($SD = 10.2$), and 53% were female. All four race/ethnicities were well represented (38.6% White, 27.3% Black, 22.0% Hispanic/Latino, and 12.0% Chinese American). CVD occurred in 8.2% of the total sample. Cigarette status was grouped into current users (13.1% of people), former users (36.6%), and non-users (50.3%). Highest level of education completed varied: less than high school (18.1%), high school/GED (18.1%), some college (including technical school certificate and associate's degree) (28.5%), and college and above (including bachelor's degree, graduate, and/or professional school) (35.3%).

Chi square tests revealed that there were significant differences in the proportion of CVD events experienced between races/ethnicities (χ^2 (3, N = 6680) = 11.36, p <.01); five individuals (0.07%) had missing data. As shown in **Table 1**, 9.3% of Hispanics experienced a CVD event compared to 8.2% of Whites, 8.6% of Blacks, and 5.4% of Chinese Americans. There were significant differences in the proportion of individuals at different levels of education across races/ethnicities (χ^2 (24, N = 6680) = 1645.46, p <.001); five individuals (0.07%) had missing data. For example, almost half of Whites completed college or above, compared to 9.9% of Hispanics who achieved this level of education. Similarly, there were significant differences in the proportion of individuals at different levels of household incomes (χ^2 (3, N = 6439) = 702.24, p <.001); 246 individuals (3.68%) had missing data. Furthermore, there were significant differences in the proportion of individuals covered by health insurance between races/ethnicities (χ^2 (3, N = 6681) = 389.49, p <.001); four individuals (0.06%) had missing data. About 19% of Chinese Americans were uninsured compared to just 2.7% of Whites. These results are also listed in **Table 1**.

There were significant differences in all MetS components between the racial/ethnic groups. First, there were significant differences in systolic (F (3, 6678) = 64.9, p < .001) and diastolic blood pressure levels (F (3, 6678) = 65.0, p < .001); seven individuals (0.10%) had missing data. Blacks had significantly higher systolic and diastolic blood pressure than all other racial/ethnic groups. There were significant differences in levels of triglycerides (F (3, 6659) = 104.0, p < .001); 26 individuals (0.39%) had missing data. Compared to all other races/ethnicities, Hispanics had the highest triglyceride levels. There were also significant differences in levels of HDL

cholesterol (F (3, 6656) = 38.8, $p < .001$); 29 individuals (0.43%) had missing data. Hispanics had significantly lower levels of HDL cholesterol than all other racial/ethnic groups. Waist circumference also significantly differed across race/ethnicity (F (3, 6680) = 218.1, $p < .001$); five individuals (0.07%) had missing data. Chinese Americans had a significantly smaller mean waist circumference compared to other racial/ethnic groups. Lastly, there were significant differences in fasting glucose (F (3, 6656) = 61.5, $p < .001$); 29 individuals (0.43%) had missing data. Whites had a significantly lower average fasting glucose compared to other races/ethnicities.

In summary, Chinese Americans had the lowest prevalence of CVD and smallest waist circumference. There were notable racial/ethnic differences in all other MetS components. Blacks had the highest systolic and diastolic blood pressure, whereas Hispanics had the highest level of triglycerides and lowest levels of HDL cholesterol. Whites had the lowest fasting glucose.

Latent variable of chronic stress

A latent variable model with four chronic stress indicators (money/financial, job/ability to work, relationship, and health problem (other) stress) was examined. The model along with unstandardized factor loadings is shown in **Figure 2.** Confidence intervals for unstandardized loadings are listed in **Table 2**. In the factor analysis literature, it is common to use a standardized loading of .30 or greater as an adequate indicator of a factor. Standardized coefficients for all indicators reached this cut-off. These standardized coefficients are listed in **Table 2** by race/ethnicity.

Model fit was evaluated based on several common fit indices [Comparative Fit Index (CFI > .95), the Root Mean Squared Error of Approximation (RMSEA < .06), and the Standardized Residuals (SRMR < .10)]. Strong measurement invariance was achieved, meaning after all factor loadings were constrained equal across races/ethnicities and the intercepts for health problem (other), job, and relationship stress were constrained equal across races/ethnicities, the model fit the data [CFI = .988; RMSEA = .019 90% CI (.004 - .031); SRMR = .020]. This model included a residual correlation between money/financial stress and job/ability to work stress.

MetS components on chronic stress

MetS components were regressed onto latent chronic stress to examine relationships in each individual MetS component. Models included age, sex, smoking status, and income as covariates. Results are presented in **Table 3**. Models were tested with and without constraints. In the unconstrained model, the path between chronic stress and the outcome was allowed to vary across races/ethnicities. In the constrained model, this path was held equal across the racial/ethnic groups. The purpose of this analysis was to determine if the relationship between chronic stress and the outcome is the same or different across the races/ethnicities. Chi square difference tests examined whether the unconstrained model fit significantly better than the constrained model, indicating racial/ethnic group differences in the relationship between chronic stress and MetS components. If the two models were not significantly different, the constrained model was retained and the prediction was assumed to be equal across groups. For all of the models analyzed, the unconstrained model did not fit significantly better than the

constrained model. In essence, this signaled that the relationships between chronic stress and MetS components are the same across race/ethnicities. Therefore, results from the constrained models only are reported below.

Metabolic syndrome components

As shown in **Table 3**, after adjusting for age, sex, smoking status, and income, chronic stress was significantly, positively related to waist circumference (B = 1.00, 95% CI: 0.30 – 1.69, $p < .01$), indicating that each unit increase in chronic stress was associated with a 1.00 cm increase in waist circumference. Chronic stress was also significantly, positively related to fasting glucose (B = 2.16, 95% CI: 0.75 – 3.56, $p < .01$).

However, chronic stress was not significantly related to HDL cholesterol (B = 0.42, 95% CI: -0.17 – 1.02, $p > .05$), triglycerides (B = 1.62, 95% CI: -2.36 – 5.61, $p > .05$), systolic (B = 0.23, 95% CI: -0.75 – 1.21, $p > .05$) or diastolic blood pressure (B = 0.01, 95% CI: -0.48 – 0.50, $p > .05$).

Psychosocial reserve capacity as a moderator

Following examination of the relationship between chronic stress and MetS outcomes, three aspects of the psychosocial reserve capacity: level of education (HS and above versus below HS), emotional support (on a continuous scale), and healthcare coverage status (insured versus uninsured), were examined as moderators of this relationship. Results of the moderation analyses are displayed in **Table 4**, which show the main effects of chronic stress and the selected moderator (level of education, emotional

support, or health insurance), as well as the interaction effects for stress x level of education, stress x emotional support, and stress x health insurance. The same covariates (age, sex, cigarette status, and income) were included in all moderation analyses.

Unsurprisingly, education level and income level were highly correlated (Pearson's r = .55, $p < .001$). Models with education were analyzed with and without income included as a covariate. Excluding income from the model did not have a significant impact on any finding. Findings that were significant with income in the model, remained significant when income was removed from the model. Findings that were not significant with income in the model remained not significant when income was removed from the model. Therefore, all reported results are from models that included income as a covariate.

Waist circumference

None of the predicted moderators significantly moderated the relationship between stress and waist circumference. As shown in **Table 4**, there was a main effect of education on waist circumference, such that fewer years of education were associated with larger waist circumference (B = -2.23, 95% CI: -3.03 – -1.43, $p < .001$). There was no main effect for emotional support. There was a main effect for health insurance on waist circumference (B = -2.51, 95% CI: -3.77 - -1.24, $p <.001$). On average, individuals with health insurance have a waist circumference that is 2.51 cm smaller than those without health insurance.

HDL cholesterol

There was a significant interaction between chronic stress and level of education (B = -1.15, 95% CI: -2.21 - -0.08, $p < .05$). This signals that there are differences in the relationship between chronic stress and HDL cholesterol, depending on level of education. To follow up this significant moderation, the interaction term (chronic stress x education level) and education level variable were removed from the model. Stratified analyses were conducted for participants achieving less than high school education (educlevel = 0) and those achieving a high school education or above (educlevel = 1). As shown in **Figure 3**, for individuals that have not completed high school, for each additional unit increase in latent chronic stress, HDL levels also increased by 1.62 mg/dL. This relationship was significant ($p <.05$). The opposite held true for individuals who completed high school or above. For these individuals, as chronic stress increases, HDL levels decrease. In fact, for each additional unit increase in latent stress, HDL levels decreased by 0.31 mg/dL. However, this simple effect was not significant. Health insurance and emotional support were not significant moderators of the relationship between chronic stress and HDL cholesterol.

There was a main effect for education on HDL (B = 1.51, 95% CI: 0.75 – 2.27, $p < .001$), such that more years of education were associated with higher HDL levels. The main effect of emotional support approached significance (B = .04, 95% CI: -0.12 – 0.20, $p = .05$), suggesting that higher levels of emotional support were associated with higher levels of HDL cholesterol. There was also a main effect of health insurance on HDL (B = -1.68, 95% CI: -2.79 - -0.57, $p < .01$). On average, individuals with health insurance have

1.68 mg/dL lower HDL than individuals without health insurance.

Triglycerides

None of the predicted moderators significantly moderated the relationship between stress and triglycerides. Of note, due to the large variance of triglycerides, the initial model examining the interaction between stress and emotional support on triglycerides did not reach convergence. To remedy this issue, triglycerides were log transformed. The results using the log transformed triglycerides as the outcome are reported in **Table 4**.

There was a significant main effect for level of education on triglycerides, such that fewer years of education were associated higher levels of triglycerides (B = -14.69, 95% CI: -20.17 - -9.21, $p < .001$). There was no significant main effect for emotional support or health insurance on triglycerides.

Fasting glucose

None of the predicted moderators significantly moderated the relationship between stress and fasting glucose. There was a main effect of education on fasting glucose such that fewer years of education were associated with higher levels of fasting glucose (B = -5.30, 95% CI: -7.16 – -3.43, $p < .001$). There was no significant main effect of emotional support or health insurance on fasting glucose.

