TOXIC STRESS, RESILIENCE AND RACE-RELATED DISPARITIES IN NEUROCOGNITIVE AND QUALITY OF LIFE CHANGE IN A NATIONALLY REPRESENTATIVE SAMPLE OF AMERICANS ≥ 50 YEARS OLD

by

ALLAN KIZZA NKWATA

(Under the Direction of Ming Zhang)

ABSTRACT

Background: Toxic stress (TS), resilience promoting factors (RPF), minority race and their interactions were evaluated as determinants of quality of life (QOL) and neurocognitive decline in a nationally representative sample of American adults ≥ 50 years with heart disease (HD) and/or type-2 diabetes (T2DM) diagnosed by 2006 as part of the Health and Retirement Study (HRS).

Methods: Data used were from the HRS 2006-2016. In Aim 1, we examined TS and conducted additional analyses within strata of racial groups to understand possible variations in TS and relationship with wellbeing (QOL) over 8 years of follow-up. In aim 2, first we examined whether TS and RPF were associated with neurocognitive impairment (NI) in our sample. We further examined whether TS and RPFs were associated with dementia incidence starting with dementia-free adults followed longitudinally from 2006-2016.

Results: The odds of declining SRH for African-Americans and Other race were respectively 1.46 (95% CI: 1.25–1.70) and 1.43 (95% CI: 1.10–1.86) times higher relative to

Caucasian race over 8 years. The odds of SRH decline were respectively 33% (OR=0.67, 95% CI: 0.50–0.89) and 17% (95% CI: 0.59–1.17) lower for individuals that experienced <2 lifetime vs. ≥2 lifetime discrimination events. Furthermore, the relationship of life course stress to SRH decline over eight years varied by race (time*stress*race, p=0.1173). Specifically, increasing lifetime stress predicted greater QOL decline among Caucasians (p=0.0063) and among African-American (p=0.0820) but not among Other race (p=0.9943). Similarly, chronic stress (OR 1.31, 95%CI: 1.01, 1.70) and discrimination (OR 2.51, 95% CI: 1.75, 3.59) were associated with higher NI risk while high vs. low mastery (OR 0.61, 95%CI: 0.47, 0.77) was associated with lower NI risk. High vs. low mastery-associated lower NI risk was evident among adults that denied experiencing discrimination (OR 0.57, 95%CI: 0.44, 0.74) but not among those that reported experience of discrimination (OR 0.93, 95%CI: 0.47, 1.81). Relative to White/Other race, African American race was associated with NI risk but only in the sub-group that achieved high mastery (OR 1.83, 95%CI: 1.20, 2.80).

Conclusion: Toxic stress and minority race are social determinants of QOL and NI declines among older Americans in this study. The types and prevalence of toxic stressors varied according to race/ethnicity. Policy interventions to address the root causes TS represent a viable strategy for mitigating racial disparities in overall wellbeing and improving health outcomes in all aging Americans regardless of race.

INDEX WORDS: Toxic Stress, Resilience promoting factors, Quality of Life, Neurocognitive Impairment, Minority Race, Older Americans, Health Disparities

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DEDICATION

I dedicate this work to my lovely wife, Florence Kizza, my daughters Alicia and Felicia, and my son Isaiah. You all have been a constant source of encouragement to me on this journey.

"He has made everything beautiful in its time. Also, he has put eternity into man's heart, yet so that he cannot find out what God has done from the beginning to the end."

Ecclesiastes 3:11

"but they who wait for the LORD shall renew their strength; they shall mount up with wings like eagles; they shall run and not be weary; they shall walk and not faint."