Systolic and diastolic blood pressure

None of the predicted moderators significantly moderated the relationship between stress and systolic or diastolic blood pressure. There was a significant main effect for level of education on both systolic (B = -2.98, 95% CI: -4.14 - -1.81, $p < .001$) and diastolic blood pressure (B = -0.87, 95% CI: -1.43 - -0.32, $p < .01$), such that fewer years of education were associated with higher systolic and diastolic blood pressure. There was also a significant main effect for emotional support on diastolic blood pressure, only (B = 0.08, 95% CI: 0.00 – 0.16, $p < .05$). Higher levels of emotional support were associated with higher levels of diastolic blood pressure. The effect of emotional support on systolic blood pressure approached significance (B = 0.15, 95% CI: -0.00 – 0.31, $p = .06$). Health insurance was not significantly related to systolic or diastolic blood pressure.

Exploratory analyses: Sex as a moderator

Although sex is not a resource in the psychosocial reserve capacity, stress may influence disease risk differently in men and women. Therefore, we elected to examine sex as a moderator of the relationship between chronic stress and MetS components, as exploratory analyses. The interaction between stress and sex was significant for waist circumference, only (B = -1.70, 95% CI: -2.88 - -0.53, $p < .01$). This relationship is depicted in **Figure 4**. In both women and men, stress is positively related to waist circumference. However, the relationship is stronger in women than in men. For women, each additional unit increase in chronic stress was associated with a 2.29 cm increase in

waist circumference ($p < .001$). For men, each additional unit increase in chronic stress was associated with a 1.68 cm increase in waist circumference ($p < .001$).

Pooled versus logistic regression

Per the MESA protocol, information was collected on time (in days) to experiencing a cardiovascular event. Time to event data can be used to examine whether or not there is acceleration or deceleration of events over time. In other words, do more events occur in the first half of data collection and fewer in the second half of data collection? This pattern would suggest an initial acceleration, or speeding up of events, followed by a deceleration, or slowing down of events. This information is useful in helping to assess risk. In the case of CVD, it is important to assess not only if an event occurs, but also how fast this happens. Understanding if acceleration occurs can help provide additional information on the role of chronic stress on CVD outcome. If there is no acceleration or deceleration, then risk is assumed to be the same across time for each individual and time to event does not matter.

To determine if there was acceleration or deceleration of CVD events over time, or if time to event matters, the data were split into two periods and coded accordingly. Individuals who had an event in the first period were given a "1" and individuals who did not have an event in the first period were given a "0." Individuals who had an event in period 1 were not included in period 2, thus the sample sizes differ for periods 1 and 2. The same coding (1 = event, 0 = no event) was applied for period 2. Two separate but simultaneous logistic regressions were analyzed with chronic stress and covariates in the model. CVD was the outcome of interest. If the estimates from the logistic regression

models for chronic stress, age, sex, or smoking status from period 1 differed significantly from period 2, we would conclude that acceleration or deceleration of events occurred.

Results showed that each variable in the model showed an overlap in 95% confidence intervals for periods 1 and 2. The results were as follows: chronic stress (OR period 1 = 0.09, 95% CI: -0.03 - 0.21) (OR period 2 = .03, 95%CI: -0.13 – 0.18); sex (OR period 1 = 0.22, 95% CI: 0.13 – 0.31) (OR period 2 = 0.15, 95% CI: 0.03 – 0.27); former smoker (OR period 1 = -0.01, 95% CI: -0.11 – 0.09) (OR period 2 = 0.07, 95% CI: -0.06 – 0.20); current smoker (OR period 1 = 0.34, 95% CI: 0.21 – 0.48) (OR period 2 = 0.29, 95% CI: 0.11 – 0.48); and age (OR period 1 = 0.03, 95% CI: 0.03 – 0.04) (OR period 2 = 0.03, 95% CI: 0.02 – 0.04). Since the odds ratios for all variables showed an overlap between period 1 and period 2, it was determined that there was no acceleration or deceleration of events. Therefore, regular logistic regression was employed for all analyses. In essence, logistic regression assigns each person the same amount of time to CVD event.

CVD on chronic stress

Next, CVD was regressed onto latent chronic stress. Each model was estimated with and without constraining the path between chronic stress and CVD equal across the grouping variable of race/ethnicity. Models were tested with and without constraints. In the unconstrained model, the path between chronic stress and the outcome was allowed to vary across races/ethnicities. In the constrained model, this path was held equal across the racial/ethnic groups. The purpose of this analysis was to determine if the relationship between chronic stress and the outcome is the same or different across the

races/ethnicities. Chi square difference tests examined whether the unconstrained model fit significantly better than the constrained model, indicating racial/ethnic group differences in the relationship between chronic stress and MetS components.

Chi square tests showed that the unconstrained model fit significantly better than the constrained model (χ^2 (3) = 11.60, p <.01). However, the relationship between stress and CVD was not significant in any one racial/ethnic group. The non-significant results are listed in **Table 5** by race/ethnicity. As shown in the table, the odds ratios were quite similar across races/ethnicities: Whites (OR = 1.12, 95% CI: 0.99 – 1.42), Blacks (OR = 1.12, 95% CI: 0.73 – 1.75), Hispanics (OR = 0.92, 95% CI: 0.72 – 1.19), Chinese Americans (OR = 1.10, 95% CI: 0.90 – 1.32), p's > .05.

Psychosocial reserve capacity as a moderator

Following examination of the relationship between chronic stress and CVD, three aspects of the psychosocial reserve capacity: level of education (HS and above versus below HS), emotional support (on a continuous scale), and healthcare coverage status (insured versus uninsured), were examined as moderators of this relationship. Since the relationship between chronic stress and CVD differed by race/ethnicity, moderation analyses were examined separately for each race/ethnicity. In other words, four separate regressions were analyzed to explore the relationship between stress, CVD, and the interaction (stress x education, stress x emotional support, and stress x health insurance) for each race/ethnicity. All models controlled for age, sex, smoking status, and income. Results of these models are listed in **Table 6** by race/ethnicity.

There was a significant main effect for health insurance for Blacks only (OR = 2.44, 95% CI: 1.15 – 5.16, p <.05). For Blacks, the odds of CVD are 2.44 times greater for individuals without health insurance compared to individuals with health insurance. There were no significant main effects for level of education or emotional support on CVD in any other race/ethnicity.

Surprisingly, none of the predicted moderators significantly moderated the relationship between stress and CVD for any race/ethnicity. Models exploring education as a moderator were run with and without income as a covariate. Excluding income from the model did not have a significant impact on any finding.

Exploratory analyses: Sex as a moderator

Although sex is not a resource in the psychosocial reserve capacity, stress may influence disease risk differently in men and women. Therefore, we elected to examine sex as a moderator of the relationship between chronic stress and CVD, as exploratory analyses. These results are listed in **Table 6**. There was a significant main effect of sex on CVD outcome in Whites, Blacks, and Hispanics. For all three races/ethnicities, men had higher odds of CVD than women. More specifically, White men had 1.77 higher odds of CVD than White women (95% CI: 1.31 – 2.39, p < .001). Black men had 1.90 higher odds of CVD than Black women (95% CI: 1.32 – 2.71, p < .001). Lastly, Hispanic men had 1.99 higher odds of CVD than Hispanic women (95% CI: 1.25 – 3.22, p < .01). Sex did not significantly moderate the relationship between stress and CVD in Chinese Americans.

Exploratory analyses: Depressive symptoms as an outcome

The lack of significant findings between chronic stress and CVD was surprising. To determine if this "resiliency" of the sample was related to mental, as well as physical health outcomes, the relationship between chronic stress and depressive symptoms, characterized by scores on the CES-D, was examined as an exploratory analysis.

Models were tested with and without constraints. In the unconstrained model, the path between chronic stress and the outcome was allowed to vary across races/ethnicities. In the constrained model, this path was held equal across the racial/ethnic groups. The purpose of this analysis was to determine if the relationship between chronic stress and the outcome is the same or different across the races/ethnicities. Chi square difference tests examined whether the unconstrained model fit significantly better than the constrained model, indicating racial/ethnic group differences in the relationship between chronic stress and MetS components. As shown in **Table 7**, there was a significant, positive relationship between chronic stress and depressive symptoms (B = 6.45, 95%CI: 5.61 - 7.29, $p < .001$).

Psychosocial reserve capacity and sex as moderators

Given the positive relationship found between chronic stress and depressive symptoms, additional analyses explored the role of the psychosocial reserve capacity (level of education, emotional support, and health insurance coverage) and sex as moderators of this relationship.

Level of education was a significant moderator (B = -2.33, 95% CI: -3.20 - -1.45, $p <.001$) of the relationship between chronic stress and depressive symptoms. As shown in **Figure 5**, the relationship between chronic stress and depressive symptoms was

stronger for less educated individuals. For individuals achieving less than a high school education, depressive symptoms start out higher and, for each additional increase in chronic stress, depressive symptoms increased by 7.73 ($p < .001$). For individuals achieving at least a high school education or above, each additional unit increase in chronic stress was associated with a 5.87 increase in depressive symptoms ($p < .001$).

Emotional support was also a significant moderator (B = -0.43, 95% CI: -0.53 - -0.33, $p < .001$). As shown in **Figure 6**, chronic stress was associated with more depressive symptoms at all levels of emotional support. However, this relationship was strongest for individuals at the lowest level of emotional support. For these individuals, each additional increase in chronic stress was associated with an 8.22 increase in depressive symptoms ($p < .001$), compared to an increase of 5.96 in depressive symptoms in those with average levels of emotional support ($p < .001$), and an increase of 3.69 in depressive symptoms in those with high levels of emotional support ($p < .001$).

Health insurance did not significantly moderate the relationship between chronic stress and depressive symptoms. Lastly, **Figure 7** depicts the significant moderation of sex on depressive symptoms. Women started out with more depressive symptoms, and each additional increase in chronic stress was associated with a 6.04 increase in depressive symptoms ($p < .001$). Men started out with fewer depressive symptoms; however, each additional increase in chronic stress was associated with a 6.44 increase in depressive symptoms ($p < .001$).

As shown in **Table 7**, there was a significant main effect of level of education, emotional support, and health insurance on depressive symptoms. More years of education were associated with lower depressive symptoms (B = -1.47, 95% CI: -1.87 - -

1.07, $p < .001$). Higher levels of emotional support were associated with lower depressive symptoms (B = -0.37, 95% CI: -0.40 – 00.34, $p < .001$). Lastly, individuals with health insurance endorsed fewer depressive symptoms than those without health insurance (B = -0.65, 95%CI: -1.22 - -0.09, $p < .05$).

Chapter 5: Discussion

The purpose of this study was to examine the relationship between chronic stress and cardiovascular health, as defined by MetS components and CVD outcome in a diverse, multi-ethnic sample of men and women who were asymptomatic of cardiovascular disease at baseline. The extent to which certain resources in the psychosocial reserve capacity (namely, level of education, emotional support, and health insurance coverage) moderate the relationship between chronic stress and cardiovascular health was also explored. Of note, prevalence of CVD nine years post-baseline was much lower in this sample (8.2%) compared to the general U.S. prevalence (~35.3%) (Go et al., 2014).

While prior research supports the finding that chronic stress is significantly, positively related to negative health outcomes (Chandola et al., 2006; Everson-Rose et al., 2014; Innes et al., 2007; Johnson et al., 2013; Juster, McEwen, & Lupien, 2010; Kershaw et al., 2015; Troxel et al., 2003), chronic stress has been inconsistently defined across studies. Some studies examine a continuous sum score of chronic stress domains, whereas others arbitrarily assign individuals to groups of stress (low, medium, high). This makes it difficult to compare across studies and generalize findings across different races/ethnicities. Therefore, the first question this study addressed was whether a latent variable model of chronic stress, comprised of four indicators of stress (money/financial, job/ability to work, health problem (other), and relationship stress), fit the data. Secondly, measurement invariance of this latent variable across the four races/ethnicities represented was assessed. Results showed that the latent model did indeed fit the data. Additionally, strong measurement invariance was achieved. These results confirm that

the latent variable of chronic stress has the same structure and can be measured in the same way across racial/ethnic groups. These findings suggest that examining chronic stress as a latent variable is appropriate, as it not only explicitly models error, which a sum score is unable to do, but also confirms that the structure, the meaning of chronic stress, and the underlying items relate equally to the construct across races/ethnicities. Future research exploring the relationship between chronic stress and other variables may benefit from examining this construct as a latent variable in order to reduce error in results and make it easier to compare across studies.

In addition, all of the indicators loaded strongly onto the factor, suggesting that each aspect of chronic stress (money/financial, job/ability to work, relationship, and health problem (other)) should be included in a latent variable model of chronic stress. However, this list is not exhaustive; indeed, there are other aspects of chronic stress that were not captured with the Chronic Burden Scale and additional variables that contribute to the severity of a stressor that requires additional study. For example, there are many factors that contribute to job stress (i.e. level of control in one's job) and marital stress (i.e. how disagreements are resolved, family finances). Furthermore, other social relationship stressors (friendships, family) that are non-marital can still be chronically stressful. These areas of chronic stress deserve attention and exploration to see if they too reliably load onto the latent factor. Additionally, more than one latent factor may be needed to accurately capture the depth and complexity of chronic stress.

Following measurement invariance, the latent variable was then considered as a predictor in analyses examining MetS and CVD outcomes. Biological studies have shown that increased stress reactivity may ultimately lead to a lowering of HDL cholesterol

concentration, impair glucose tolerance, and elevate blood pressure and lipid levels (Bonora et al., 2003; Innes et al., 2007; Krotkiewski et al., 1983; Liu et al., 2006; Vrijkotte et al., 2000). A systematic review of prospective cohort studies supports the finding between psychological stress and MetS diagnosis (Bergmann et al., 2014). These studies provided a solid foundation to explore how chronic stress is associated with components of MetS. In the current study, the path between chronic stress and MetS components were compared across races/ethnicities. Results from chi square difference tests comparing models with the same or different paths between chronic stress and Mets showed that the relationship between chronic stress and MetS was the same across all four races/ethnicities. For all racial/ethnic groups, higher levels of latent chronic stress were associated with larger waist circumference and higher levels of fasting glucose, after adjusting for relevant covariates. Consistent with the findings from this study, stress (defined as perceived stress, psychological distress, marital stress, or job stress) was positively related to weight gain in several other studies (Allard et al., 2011; Block et al., 2009; Kouvonen et al., 2011; Puustinen et al., 2011; Roos et al., 2013). Prior research has shown mixed results regarding the relationship between chronic stress and fasting glucose. Some have found a positive relationship between stress and glucose (Rod et al., 2009), whereas others have found no relationship, or even a negative association (Eriksson et al., 2013; Kawakami et al., 1999). Overall, findings from our study suggest that waist circumference and fasting glucose may be more susceptible to chronic stress than lipids or blood pressure.

The relationships between chronic stress and other MetS components, including blood pressure, HDL cholesterol, and triglycerides, were not significant in the present

study. Similar to the findings from this study, several others have found no significant relationship between psychological stress and blood pressure (Fauvel et al., 2003; Kivimaki et al., 2007; Puustinen et al., 2011). Certain aspects of job stress, including worrying about keeping one's job, low workplace social capital, and low feeling of justice, have been associated with an increase in blood pressure among men, whereas dissatisfaction with one's job and effort-reward imbalance have been associated with increased blood pressure among women (Gimeno et al., 2010; Levenstein, Smith, & Kaplan, 2001; Oksanen et al., 2012). These results suggest that there are certain aspects of job stress that relate to blood pressure differently in men and women. Job stress in general has been shown to be positively related to triglycerides, but the research on its relationship to HDL cholesterol is mixed (Gimeno et al., 2010; Puustinen et al., 2011).

Other studies have examined MetS diagnosis, rather than examining individual components. For example, Chandola et al. (2006) found that chronic job stress was related to increased risk of MetS diagnosis. In this study, job stress was defined using the Job Strain Questionnaire and participants were categorized into one of four quartiles of job stress. The Job Strain Questionnaire assesses physical and psychological demands of the job, job insecurity, and level or authority or control in one's job. These specific stressors are not assessed in the Chronic Burden Scale. Differences in the operational definition of stress may have contributed to the difference in significant findings. More specifically, job stress in general may not directly influence MetS risk, but rather exposure to specific job stressors (for example, level of control in one's job) may negatively impact other factors of metabolic health.

Certain components may contribute to a chronic stressor becoming deleterious to one's health. Not only with job stress, as seen with the Job Strain Questionnaire, but also with all other aspects of chronic stress, this may be seen. Specific factors of marital stress, health problem (other)/caregiver stress, and money/financial stress can be assessed with other reliable and valid questionnaires to pinpoint aforementioned components. Examining these more detailed aspects of the stressors may help create an ideal measure of chronic stress, which takes into account several aspects of why a situation or relationship may be stressful, above and beyond mere presence of a stressor.

For example, measures of marital satisfaction, such as the Locke Wallace Short Marital Adjustment Test (LWSMAT) (Locke & Wallace, 1959) may help clarify which aspects of the marital relationship may contribute to perceived stress. This scale contains 15 questions that are answered using a Likert scale and summed for a total score. Questions address the extent to which couples agree or disagree on handling family finances, demonstration of affection, intimacy, philosophy of life, among other topics. Sample questions include: "Do you ever wish you had not married?"; "Do you and your mate engage in outside interests together?"; and "When disagreements arise, they usually result in [husband giving in] [wife giving in] or [agreement by mutual give and take]?" The Caregiver Self-Assessment Questionnaire (Epstein-Lubow, Gaudiano, Hinckley, Salloway, & Miller, 2010) is an 18-item self-report measure devised by the American Medical Association to help physicians assess stress levels of family caregivers. Items are answered either yes or no: "I have felt completely overwhelmed"; "I have felt a loss of privacy and/or personal time"; and "I have found my relative's living situation to be inconvenient or a barrier to care." Chronic financial stress has been measured using a 4-

item scale, which assesses how often an individual did not have enough money to afford food, medical care, clothing, and leisure activities (Pearlin & Lieberman, 1979; Pearlin, Menaghan, Lieberman, & Mullan, 1981; Peirce, Frone, Russell, & Cooper, 1996). The Psychiatric Epidemiologic Research Inventory Life Events Scale (B. S. Dohrenwend, Krasnoff, Askenasy, & Dohrenwend, 1978) also assess aspects of financial stress including: having less money than usual, having to borrow money, going on welfare, or experiencing a foreclosure on a loan or mortgage. Taken together, these questionnaires provide more detailed information on the degree of stress an individual may be experiencing above and beyond assessing mere presence and perceived stressfulness of a stressor, as done by the Chronic Burden Scale.

An important follow-up study might take these more detailed examinations of chronic stress domains and import these data into a second-order or a bi-factor latent model. This would enhance the definition of latent chronic stress by including more information on what contributes to the individual sources of stress. At level one, there would be a latent factor of job stress comprised of certain indicators (physical demands, psychological demands, insecurity, level of control/authority), marital stress (disagreements, affection/intimacy, recreation), caregiver stress (number of hours caregiving, physical burden, mental burden), and money/financial stress (chronic financial stress, life events scale, level of income). Next, how reliably these first-order latents load onto the second-order latent variable of chronic stress would be examined. Having these additional items would make the definition of latent chronic stress more precise by including more information on what contributes to the presence and perceived stressfulness of chronic stress.

Furthermore, moderators may help explain the strength of the relationship between chronic stress and MetS and elucidate for whom this relationship holds. Few empirical studies have examined potential moderators of the relationship between chronic stress and MetS. With strong theoretical support from literature on the psychosocial reserve capacity (Gallo & Matthews, 2003), it was hypothesized that level of education, emotional support, and healthcare coverage status would moderate the relationship between chronic stress and MetS. Although there was a significant main effect of level of education on health, such that more years of education were associated with better health outcomes (smaller waist circumference, higher HDL cholesterol, lower triglycerides, lower fasting glucose, and lower systolic and diastolic blood pressure), level of education was also a significant moderator in the relationship between chronic stress and HDL cholesterol, only. Surprisingly, for less educated individuals (those achieving a less than high school education), higher levels of chronic stress were associated with an increase in HDL cholesterol. Individuals who do not complete high school are more likely to enter into manual labor jobs, often requiring many hours of physically demanding work (Rho, 2010). One important way to raise HDL cholesterol levels is by increasing physical activity (Lopez, Vial, Balart, & Arroyave, 1974). It is possible that one reason greater stress is associated with higher HDL cholesterol in this population is that, despite high stress, engaging in more physically active work during the daytime leads to elevated HDL cholesterol levels. This hypothesis deserves greater attention and more structured follow up. In addition to measures of chronic stress, this type of follow-up would require collecting data on type of job and physical demands of that job. With this information, the correlation between level of education and physical demands of job could be

examined. Next, physical demands of job would be an important moderator to examine. In other words, is the relationship between chronic stress and HDL positive in those with physically demanding jobs, but not significant (or negative) in those without physically demanding jobs? This type of analysis would help clarify why we see a positive relationship between chronic stress and HDL cholesterol in less educated individuals. This also reinforces the idea that a more detailed and well-informed latent variable of chronic stress is needed. As described above, including physical and psychological demands of the job as indicators of a latent job stress variable may help us better understand the relationship between chronic stress and HDL cholesterol.