Isaiah 40:31

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CHAPTER 1

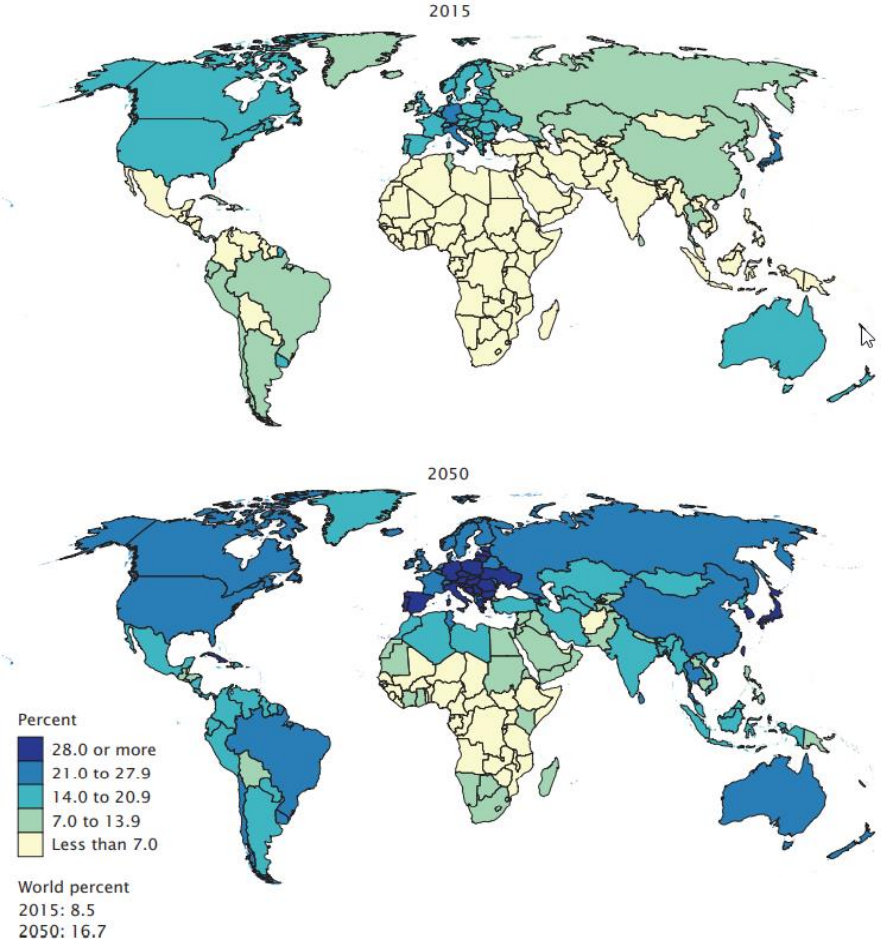
INTRODUCTION

Background and Motivation

The population of the world continues to grow older rapidly as fertility rates have fallen to very low levels in most world regions and people tend to live longer. Not only are more people living longer, the proportion of the world population that is 65 years old and above is also growing. In 2015, the population of people 65 years and older around the world was estimated at 617 million (8.5 percent of the total population). This population is projected to increase to 1.6 billion globally by 2050 (16.7 percent of the total population).[1]

A distinct feature of global population aging is that it has been happening at uneven rates across world regions and by levels of economic development. For instance, most of the more developed countries in Europe have observed aging populations for decades, and the post-World War II baby boom generation in the United States turning 65 in the last 10 years.[2] In 2015, more than a third of the world population aged 65 and older lived in developed countries. However, with the accelerated growth of older populations in Asia and Latin America, it is projected that more than four-fifths of the world's population aged 65 and older will live in the less developed countries (Figure 1.1).[1]

Figure 1.1: Percentage of the World's Population aged ≥ 65: 2015 and 2050

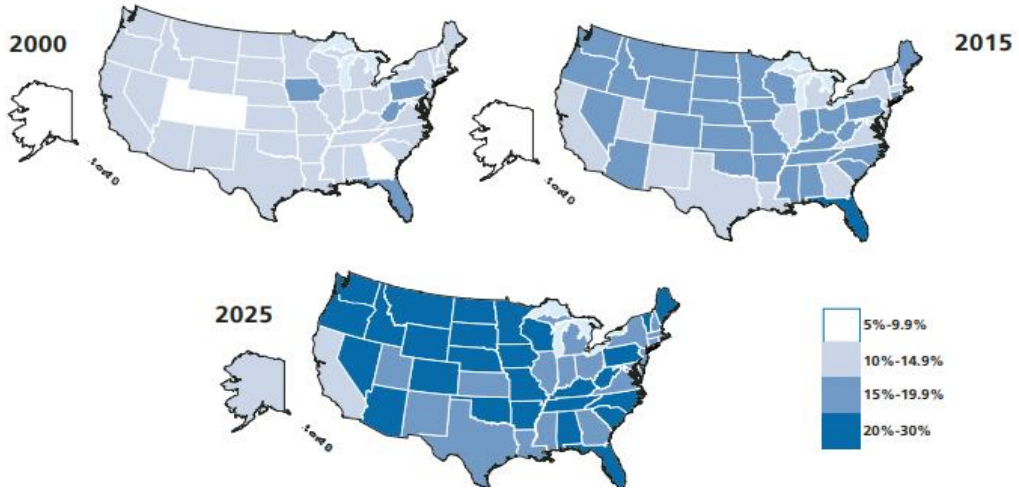


Sources: U.S. Census Bureau, 2013, 2014; International Data Base, U.S. population projections

The United States is undergoing a major shift in the demographic composition of its adult population due to increases in life expectancy at older ages. In 2012, the population of adults aged 65 and over was estimated at 43.1 million, and this increase was largely driven by aging of the post-World war II baby boomers around that time (Figure 1.2). This population is expected to double by 2050, as people tend to live longer.[2] This has been termed the "Graying of America". The growing shift in the numbers and proportions of older adults is expected to be accompanied by a considerable burden on the public health systems, and the medical and social services.[3,4]

This burden includes a disproportionate increase in prevalence and incidence of chronic conditions such as cancers, diabetes and heart diseases among older adults that represent a primary source of health care services and costs. For example, in 2012, 60% of older adults had two or more chronic conditions, such as heart disease, cancer, stroke, emphysema, diabetes mellitus, and Alzheimer's disease.[5] Chronic conditions lower the quality of life for older adults and are the leading causes of disability and death in the United States and all developed countries.[6,7] Although the overall life-expectancy is increasing in all racial groups, notable racial disparity in life expectancy persists.[8] Further still, increase in life-expectancy is not accompanied by corresponding increase in years of life lived without a major health condition or healthy life expectancy (HLE). [9,10] Due to this, the National Institutes of Aging (NIA) is encouraging scientific research on understanding modifiable determinants that would lead to improving HLE in aging populations in the United States.[11]

Figure 1.2: Percentage of the United States' Population aged ≥ 65: 2000, 2015 and 2025