Surprisingly, emotional support and health insurance did not significantly moderate the relationship between chronic stress and any MetS component. Prior research supports the finding that emotional supports buffers the negative effects of stress on physical health outcomes (Cobb, 1976; Cohen & Hoberman, 1983; Ozbay et al., 2007). However, evidence for the buffering model is found when the emotional/social support responds directly to the needs elicited by the stressor (Cohen & Wills, 1985). In other words, the process by which emotional support buffers the effects of stress on health occurs only when that support is obtained in response to the stressor. It is possible that for certain indicators of chronic stress, social support might not be a useful resource. For example, despite high emotional/social support, money/financial stress may still negatively impact health, since financial support might be a more important resource than social support.

Few studies have examined the moderating role of health insurance. The non-significant finding suggests that the relationship between stress and MetS does not differ

between those with or without access to healthcare. However, there are additional unmeasured variables at play here. For example, health literacy, proximity to a healthcare provider, and attendance at scheduled physical appointments may also have a direct and moderating impact on the way in which stress affects metabolic health. Attendance at appointments, for example, targets a health behavior that is not necessarily correlated with health insurance coverage. This pathway, entitled "healthcare access and utilization," as outlined in the Myers (2009) lifespan biospsychosocial model of cumulative vulnerability and minority health, requires additional exploration in future studies. More specifically, it is important to assess these other important aspects of health care (literacy, proximity, attendance at appointments) to understand the relationship between health insurance coverage and health status. Answering these questions may clarify what factors influence an individual to seek help from a healthcare provider before disease develops.

As an exploratory analysis, sex was examined as a moderator of the relationship between chronic stress and MetS components. The interaction between stress and sex was significant for waist circumference, such that the relationship between chronic stress and waist circumference was stronger in women than in men. Many studies support the finding that stress is associated with larger waist circumference or weight gain, especially in women (Block et al., 2009; Brunner, Chandola, & Marmot, 2007; Fowler-Brown et al., 2009; Gram Quist et al., 2013). It is not abundantly clear why this relationship is stronger in women than in men; however, a working hypothesis suggests that stress may affect eating behavior differently in women and men, such that women are more likely to

overeat and men are more likely to turn to alcohol or smoking (Conway, Vickers, Ward, & Rahe, 1981; Grunberg & Straub, 1992; Laitinen, Ek, & Sovio, 2002; Mehlum, 1999).

In addition to a positive relationship between stress and MetS, several reports have shown that chronic stress is implicated in CVD (Janczura et al., 2015; Kershaw et al., 2015; Mujahid et al., 2011; Troxel et al., 2003). In the current study, the path between chronic stress and CVD outcome was compared across the four races/ethnicities. The relationship between chronic stress and CVD was found to differ across races/ethnicities. However, the relationship between stress and CVD was not significant in any one race/ethnicity. In fact, the odds ratios were quite similar. CVD events were rare in the sample, and it is possible that a relationship might have emerged with a larger number of CVD events. This is in contrast to the Kershaw et al. (2015) study, which found that race/ethnicity was not a significant moderator of the relationship between stress and CHD outcome.

The Kershaw et al. (2015) study highlighted the importance of presence and perceived stressfulness of individual level sources of chronic stress and found that individuals in the highest category of stress had a 65% higher odds of CHD than those in the lowest category. There were several important distinctions in the current study, which may account for the differences in significant findings. Most importantly, the measure of chronic stress was different. The latent variable of chronic stress did not include a measure of stress due to self-reported health status. As a reminder, the question asking whether or not health problem (self) was a significant source of stress for a participant was not included as an indicator for the latent variable, so as to not use one's own health status to predict later health status. Secondly, in the Kershaw et al. (2015) paper,

individuals were assigned to one of three categories of stress. Lastly, the present study examined CVD, as opposed to CHD. It is possible that these measurement differences are responsible for the differences in significant findings. Despite a non-significant finding, the present study adds to the knowledge of literature by strengthening the measure of chronic stress and addressing certain measurement limitations in the Kershaw study. Although this paper reported significant findings, categorizing individuals into levels of chronic stress is not a recommended practice as, among other consequences, arbitrarily draws a line between those who may, in fact, not be that dissimilar in their stress response (MacCallum, Zhang, Preacher, & Rucker, 2002).

Another potential reason for the non-significant findings with CVD outcome could be the timing of both stress exposure and CVD. Chronic stress was assessed at baseline, and CVD was assessed up to nine years later. Perhaps an individual who endorsed chronic stress at baseline eventually located the necessary resources to alleviate the stressor, thereby reducing CVD risk. This may also explain why more components of MetS emerged as significant, given that the MetS components were also measured at baseline. Essentially, the significant MetS findings demonstrate the relationship between chronic stress exposure for the past six months (or more) and current metabolic health. How long a stressor must be present before it becomes detrimental to cardiovascular health remains unknown. Results from this study suggest that six months of exposure is sufficient to negatively impact waist circumference and fasting glucose. However, additional research is warranted to further explore length of chronic stress exposure to metabolic health and disease outcomes. Longitudinal studies are best suited to help determine the length of time it takes for a stressor to become metabolically toxic. If the

Chronic Burden Scale is given at baseline, at each follow-up, the questionnaire ought to assess if the initial stressor has dissipated, remained the same, or worsened. At the same time, it would be important to assess if any new stressors have developed. These follow-ups could be in-person, emailed, or texted to the participant to fill out, for ease of responding. Ecological momentary assessments could also help determine length of time until a stressor dissipates; for example, a participant who endorses any chronic stressor may then be prompted at random times to respond to the Chronic Burden Scale to get a more accurate sense of when a stressor is eliminated. Additional questionnaires ought to assess coping techniques, health behaviors, and personality factors to explore as potential moderators or mediators. It would also be important to include physical assessments to examine metabolic and cardiovascular health outcomes at various time points. Such designs may help elucidate the time it takes for a stressor to dissipate, what coping techniques, behaviors, or personality factors aid in the reduction of a stressor, and/or how long it takes for a stressor to impact the body at a cardiovascular level.

This study attempted to explore what moderates the relationship between chronic stress and CVD. Surprisingly, none of the proposed moderators (level of education, emotional support, or health insurance coverage) emerged as significant. Sex, which was entered as an exploratory moderator, was found to significantly moderate the relationship between stress and CVD in Whites, Blacks, and Hispanics, but not Chinese Americans. In three of the four racial ethnic groups, men had higher odds of CVD than women, which is consistent with findings from other research studies (Galiuto & Locorotondo, 2015; Naqvi, Naqvi, & Merz, 2005). It is possible that personality factors such as optimism and sense of mastery/self-control may be relevant or more impactful

moderators on the stress to cardiovascular health pathway (Elliot, Mooney, Infurna, & Chapman, 2017; Roepke et al., 2011). Future studies should also focus on behavioral variables as mediators of the chronic stress to CVD relationship. Returning to the lifespan biopsychosocial model of cumulative vulnerability and minority health, there is, indeed, a pathway from chronic stress to health behaviors to health status, which bypasses the psychosocial reserve capacity. Empirically testing these other pathways (e.g., diet, exercise) is an area for future research.

The lack of significant findings between chronic stress and CVD was surprising. To determine if this "resiliency" of the sample was related to mental, as well as physical health outcomes, the relationship between chronic stress and depressive symptoms was also examined as an exploratory analysis. In the current sample, despite risk, based on increasing levels of chronic stress, there was some degree of physical resiliency with respect to certain MetS factors and CVD. However, the relationship between chronic stress and depressive symptoms was strong. Moreover, this relationship was moderated by level of education and emotional support, in the expected directions. The relationship between chronic stress and depressive symptoms was stronger for less educated individuals and for individuals at the lowest level of emotional support. These results highlight the importance of both education and emotional support as important resources in the reserve capacity to buffer the negative effects of chronic stress on mental health. Poor mental health is a risk factor for chronic physical conditions, including cardiovascular disease (Bradley & Rumsfeld, 2015; Elderon & Whooley, 2013; Whooley, 2006). Given that depression is a risk factor itself for cardiovascular disease, early intervention for those suffering from chronic stress is paramount to prevention of later

disease. Although this study did not find a significant relationship between stress and CVD, the fact that depressive symptoms were strongly related to chronic stress puts those highly stressed individuals at heightened risk for later disease development. Clinically, this has relevance for healthcare providers to assess for the presence and perceived stressfulness of chronic stressors in various domains to accurately identify individuals at elevated risk for depression, and potentially, CVD.

Additionally, sex significantly moderated the relationship between chronic stress and depressive symptoms. Although men started out with fewer depressive symptoms than women did, each additional unit increase in chronic stress was associated with a steeper increase in depressive symptoms. Men, in particular, may be more susceptible to depression when chronically stressed. Research suggests that men and women may cope differently with stress, such that women engage more frequently in emotion-focused coping and men engage more frequently in problem-focused coping (Ptacek, Smith, & Dodge, 1994). It is possible that when a chronic stressor cannot be eliminated with problem-focused coping, men are more likely to develop symptoms of depression than women, who seek out social support to a greater extent than men.

This is the first study to examine measurement invariance of a latent variable of chronic stress and analyze its relationship with longitudinal health outcomes. Additional strengths of the study include its large, diverse sample from multiple sites. CVD outcomes were adjudicated, and multiple covariates were accounted for. Moreover, the Chronic Burden Scale is a reliable and valid measure of stress, which assesses cognitive appraisal of the stressor, above and beyond the mere presence of the stressor.

The study was limited to a select number of moderators; however, many additional external factors may influence both perceived stressfulness and may moderate the relationship between chronic stress and health outcomes. Indeed, more research is needed to understand what moderates the relationship between chronic stress and cardiovascular health. Future studies may wish to focus on personality factor moderators (e.g. optimism, self-control) or behavioral mediators, such as diet and/or exercise to help understand this relationship. Furthermore, this study did not examine biological pathways that contribute to disease development. Further research is needed to understand the mechanisms by which chronic stress functions to influence metabolic change over time.

Notwithstanding these limitations, these findings enhance our understanding of the concept of chronic stress in a multi-ethnic sample. Results from this study suggests that future research examining the role of chronic stress in multiple populations could utilize a latent variable over a sum score or assigning individuals to groups of stress (high, medium, low), since all indicators loaded reliably onto a latent factor in an invariant manner across races/ethnicities. The finding that greater levels of chronic stress positively related to larger waist circumference, higher fasting glucose, and more depressive symptoms suggest that it is an important domain for healthcare providers to assess. Understanding the role that chronic stress plays on both mental and physical health can help clarify when and where to intervene. Higher levels of education and greater levels of emotional support buffered the negative effects of chronic stress on depressive symptoms. This finding highlights the role of these important resources in the psychosocial reserve capacity. Additional research is needed to illuminate what moderators act upon the chronic stress-CVD path.

Summary/conclusions

This study supports the finding that chronic stress is related to negative health outcomes and provides support for examining stress as a latent variable, but points to the need to more comprehensively measure its various aspects. In a large, ethnically diverse sample of asymptomatic men and women at baseline, latent chronic stress was positively associated with waist circumference and fasting glucose. Level of education significantly moderated the relationship between chronic stress and HDL cholesterol, such that for less educated individuals, as chronic stress increases, HDL also increases. Chronic stress was significantly, positively related to depressive symptoms. Lastly, higher levels of education and emotional support buffer the negative effects of chronic stress on depressive symptoms. Future studies should focus on identifying moderators in the chronic stress-cardiovascular health pathway.

Funding

This research was supported by Supported by contracts N01-HC-95159 through N01-HC-95169 from the National Heart, Lung, and Blood Institute (NHLBI) and by grants UL1-RR-024156 and UL1-RR-025005 from National Center for Research Resources (NCRR). SAF was supported by NHLBI T32 institutional training grant HL007426-37.

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Table 1. Descriptive characteristics (mean and standard deviation) of the total sample and by race/ethnicity.

Variable	Total Sample N = 6685	Whites N = 2583	Blacks N = 1827	Hispanics N = 1473	Chinese American N = 802
	M (SD)				
Age (years)	62.1 (10.2)	62.5 (10.2)	62.1 (10.0)	61.3 (10.3)	62.4 (10.3)
Waist circumference (cm)	98.1 (14.4)	98.0 (14.4)	101.2 (14.7)	100.5 (13.0)	87.1 (9.9)
Systolic blood pressure (mmHg)	126.5 (21.4)	123.4 (20.4)	131.7 (21.5)	126.8 (21.9)	124.6 (21.6)
Diastolic blood pressure (mmHg)	71.9 (10.3)	70.2 (9.98)	74.5 (10.2)	71.6 (10.1)	72.0 (10.3)
HDL cholesterol (mg/dL)	50.9 (14.8)	52.2 (15.7)	52.3 (15.2)	47.7 (13.1)	49.5 (12.7)
Triglycerides (mg/dL)	131.6 (89.1)	133.2 (90.5)	104.9 (69.0)	157.2 (101.2)	142.8 (84.7)
Fasting glucose (mg/dL)	97.4 (30.4)	91.4 (21.7)	100.0 (32.2)	103.8 (39.1)	99.0 (28.3)
Emotional support	24.2 (5.3)	24.1 (5.2)	24.3 (5.2)	24.3 (5.6)	23.8 (5.0)
CES-D	7.6 (7.6)	7.0 (7.0)	7.3 (7.3)	9.5 (7.0)	6.3 (6.5)
	N (%)				
Sex (Females)	3525 (52.7)	1339 (51.8)	1011 (55.3)	761 (51.7)	414 (51.6)
Cigarette Status (Users)					
Current	872 (13.1)	298 (11.5)	328 (18.0)	201 (13.6)	45 (5.6)
Former	2449 (36.7)	1145 (44.3)	672 (36.8)	479 (32.5)	153 (19.1)
Never	3360 (50.3)	1139 (44.1)	825 (45.2)	793 (53.8)	603 (75.3)
Education					
Less than HS	1210 (18.1)	126 (4.9)	222 (12.2)	662 (44.9)	199 (24.8)
HS/GED	1089 (18.1)	431 (16.7)	346 (19.0)	301 (20.4)	130 (16.3)
Some college	1906 (28.5)	741 (28.7)	641 (35.1)	364 (24.8)	160 (19.9)
College and above	2356 (35.3)	1282 (49.7)	616 (33.7)	146 (9.9)	312 (39.0)
Income					
Below $30k	2408 (37.4)	511 (20.3)	613 (36.4)	846 (58.8)	438 (55.0)
Above $30k	4031 (62.6)	2009 (79.7)	1070 (63.6)	594 (41.3)	358 (45.0)
Health insurance (No)	609 (9.0)	70 (2.7)	113 (6.2)	265 (18.0)	154 (19.2)
CVD	551 (8.2)	221 (8.6)	150 (8.2)	137 (9.3)	43 (5.4)

Figure 1. Lifespan biopsychosocial model of cumulative vulnerability and minority health. Reprinted from Myers (2009).

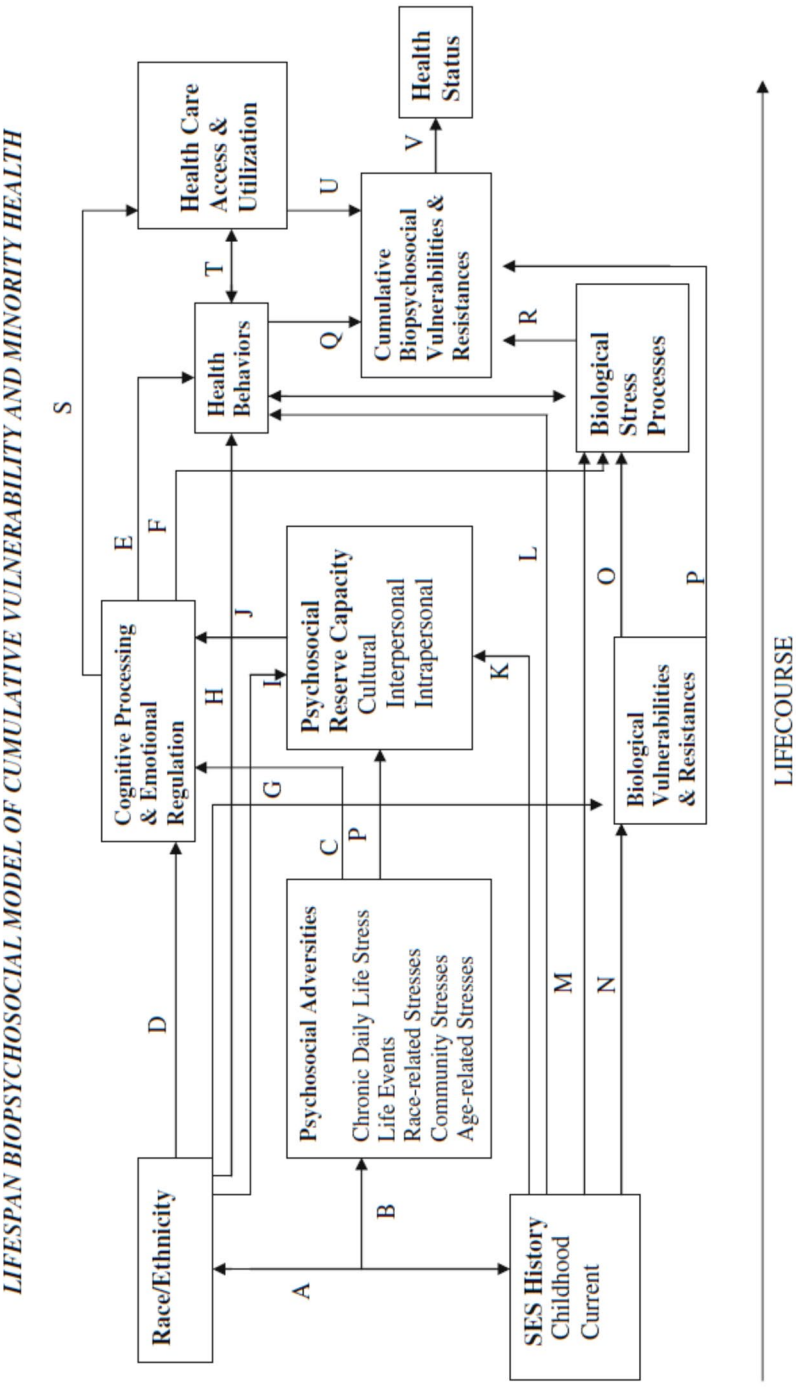
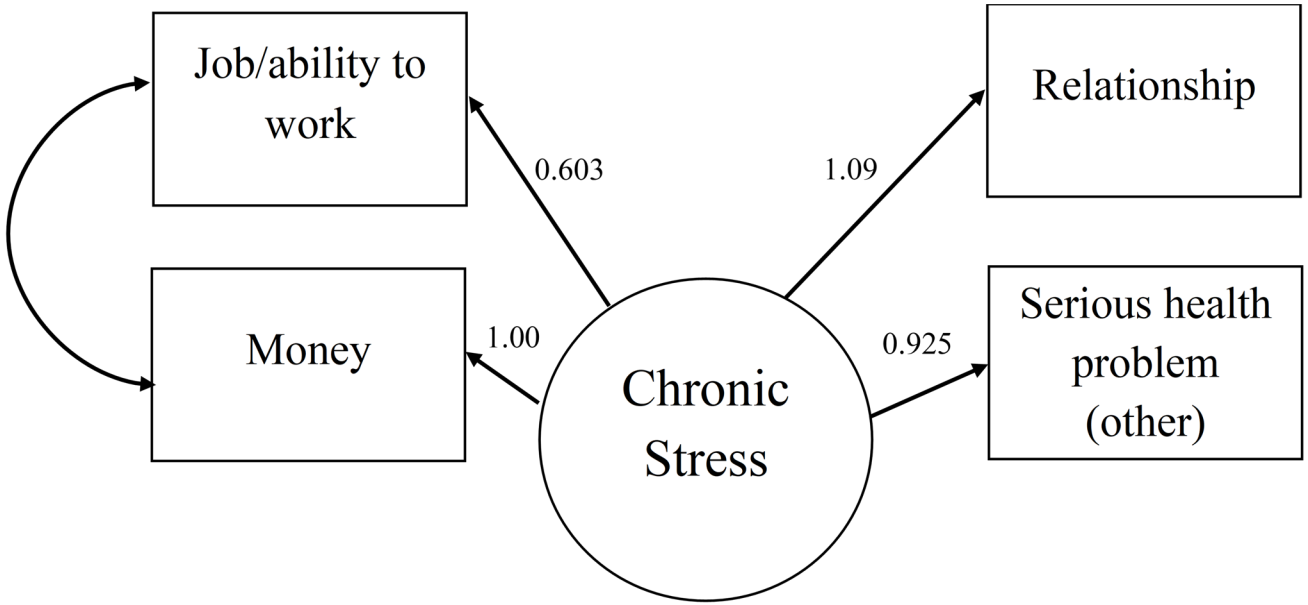