Source: US Bureau of the Census, 2003

Despite decades of efforts to reduce racial discrimination, race-related disadvantages in access to healthcare, chronic disease prevalence, incidence and health outcomes persist for racial/ethnic minority populations compared to whites in the United States (US).[12] These disparities in health and healthcare are well established across various health outcomes[13] including morbidity, mortality, disability and injury[14] and are largely the result of excessive rates of chronic disease among racial minorities.[15,16] Compared to non-Hispanic whites, the rates of hypertension, diabetes and obesity are 25%, 49% and 59% higher respectively amongst African Americans/ blacks. Similarly, compared to non- Hispanic whites, Hispanics experience rates of diabetes and obesity that are 25% and 20% higher respectively.[17]

Racial disparities have also been observed in mortality rates. For example, when age-adjusted mortality rates are compared, African Americans remain significantly at risk for early death compared to whites in general. Of note, the overall death rate of African Americans in the US today is equivalent to that of whites over 30 years ago.[18,19] Also, minorities and the less educated have higher mortality rates for a wide range of diseases, including stroke, Type 2 diabetes (T2DM), cancer, cardiovascular diseases (CVD), acquired immunodeficiency syndrome (AIDS), and lung disease.[20] Due to this, the Healthy People 2030 initiative keeps the elimination of health disparities and advancing health equity across all groups as one of its key goals.[21]

In addition to sub-optimal health outcomes and inappropriate health care utilization, racial disparities have been linked to significant economic costs. In a study on the economic burden of health disparities in the US, the authors found that 31% of direct medical care expenditures for African Americans, Asians, and Hispanics were avoidable excess costs attributable to health inequalities. The authors estimated that eliminating health disparities for minority communities reduced direct medical care expenditures by about US $230 billion, and

indirect costs associated with illness and premature death by more than one trillion dollars between 2003 and 2006. Further still, the combined costs of health inequalities and premature deaths in the US were estimated at US $1.24 trillion.[22]

Statement of the Problem

Despite marked improvements in life expectancy and overall health of the population in United States, racial and ethnic minorities by and large continue to experience higher rates of morbidity and mortality than non-minority populations.[23,24]African Americans, for example, have the highest rates of mortality from heart disease, cancer, cerebrovascular disease, and HIV/AIDs than any other US racial or ethnic group.[25,26] Similarly, compared to non-Hispanic whites, African American adults have a higher prevalence of diabetes, high blood pressure, stroke and heart disease. [25,26] African American compared to Non-Hispanic white race is also associated with markedly higher rates of disability[27], functional limitations[28,29] and lower overall life expectancy.[30] Reasons for race-related differences in health status in the US population are complex, under investigated and overall still poorly understood in many key respects. Undeniable differences in a range of outcomes by race reflect to varying degrees disparities in socio-economic status, health-related risk behaviors, environmental degradation, and the direct and indirect consequences of discrimination, which this dissertation identifies as a major psychosocial stressor.[31]

Additionally, the pervasiveness of racial disparities in prevalence and incidence of chronic conditions are not new. However, the proximate mechanisms of racial disparities – including their potential mediators or moderators, for respective health outcomes are poorly understood yet prevalent among Americans at highest risk of chronic diseases. This dissertation seeks to evaluate the prevalence and severity of toxic stress (TS) and resiliency promoting

factors (RPF) as modifiable independent risk factors for non-communicable diseases (NCDs) unevenly distributed by race/ethnicity in the United States.

Purpose of Research

This dissertation goes beyond demonstration of racial/ethnic disparities in chronic disease endpoints and specifically investigates toxic stressors and deficits in resiliency promoting factors as key mediators of race-related differences in quality of life and neuro-cognitive declines in an aging population of retired and semi-retired adults with heart disease and/or diabetes. Discrimination as a component of psychosocial stress may be blatant or perceived resulting in a range of physiological responses (e.g., elevated blood pressure and heart rate, production of biochemical reactions, hypervigilance) that ultimately contribute to dysregulated blood pressure, worse quality of life/self-rated health[32] and predicts adverse health behavior in affected populations.[33] With respect to onset and progression of major non-communicable diseases, the role of a range of psychosocial stressors remains poorly understood. The health impact of toxic stress depends on the nature, number, and persistence of the stressors as well as the individual's biological vulnerability (that is, genetics, constitutional factors), available psychosocial resources, and learned patterns of coping.[34] Of importance, the severity and persistence of toxic stressors – including the presence and quality of coping strategies is almost always linked with a lower socio-economic status (SES) in the United States and around the world.[35]

This research investigated the etiologic role of toxic psychosocial stressors and measures of resiliency, as independent predictors, or mediators of racial disparities in the onset of dementia, general neurocognitive and overall quality of life decline in adults 50 years or older with recent diagnosis of cardiovascular disease and diabetes. We used the theory of allostatic load as an important conceptual framework for defining and evaluating toxic stress as a mediator

of race/ethnicity related disparities in these outcomes among a vulnerable nationally representative sample of US adults with recently diagnosed heart disease or diabetes. We hypothesized that Blacks would report higher rates of decline than Whites in our study outcomes in our sample, as observed in prior research. We further hypothesized that experiences of higher levels of toxic stress (TS) and lower levels of resilience -promoting factors (RPF) will partly mediate these race/ethnicity associations by inducing faster quality of life and neurocognitive decline in this vulnerable sub-group of older Americans.

Research Questions and Specific Aims

Proposed investigations utilized data from a longitudinal cohort design – the Health and Retirement Study (HRS). The HRS tracks health, life course events and aging among semi-retired and retired adults in the US. The study is conducted under the University of Michigan and sponsored by the National Institute on Aging. The study population includes a representative sample of about 20,000 US adults older than 50 years along with their partners who may be younger. Participants are interviewed every two years about their physical health and functioning, cognitive abilities, health insurance and healthcare expenses, and financial information such as income, assets, wills, trusts and pension plans. Data used were from the 2006, 2008, 2010, 2012, 2014 and 2016 waves of the HRS.

Two specific aims were addressed in this study.

1) To evaluate the independent roles of toxic stress, measures of resiliency and race/ethnicity in relationship to change in quality of life (QOL) among older US adults with diagnosed cardiovascular/ heart disease or type-2 diabetes.

   Hypotheses: There will be racial differences in QOL declines, and individuals higher levels of Toxic stress and lower levels of resilience promoting factors will have lower QOL.

General approach: Data from 2006-2014 HRS waves were used. To answer the first research question, generalized estimating equations (GEE) models controlling for age, gender, SES, multiple chronic conditions were implemented. Race/Ethnicity categories, different types of stressors and resilience measures were examined as primary determinants. The main outcome was rates of change in QOL as measured by change in self-rated health since the previous wave.

2) To evaluate the role of toxic stress and resilience in change in neurocognitive function.
   a) To determine the correlates of dementia in a representative sample of US adults 50 years and above enrolled in the HRS.

Hypotheses: Higher levels of toxic stress and lower levels of resilience promoting factors will be associated with higher rates of neurocognitive impairment in older American adults; the relationship between race/ethnicity and neurocognitive impairment varies according to levels of toxic stress and resilience promoting factors; and c) respective relationships between toxic stress, resilience promoting factors and neurocognitive impairment in older adults vary according to race ethnicity.

General approach: To answer the second research question, predictors of cognitive decline were evaluated in 2014 HRS wave. Multivariable logistic regression models were performed to evaluate associations between toxic stress/ resilience measures and race/ethnicity as independent predictors of cognitive decline in these older adults.

   b) To evaluate toxic stress and resilience promoting factors as independent contributors of change in neuro-cognitive function among American adults with normal cognitive functioning at enrollment over 10 years**.**

Hypotheses: Higher levels of toxic stress and lower levels of resilience promoting factors will be associated with higher rates of cognitive impairment in older American adults;

Race/ethnicity will be associated with earlier onset of cognitive decline over 10 years; and the relationship between race and earlier onset of cognitive decline varies according to levels of toxic stress and resilience promoting factors.

General approach: Data from 2016-2016 waves of HRS were used. Cox proportional hazard models and Kaplan Meier curves were used to analyze the incidence of cognitive decline in ten-year period. The main outcome was a new report of dementia as determined by responses to the question on memory loss as diagnosed by a physician.

Organization of the Study

Chapter 2 of this dissertation details the literature that is relevant to a full understanding of how racial disparities, sustained levels of toxic stressors and lower levels of resilience (coping) resources combine in complex ways to affect health outcomes and gaps identified in the literature. Chapter 3 outlines the general analytic methods that were used in conducting this research. Chapters 4 and 5 describe specific aim 1, while chapters 6 and 7 describe specific aims 2 a), and 2b) respectively. Each of chapters 4-7 is in a manuscript-style format, with a standalone abstract, introduction, methodology, results, discussion, conclusions, and references. Chapter 8 summarizes the major conclusions and implications from the study's two main aims.

CHAPTER 2

LITERATURE REVIEW

Persistence of Health Disparities

The United States (US) is racially and ethnically diverse, and the nation's diversity is growing over time. The major racial/ ethnic groups include, non-Hispanic whites, Latino, African American, Asian / Pacific Islander, and American Indian/Alaska natives. As of 2014, nearly one-third of the US population identified themselves as a member of a racial or ethnic minority group.[36] By the year 2050, this proportion is expected to increase to nearly half.[37]

There is a long history of collecting and reporting health statistics by race in the US[14] as seen in the US mortality statistics that have been compiled and published since the 1930s. In these reports, health status variations among the population on the basis of race rather than social class have been obtainable allowing trends to be tracked over time.[38]

Health disparities are inequalities that occur in the provision of healthcare and access to healthcare across different racial, ethnic, and socioeconomic groups. Health disparities among racial and ethnic groups have a long history and continue to exist in the United States[39] having been perpetuated by unfair policies of the past like slavery and racial segregation. People of color are more likely than non-Hispanic whites to have lower incomes, which may have implications for both their health and insurance status.[37]

Early researchers approached the study of race and health within the context of genetic and biological differences between the races. They posited that observed differences in health conditions at the time were due to underlying genetic or biologic differences[40-42] and documented

that African Americans were biologically inferior, making them more susceptible to a myriad of illnesses. This fueled controversies between innate versus acquired bases for health differences between ethnic groups.[43] However, with the emergence of newer knowledge, this notion was later dispelled as false, as much of the earlier research attempted to justify policies that fostered racial inequality.[44] Furthermore, earlier research did not take into account the variations in social contexts and environments that different racial groups experienced, such as zoning along racial lines, segregation and housing policies.