Figure 2. Latent variable model of chronic stress.



Model fit statistics: CFI = .988; RMSEA = .019 (90% CI: .004 - .031); SRMR = .020.

Unstandardized loadings are reported.

Table 2. Unstandardized and standardized factor loadings for the chronic stress latent variable

	Unstandardized loading* (95% Confidence Interval)	Standardized loading
White		
Money/Financial	1.000 (1.000 – 1.000)	0.453
Job	0.603 (0.511 – 0.696)	0.300
Relationship	1.096 (0.929 – 1.263)	0.463
Health problem (other)	0.925 (0.781 – 1.069)	0.346
Black		
Money/Financial		0.489
Job		0.366
Relationship		0.572
Health problem (other)		0.420
Hispanic		
Money		0.446
Job		0.353
Relationship		0.525
Health problem (other)		0.383
Chinese-American		
Money		0.478
Job		0.359
Relationship		0.585
Health problem (other)		0.371

*Unstandardized loadings are the same across all four races/ethnicities

Table 3. Linear regression results examining chronic stress with MetS components.

Variable	Waist B (95% CI)	HDL	Triglycerides	Glucose	Systolic BP	Diastolic BP
Chronic stress	1.00** (0.30 – 1.69)	0.42 (-0.17 – 1.02)	1.62 (-2.36 – 5.61)	2.16** (0.75 – 3.56)	0.23 (-0.75 – 1.21)	-0.03 (-0.48 – 0.42)
Age	0.05 (-0.01 – 0.11)	0.14*** (0.08 – 0.20)	-0.44* (-0.79 - -0.09)	0.27*** (0.17 – 0.36)	0.72*** (0.64 – 0.80)	-0.05* (-0.09 - -0.01)
Sex	6.88*** (5.78 – 7.97)	-14.66*** (-15.78 – -13.54)	8.76* (1.20 – 16.31)	7.78*** (6.00 – 9.59)	2.12** (0.63 – 3.61)	6.99*** (6.24 -7.74)
Cigarette status			-5.51	-0.02	-0.62	-0.26
Former	0.34	2.21***	(-12.84 – 1.82)	(-1.81 – 1.78)	(-2.16 – 0.93)	(-1.03 – 0.52)
Current	(-0.81 – 1.49)	(1.05 -3.38)	13.72	-0.71	-2.15	-0.82
	-1.44	-1.07	(-0.06 – 27.50)	(-3.39 – 1.97)	(-4.57 – 0.28)	(-2.08 – 0.44)
	(-3.28 – 0.41)	(-2.90 – 0.75)				
Income	-0.57*** (-0.77 - -0.36)	0.69*** (0.49 – 0.90)	-3.73*** (-5.10 - -2.35)	-0.43* (-0.81 - -0.06)	-0.65*** (-0.89 - -0.37)	-0.03 (-0.17 – 0.10)

*$p < .05$, **$p < .01$, *** $p <. 001$

Table 4. Results from moderation analyses examining level of education, emotional support, and health insurance status as moderators of the relationship between chronic stress and MetS components.

Interaction	Waist B (95% CI)	HDL	Triglycerides	Glucose	Systolic BP	Diastolic BP
Chronic stress	1.85*** (0.80 – 2.90)	1.04* (0.06 – 2.01)	-2.21 (-12.05 – 7.64)	3.81 (-0.23 – 7.85)	-0.10 (-1.69 – 1.49)	0.14 (-0.56 – 0.84)
Level of education	-2.23*** (-3.03 – 1.43)	1.51*** (0.75 – 2.27)	-14.69*** (-20.17 - -9.21)	-5.30*** (-7.16 - -3.43)	-2.98*** (-4.14 - -1.81)	-0.87** (-1.43 - -0.32)
Interaction	0.65 (-0.50 – 1.79)	-1.15* (-2.21 - -0.08)	3.28 (-6.60 – 13.16)	-1.99 (-5.98 – 2.01)	1.26 (-0.46 – 2.99)	0.01 (-0.79 – 0.80)
Chronic stress	2.05* (0.44 – 3.65)	-0.35 (-1.97 – 1.27)	0.03 (-0.03 – 0.09)	2.34** (0.81 – 3.87)	0.32 (-1.61 – 2.25)	0.24 (-0.81 – 1.28)
Emotional support	0.05 (-0.07 – 0.16)	-0.11 (-0.23 – 0.00)	0.00 (-0.00 – 0.01)	0.03 (-0.12 – 0.19)	0.15 (-0.00 – 0.31)	0.08* (0.00 – 0.16)
Interaction	-0.01 (-0.21 – 0.18)	0.04 (-0.12 – 0.20)	-0.00 (-0.01 – 0.01)	0.20 (-0.00 – 0.39)	0.06 (-0.17 – 0.30)	-0.03 (-0.16 – 0.09)
Chronic stress	2.26*** (1.50 -3.02)	0.28 (-0.34 – 0.90)	0.04 (-4.71 – 4.80)	1.89** (0.62 – 3.16)	0.60 (-0.29 – 1.49)	0.12 (-0.33 – 0.57)
Health insurance	-2.51*** (-3.77 - -1.24)	-1.68** (-2.79 - -0.57)	16.20 (-21.30 – 53.69)	5.13 (-0.72 – 10.97)	0.59 (-1.33 – 2.51)	0.03 (-0.92 – 0.97)
Interaction	-1.24 (-2.76 -0.28)	0.48 (-0.82 – 1.78)	-25.86 (-162.44 – 110.72)	0.17 (-18.0 – 18.39)	-0.06 (-2.76 – 2.65)	-0.28 (-1.65 – 1.08)

All models adjusted for age, sex, cigarette status, and income
*$p < .05$, **$p < .01$, *** $p <. 001$

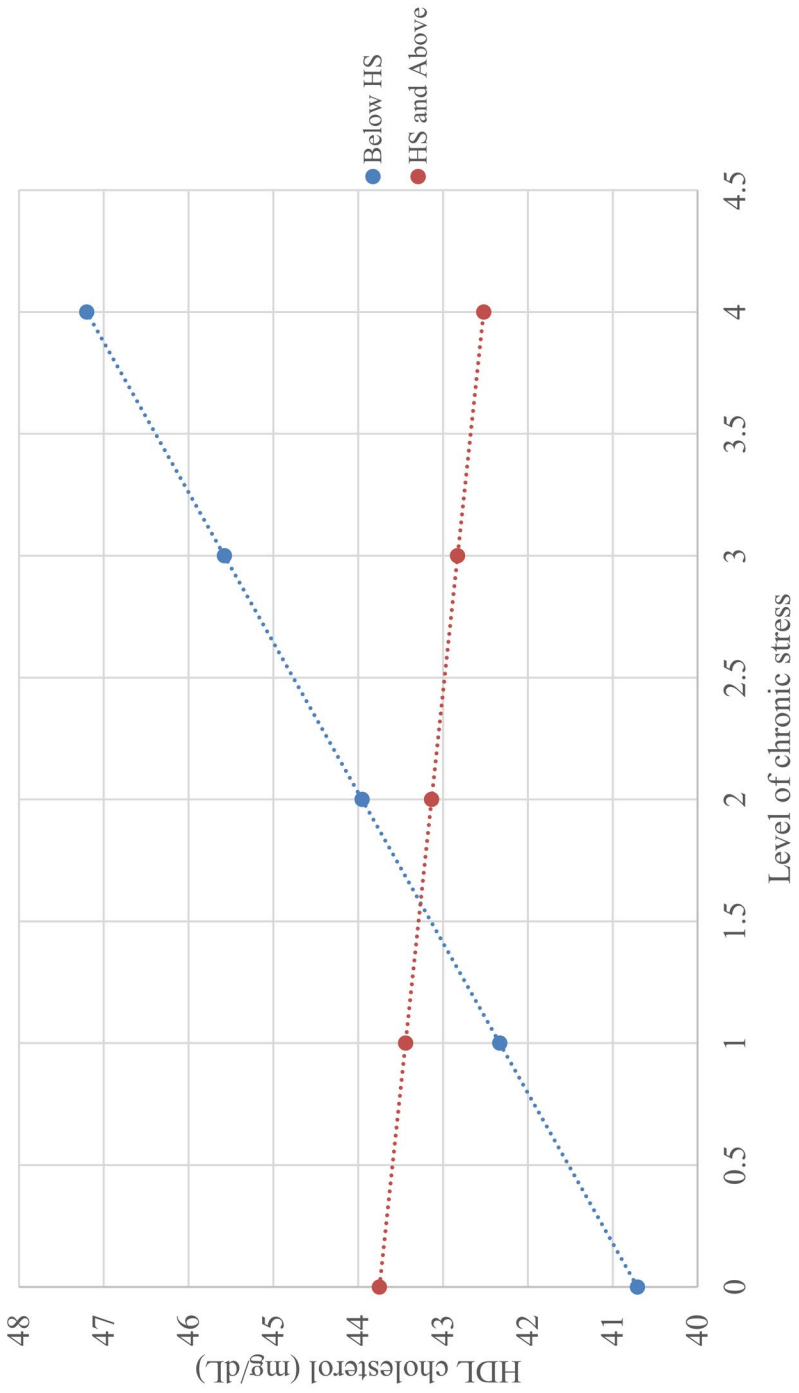


Figure 3. The relationship between chronic stress and HDL cholesterol, moderated by level of education