Despite steady improvement in the overall health of the US population, racial and ethnic minorities, with few exceptions, experience higher rates of morbidity and mortality than non-minorities.[45] African Americans, for example, experience the highest rates of mortality from heart disease, cancer, cerebrovascular disease, and HIV/AIDs than any other US racial or ethnic group. American Indians disproportionately die from diabetes, liver disease and cirrhosis, and unintentional injuries. In addition, some Asian American sub populations experience rates of stomach, liver, and cervical cancers that are well above national averages. The reasons for these differences in health status are complex and poorly understood, but may largely reflect differences in SES, health-related risk factors, environmental degradation, and direct and indirect consequences of discrimination.[31]

Racial and ethnic inequities in health and health care can impose significant costs on various segments of society, including individuals, families, communities, health care organizations, employers, health plans, and government programs, including, Medicare and Medicaid. These costs can include direct expenses associated with the provision of care to a sicker and more disadvantaged population, as well as indirect cost such as lost productivity, lost wages, absenteeism, family leave to deal with avoidable illnesses, and lower quality of life.

Premature mortality imposes considerable cost on society in the form of lower wages, lost tax revenues, additional services, and benefits for families of the deceased, and lower quality of life for survivors.

In one such study, La Veist and colleagues estimated the economic burden of health disparities in the US using three measures; 1) direct medical costs of health inequalities, 2) indirect costs of health inequalities, and 3) costs of premature death, using data from the Medical Expenditure Panel Survey (MEPS) and National Vital Statistics reports for the years 2002-2006. The authors found that about 31% of direct medical care expenditures for blacks / African Americans, Asians, and Hispanics were excess costs due to health inequalities. The authors estimated that eliminating health disparities for minorities would have reduced direct medical care expenditures by about US $230 billion, and indirect costs associated with illness and premature death by more than one trillion dollars between 2003 and 2006. Further still, the combined costs of health inequalities and premature deaths in the US were estimated at US $1.24 trillion.[22]

This dissertation did not treat race as a genetic or biologic construct. Instead, we used a social determinants of health framework which posits that race is a socio-cultural construct that is socially determined and that racial and ethnic minorities suffer from worse health outcomes compared to non-Hispanic whites due to their environments, social status, limited opportunities and experiences with discrimination in the United States.[46-48]

Racial discrimination

Racism is the belief that members of one or more races are inferior to members of other races. Racism in the US has been directed mainly by the white majority against racial and ethnic

minorities. Historically, the white majority has singled out racial/ ethnic minority groups for differential and unequal treatment in the areas of housing, employment, education, and criminal justice.[44,49]

Racism operates on multiple levels; institutionalized, personally mediated, and internalized.[50] Institutionalized racism is embedded in systems and institutional structures and permeates politics, medicine, housing, education, and employment. For instance, existing patterns in housing and education are the result of historical legacies of forced segregation and legalized discrimination. Personally mediated racism, on the other hand, refers to attitudes and beliefs about the inferiority of minority racial groups (prejudice) and differential treatment of people on the basis of race (discrimination) which is directly experienced at the individual level. Internalized racism, as opposed to personally mediated racism which has an identifiable perpetrator, refers to the acceptance of negative sociocultural beliefs about the intrinsic worth of one's own racial group.[51]

Experiences of racial discrimination may impact health directly or indirectly through various processes. Health may be physically impacted through the victimization that follows racial profiling or deaths from police brutality towards African Americans. Micro-aggressions, such as being treated without respect or courtesy in the workplace can also chronically impact health.[52-54] Additionally, subtle forms, based on assumptions about the work ethics or dispositions of racial groups also directly impact health and disease outcomes. Indirect health effects of racial discrimination are mostly observed through its impact on housing, employment, education, and other socioeconomic indicators.

Racial discrimination may also exert direct effects on mental and behavioral health. Unfair treatment may lead to negative psychological responses, including depression and

anxiety.[55,56] Discrimination may also increase the risk of engaging in unhealthy behaviors, including illicit substance use, smoking, and alcohol consumption.[57-59]

Evidence for racial disparities in the US

Racial disparities in the delivery of healthcare, health outcomes and health status have been observed in the US and in many societies around the world.[14,60] These inequalities exist in socio-economic status, access to the health care system, discrimination, and social and cultural attitudes about health and the healthcare system. In the US, African Americans have higher rates of death, disease and disability than whites have[44] and this trend has persisted for a very long time.[61] For example, African Americans face rates of hypertension, diabetes and obesity that are 25%, 49% and 59% higher, respectively than those found among non-Hispanic whites while Hispanics experience rates of diabetes and obesity that are 25% and 20% higher respectively than their non- Hispanic white counterparts.[17]

Mortality statistics: Mortality data reveal a lot about the health status of racial/ ethnic groups in the US.[13] In 2014, blacks had an age-adjusted death rate that was 20 percent higher than that of whites for all causes. African Americans had higher death rates than whites for 09 of the 15 leading causes of death (Table 2.1).[62]

Table 2.1: Leading causes of death in the United States: 2014

Rank	Cause of death	No. (%)	Crude Death rate	Age-adjusted Death rate	Black:White ratio
	All causes	2,626,418 (100.0)	823.7	724.6	1.2
1	Heart diseases	616,348 (23.4)	192.7	167.0	1.2
2	Cancers	591,700 (22.5)	185.6	161.2	1.1
3	Chronic Lower respiratory diseases	147,101 (5.6)	46.1	40.5	0.7

4	Accidents (unintentional injuries)	135,928 (5.2)	42.6	40.5	0.8
5	Stroke (cerebrovascular diseases)	133,103 (5.1)	41.7	36.5	1.4
6	Alzheimer's disease	93,541 (3.6)	29.3	25.4	0.8
7	Diabetes	76,488 (2.9)	24.0	20.9	1.9
8	Flu and pneumonia	55,227 (2.1)	17.3	15.1	1.1
9	Kidney disease	48,146 (1.8)	15.1	13.2	2.0
10	Suicides (intentional self-harm)	42,826 (1.6)	13.4	13.0	0.4
11	Septicemia	38,940 (1.5)	12.2	10.7	1.8
12	Liver cirrhosis	38,170 (1.5)	12.0	10.4	0.6
13	Hypertension	30,221 (1.2)	9.5	8.2	2.1
14	Parkinson's disease	26,150 (1.0)	8.2	7.4	0.5
15	Pneumonitis due to solids and liquids	18,792 (0.7)	5.9	5.1	1.0
	All other causes	535,737 (20.4)	168.0		

Source: Adapted from Kochanek et al. (2016)

Earlier onset of disease: Minorities also get sick at younger ages and die sooner than Whites. In an earlier classic study, Geronimus (1992) showed that the national infant death rates were lower for white and Mexican American women who delayed first births to their 20s compared with those who gave birth in their teenage years. The opposite pattern was evident for black and Puerto Rican women, with infant mortality lower for 15-19 year old than for women who had their first baby in their 20s. Geronimus argued that this pattern was due to "weathering" –the idea that early physiological deterioration was a result of multiple social disadvantages.[63] More recent studies provide evidence of this earlier onset of disease or accelerated aging for minority populations across multiple health indicators. White women have a higher incidence of breast cancer than black women, but the incidence rate under the age of 40 is higher for black than white women.[64] Similarly a 20-year follow up study found that the incident heart failure before the age of 50 was 20 times more common in blacks than whites, with the average age of

onset being 39 years for African Americans.[65] National data also show that cardiovascular disease develops earlier in blacks than whites, with 28 percent of CVD deaths among blacks occurring before age 65 compared 13 percent among whites.[66]

Another study also showed that the early health deterioration of black adults is evident across multiple biological systems. Using a global measure of allostatic load that summed 10 indicators of clinical and sub-clinical status, they found that African Americans were more likely than whites to score high on allostatic load (high on four or more indicators) at all ages, and the size of the black-white gap increased with age. In each age group, the average score for blacks was comparable with that of whites who were 10 years older. Moreover, blacks continued to have higher allostatic load scores even after adjustment for poverty.[67]

Severity and progression of disease: Racial disparities are also evident in the severity and progression of disease. For example, blacks have a higher prevalence of chronic kidney disease (CKD) than whites, require dialysis or kidney transplantation at younger ages, and have a higher incidence of end-stage renal disease at each decade of life, and their level of CKD risk factors does not adequately account for their faster progression of CKD to end-stage renal disease.[68] Disparities in the severity and progression of illness have been documented of even for outcomes that are less prevalent in Blacks, Breast cancer is one example. Although black- are less likely than white- women to get breast cancer, they are more likely to have tumors that grow quickly, recur more often, are resistant to treatment, and kill more frequently.[69] In addition, black and Hispanic women continue to be diagnosed at a later stage of breast cancer compared to white women,[70] and this partly explains the higher breast cancer mortality observed in black than white women in the US.[71]

Depression is another example. Blacks tend to have lower lifetime and current rates of depression than Whites, but depressed Blacks are more likely than their White peers to have higher levels of impairment, more severe symptoms, to be chronically depressed, and not to receive any treatment.[72]

Unhealthy behaviors: Racial disparities have been observed in unhealthy lifestyle behaviors. Unhealthy lifestyle behaviors include cigarette smoking, lack of regular moderate or vigorous physical activity, excessive alcohol use and poor dietary habits. Although cigarette smoking rates among Blacks adults are comparable to those of Whites,[13,73] Blacks suffer more from tobacco-related morbidity and mortality than Whites.[74-76] Blacks are less likely to quit smoking, hence will smoke for longer periods, contributing to the observed mortality disparities.[77] One third of all cancer deaths in the US are attributed to smoking.[78] For example, Blacks have the highest incidence, death rate and shortest survival for most cancers than any other racial or ethnic group. Each year, more than 72,000 Blacks are diagnosed with a tobacco-related cancer and more than 39,000 die from a tobacco related cancer.[79] Smoking is responsible for 87 percent of lung cancer deaths in the US.[78]

Similarly, despite comparable levels of alcohol consumption,[80] Blacks tend to develop more serious problems arising from excessive alcohol use than Whites, and their alcohol-related mortality is twice as high compared to that in whites. Obesity is more common among Blacks and Latinos than in Whites.[81]

Life course: Life expectancy data also illustrate striking racial disparities that have persisted in the US over many years.[13] In 1950, for instance, Blacks had a life expectancy at birth of 60.8 years, compared with 69.1 years for Whites.[82] Despite improvements over time, it was not until 1990 that Blacks achieved the life expectancy that Whites had in 1950.[18-19] Farther

more, there was still an almost 4- year gap in life expectancy in 2013 between Blacks and Whites (75.5 vs 79.0 years respectively). Data from the Indian Health Service (2014) also provide numerous examples of persisting disparities for specific causes of death overtime for American Indians compared to Whites.[14,83]

Race and Socioeconomic Status (SES)

Race and SES combine in complex ways to affect health outcomes. Existing literature suggests that SES not only confounds the relationship between race and health, but part of the causal pathway that links race to health.[72] Studies have documented significant relationship between race/ ethnicity and socio-economic status in various health outcomes across the life-course.[84] However, it is important to point out that racial and ethnic differences in health cannot be entirely explained by between- group differences in socio-economic status (SES).[85] The causes of racial and ethnic disparities in health are multi-factorial; they reflect underlying differences in biological vulnerability to disease as well as differences in social resources, environmental conditions, and healthcare interventions.[19] Understanding disparities requires the examination of multiple, complex and sometimes subtle relationships between genetic susceptibility, individual behavior, the social environment, physical surroundings, disease prevention, and medical treatment that lead to the observed differences in health status and health outcomes.