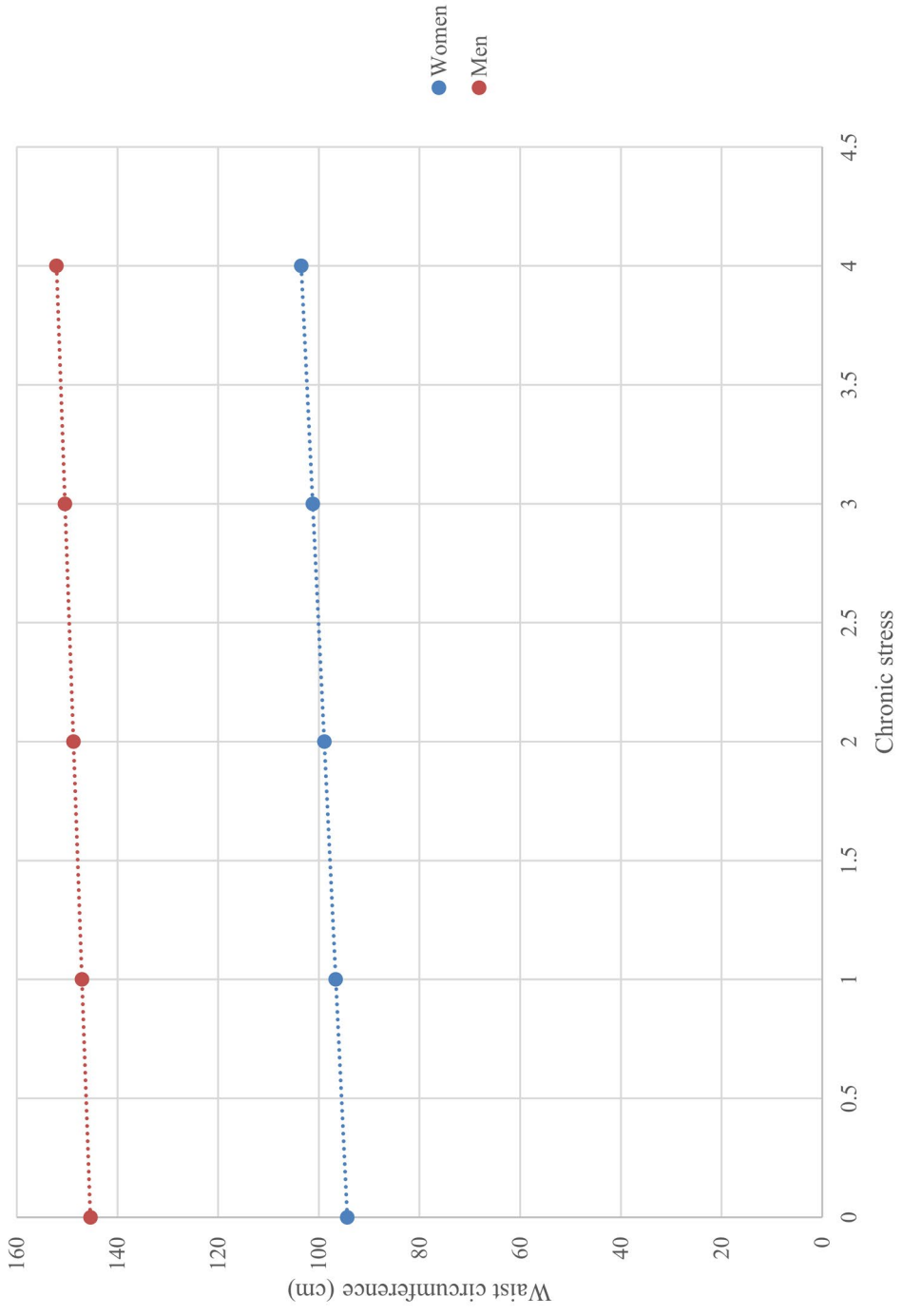


Figure 4. The relationship between chronic stress and waist circumference, moderated by sex.

Table 5. Results of logistic regression analyses examining the relationship between chronic stress and CVD outcome, separated by race/ethnicity.

	CVD Outcome Odds Ratio	95% CI
Whites	1.12	0.99 – 1.42
Blacks	1.12	0.73 – 1.75
Hispanics	0.92	0.72 – 1.19
Chinese Americans	1.10	0.90 – 1.32

All models adjusted for age, sex, cigarette status, and income
*$p < .05$, **$p < .01$, *** $p <. 001$

Table 6. Results from moderation analyses examining level of education, emotional support, and health insurance status as moderators of the relationship between chronic stress and CVD.

Interaction	Whites B (95% CI)	Blacks	Chinese-Americans	Hispanics
Chronic stress	0.06 (-0.55 – 0.66)	0.28 (-0.06 – 0.62)	-0.67 (-2.98 – 1.64)	0.02 (-0.69 – 0.72)
Level of education	0.00 (-0.38 – 0.38)	-0.23 (-0.62 – 0.16)	-0.46 (-1.24 – 0.32)	0.28 (-0.15 – 0.71)
Interaction	0.22 (-0.39 – 0.84)	-0.31 (-0.74 – 0.12)	1.12 (-1.65 – 3.89)	-0.90 (-2.04 – 0.24)
Chronic stress	0.25 (-0.13– 0.63)	0.07 (-0.18 – 0.32)	0.10 (-1.27 – 1.47)	-0.24 (-0.90 – 0.42)
Emotional support	0.01 (-0.02 – 0.03)	-0.00 (-0.04 – 0.03)	-0.02 (-0.10 – 0.05)	-0.00 (-0.04 – 0.03)
Interaction	0.01 (-0.03 – 0.05)	-0.01 (-0.05 – 0.03)	0.11 (-0.25 – 0.47)	0.03 (-0.04 – 0.10)
Chronic stress	0.27 (-0.09 – 0.63)	0.10 (-0.17 – 0.36)	-0.05 (-1.52 – 1.41)	-0.10 (-0.77 – 0.58)
Health insurance	0.44 (-0.51 – 1.39)	0.89* (0.14 – 1.64)	0.14 (-0.81 – 1.08)	-0.53 (-1.25 – 0.20)
Interaction	-1.27 (-2.96 – 0.43)	-0.21 (-0.82 – 0.41)	0.14 (-2.47 – 2.75)	-1.29 (-2.63 – 0.05)
Chronic stress	0.18 (-0.25 – 0.60)	0.15 (-0.15 – 0.45)	-0.12 (-1.40 – 1.16)	-0.96 (-2.21 – 0.30)
Sex	0.57*** (0.27 – 0.87)	0.64*** (0.28 – 1.00)	0.38 (-0.37 – 1.12)	0.69** (0.22 – 1.17)
Interaction	0.10 (-0.42 – 0.63)	-0.11 (-0.52 – 0.31)	0.71 (-0.92 – 2.33)	1.17 (-0.13 – 2.47)

All models adjusted for age, sex, cigarette status, and income

*$p < .05$, **$p < .01$, *** $p <. 001$

Table 7. Results from analyses examining level of education, emotional support, and health insurance status as moderators of the relationship between chronic stress and depressive symptoms.

	Depressive symptoms	
	B	95% CI
Model 1		
Chronic Stress	6.45***	5.61 – 7.29
Age	0.14***	0.11 – 0.18
Sex	0.09	-0.49 – 0.68
Cigarette status		
Former	0.16	-0.41 – 0.73
Current	0.94	-0.12 – 2.00
Income	-0.16**	-0.28 - -0.04
Model 2		
Chronic Stress	8.13***	7.07 – 9.29
Education	-1.47***	-1.87 - -1.07
Chronic Stress x Education	-2.33***	-3.20 - -1.45
Model 3		
Chronic Stress	5.96***	4.91 – 7.00
Emotional support	-0.37***	-0.40 - -0.34
Chronic Stress x Emotional support	-0.43***	-0.53 - -0.33
Model 4		
Chronic Stress	6.06***	5.30 – 6.82
Health insurance	-0.65*	-1.22 - -0.09
Chronic Stress x Health insurance	1.42	-0.04 – 2.87
Model 5		
Chronic Stress	7.45***	6.35 – 8.54
Sex	-0.33	-0.71 – 0.06
Chronic Stress x Sex	-2.01***	-2.90 - -1.12

All models adjusted for age, sex, cigarette status, and income
*$p < .05$, **$p < .01$, *** $p <. 001$

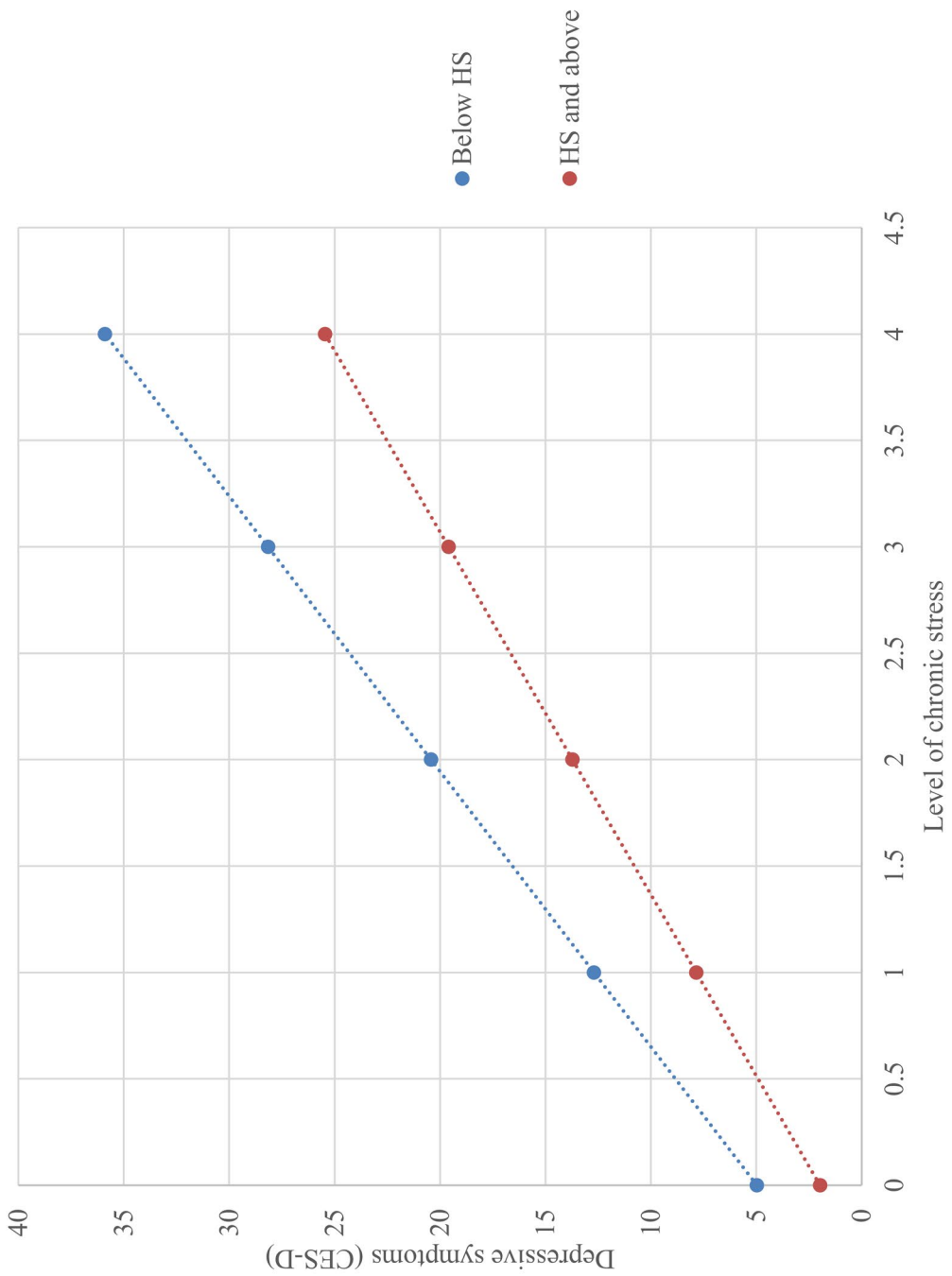


Figure 5. Relationship between chronic stress and depressive symptoms, moderated by level of education.

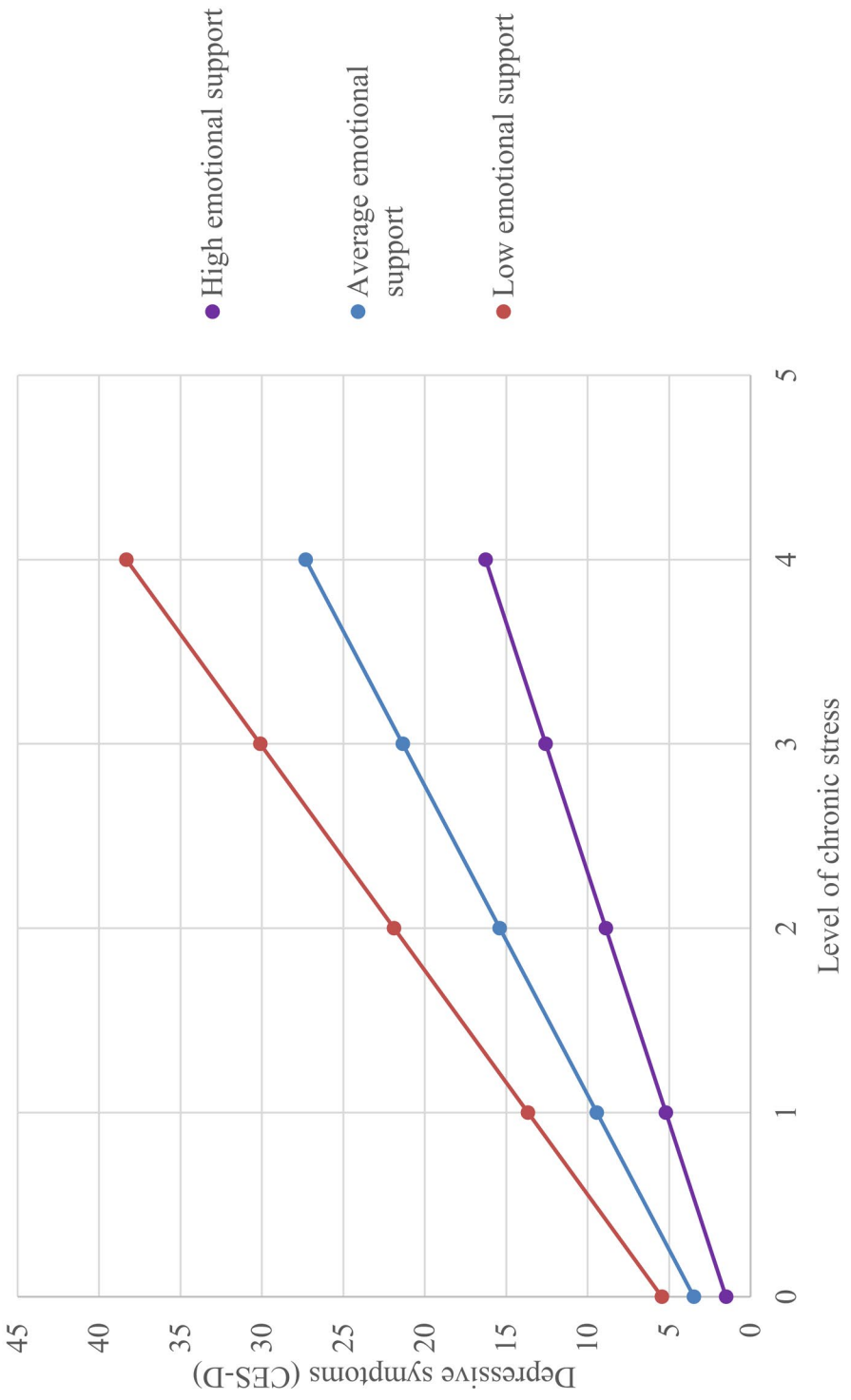


Figure 6. Relationship between chronic stress and depressive symptoms, moderated by emotional support.

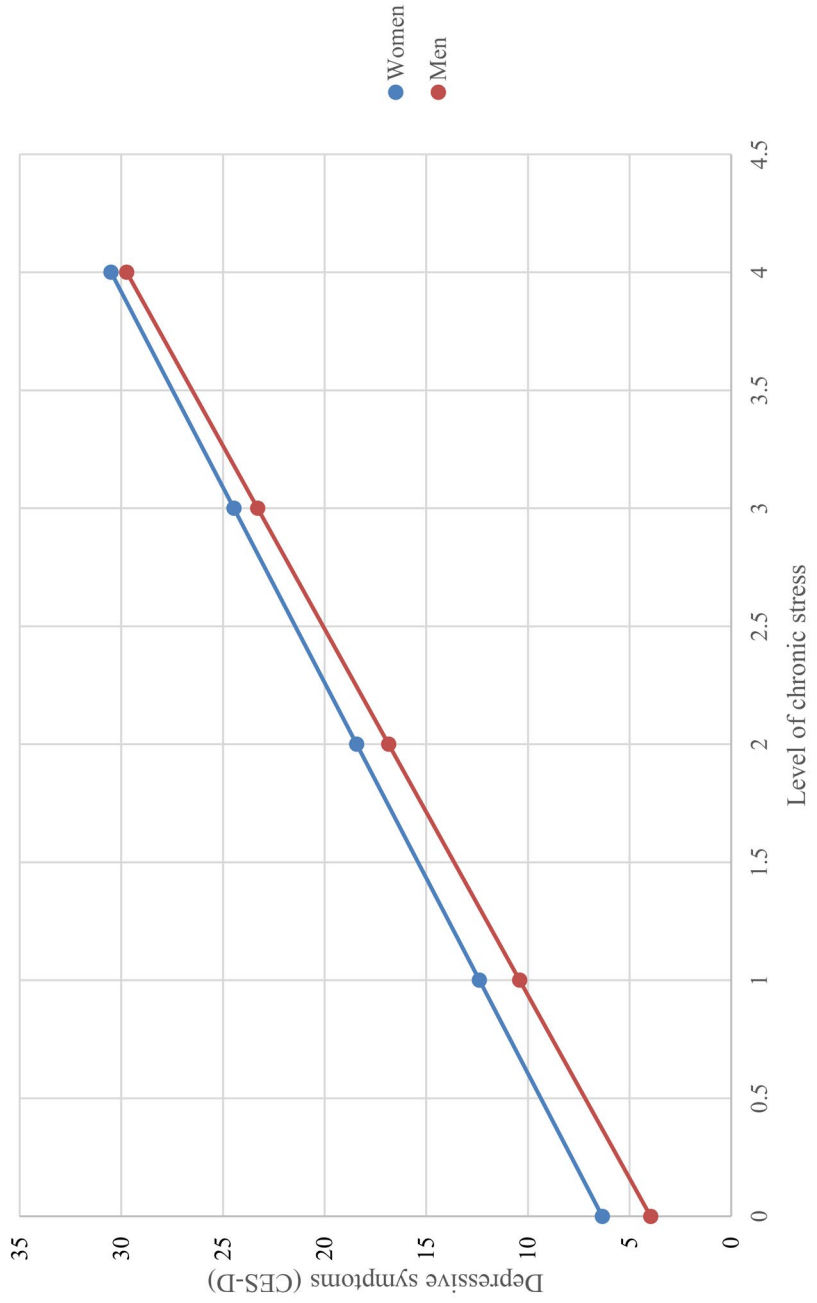


Figure 7. Relationship between chronic stress and depressive symptoms, moderated by sex.