Many Blacks live in chronically precarious and difficult environments[47,86] that lack the resources necessary to foster and sustain health. These environments produce stressful living conditions, and often the most easily accessible options for addressing stress are various unhealthy behaviors like smoking, drinking, drug use and others.[87]Farther more, when the

relationship between race and access to healthcare is examined, whites are more likely than any other group to have health insurance coverage and a usual source of medical care.[39] Having health insurance coverage and the existence of a usual source of care are both important for timely access to healthcare.[39]

Race and chronic stress

The harmful effects of chronic stress experiences on health have been studied within the context of racial discrimination as a stressor.[12] Experiences of racial discrimination may be blatant or perceived, and can lead to a range of physiological responses (e.g., elevated blood pressure and heart rate, production of biochemical reactions, hypervigilance) that ultimately result in disease and death. A number of studies have now documented health effects of discrimination.[84,88,89] In one such study, experiences of perceived race-based discrimination were positively associated with raised blood pressure and poorer self-rated health[32]. Perceived race-based discrimination was also found to be a predictor of smoking among African American adults in two studies.[33] Moreover, smokers, compared with nonsmokers, reported finding the experience of discrimination as subjectively more stressful.

The relationship between psychosocial stressors and chronic disease is affected by several factors. These include the nature, number, and persistence of the stressors as well as by the individual's biological vulnerability (that is, genetics, constitutional factors), psychosocial resources, and learned patterns of coping.[34] It is worth noting that the prevalence of these stressors is almost always linked with a lower socio-economic status (SES).[35]

The Stress response

Stress occurs when the body responds to stimuli that threaten the maintenance of homeostasis, causing bodily or mental tension. The stress response is also called the "fight or flight" response or general adaptation syndrome[90]. The stress response is mediated by both the nervous and endocrine systems, to exert effects on other systems and peripheral body organs.[91] The stress response results in increased activity of the sympathetic nervous system and increased secretion of adrenal hormones in response to adverse events.[92,93] The sympathetic nervous system secretes the cytokines, epinephrine and norepinephrine while the adrenal glands release glucocorticoids into the blood stream.[94] The effects of these cytokines and hormones usually include increased respirations, heart rate, blood pressure, and overall oxygen consumption.[95] In most situations, the physiological changes associated with the stress response are temporary, with the body returning to its baseline state when the stressor is removed.

Types of stress: Stress differs in its nature, duration, and severity. There are different kinds of stress; it can be harmful (toxic), tolerable, or beneficial (positive) depending on the severity of the stress, a child's ability to cope, and how long the stress response lasts. Stressors may be physical, psychological or a combination of both types. Physical stress results from environmental factors that are harmful or potentially harmful to body tissues.[92] These include extreme heat or cold, decreased oxygen concentration, infections, injuries, prolonged heavy exercise, and loud sounds. Psychological stress is internal and results from thoughts about real or imagined (perceived) dangers. Examples of these include personal losses, unpleasant social interactions (or lack of social interactions), illness or perceived effects of a medical procedure. Feelings of anger, fear, grief, anxiety, depression, and guilt cause psychological stress. Psychological stress may also stem from pleasant stimuli such as friendly social contact, feelings

of joy or happiness or sexual arousal. Worth noting is the factors that produce psychological stress vary with the individual, the situation and time

The stress response can also be classified as positive, tolerable, or toxic depending on the magnitude and duration of the stressor. A positive stress response may be adaptive and typically does not impose a health burden as it is short-lived and moderate to mild in magnitude. This type may be either harmful or beneficial.[96] Examples may include dealing with first experiences in childhood, like meeting new people, getting shots, starting a new day care arrangement, and frustration. Tolerable stress, however, arises from exposure to a stressor that is not always normal and at a higher magnitude of threat. This can be triggered by a natural disaster or a serious illness. This too, may be marked with recovery after the stressor dissipates.

Toxic stress: Toxic stress (TS) results from strong, prolonged or permanent abnormal physiological responses to a stressor that increase risk of disease or ill health in the absence of coping mechanisms.[97] Toxic stress emerges and evolves throughout life[98] and manifests as negative emotional disorders like depression and anxiety, anger or hostility and external stressors resulting from repeated exposure to stressful conditions,[99] leading to the body's failure to fully recover even after the stressor is removed.[93] Toxic stress (TS) burdens society and everyone is susceptible to its effects.[93] Adverse effects of toxic stressors include job loss, lifestyle habits such as smoking, alcohol and drug abuse, onset of conditions like depression and obesity and chronic diseases such as diabetes and cardiovascular diseases (CVD). Early detection of it is key to prevention and mitigating its consequences. The role of psychosocial factors, specifically toxic/chronic and stress resilience in the etiology and prognosis of chronic diseases remains poorly understood. This is perhaps due to the fact that there are several

different dimensions of health that could be measured, and no gold standard exists for what could qualify as toxic stress in published studies.[100]

Resilience: Resilience on the other hand is the ability to properly adapt to and emerge from adverse conditions.[93] It refers to the idea that strategies/ mechanisms to overcome and withstand life's challenges exist. These resources include social support in the form of social networks, personal mastery, self-esteem, purpose in life and others.[100] A sense of control or personal mastery is a generalized belief that most circumstances in one's life are under one's personal control and not due to chance, fate or the actions of other people [101]. High self-esteem is a perception of oneself as a good, valued, and competent person. Social support refers to emotional, informational, or practical assistance from significant others such as family members, friends, or co-workers.[102] This support may actually be received from others or simply perceived to be available when needed. All of these resources augment individuals' abilities to cope with stressful demands. Mastery and self-esteem encourage active attempts at problem-solving, and perceived social support, especially perceived emotional support diminishes stress-induced psychological distress and physiological arousal.[103,104] A stronger sense of personal mastery (control) has been associated with better self-reported physical and mental health, lower risk of heart disease and diabetes, better chronic disease outcomes, and lower mortality.

Lower status, disadvantaged groups (women, minorities, unmarried persons, working class and poor individuals) generally have lower levels of these coping resources,[104 105] implying that they are doubly at risk of developing ill health and mental health problems. Acute and chronic stressors are concentrated in the very groups that are deficient in these stress-buffering assets.

Stress across the life span

A wealth of literature exists on toxic stress in pediatric populations. In this sub-group, toxic stress has been defined as adverse childhood experiences (ACEs). These range from experiences of extreme abuse and neglect to negative emotional environments and living in impoverished settings.[106] Children who experience toxic stress in early life are at risk of long-term poor health outcomes that may manifest later in their adulthood.[107,108]

The toxic stress response is believed to play a role in the pathophysiology of depressive disorders, behavioral dysregulation, post-traumatic stress disorder (PTSD), and psychosis.[109,110] In adolescents and adults, toxic stress has been linked with the uptake of unhealthy lifestyles. Adolescents with a history of early childhood adversity are more likely to initiate alcohol use at younger ages and will more likely use alcohol as a stress coping mechanism than for social reasons.[111] Other unhealthy adult behaviors associated with toxic stress exposures include tobacco use, illicit drug abuse, obesity, promiscuity[112,113] and pathologic gambling.[114]

Adolescents and adults with higher rates of risk-taking behaviors are also less likely to maintain supportive social networks and are at higher risk of school failure, membership in gangs, unemployment, poverty, homelessness, violent crime, incarceration, and becoming single parents. Furthermore, adults in this high-risk group who become parents themselves are less likely to be able to provide the kind of stable and supportive relationships that are needed to protect their children from the dangers of toxic stress.[115]

Adults who endured various forms of early childhood adversity also experience more physical illness and poor health outcomes.[113,116-120] These poor health outcomes are varied and include, chronic obstructive pulmonary disease, depression, cancer, obesity, suicide attempts, ischemic heart disease and a multitude of other disease conditions.[116,121,122]

Toxic stress and social economic status: The idea that social and economic status (SES) influences the health of populations is well established.[123] In every society, the poor tend to have worse health outcomes and shorter life expectancies than the wealthy. [15,124] Several studies have shown that toxic stress exposure is in many ways tied to social disadvantage. Socio-economic disparities in health persist at almost every stage in the life course, from birth (neonatal outcomes, infant mortality) to working age (e.g. cardio-vascular disease, accidents) and in old age (functional disability). Lower SES is almost always correlated with nearly every cause of morbidity and premature mortality.[124] There also seems to exist a gradient of health in as you move up the SES range, where those in the middleclass experiences better health than the poor, while the wealthy enjoy better health than the middle class.[125]

Toxic stress and behavioral issues: An extensive body of literature links chronic stress to multiple behavioral issues including smoking, excessive alcohol use, poor sleep as well as physical inactivity in adulthood.[126] More directly studies indicate racial disparities in allostatic load- a multi-systemic physiological wear and tear through long term exposure to stress-induced fluctuations or elevations in neuro-endocrine response.[127]

Racial disparities and Toxic stress

Relatively fewer studies have examined racial differences in stress. In a study evaluating the association between stressors and health in a community sample of African American, White, and Hispanic adults, the authors found significant racial differences in both the levels and clustering of stressors. African Americans reported a higher prevalence of stress overall, and compared to whites, multiple stressors were more common among African Americans reporting any stressors. When stratified by nativity status, American born-Hispanics had greater stressor-exposure compared to Whites and foreign-born Latinos, although their exposure level was

comparable to that of African Americans. In contrast, foreign-born Hispanics reported stress levels similar or lower than that of whites.[60]

Traumatic life events include divorce/ separation, motor vehicle crashes, physical assault, violence, disasters, and tragic deaths of individuals among others.[128] Previous research shows conflicting evidence on the distribution of traumatic events by race/ ethnicity. Breslau et al. (1991) found the overall lifetime prevalence of traumatic events was lowest among African-Americans in a study of 1007 adults, aged 21-30 years, in Detroit Michigan.[129] In a later study of a general population household sample of 2181 adults aged 18-45 years, the authors found a significantly greater prevalence of lifetime exposure to violence in non-whites compared to whites.[130] In another study examining the frequency and impact of various traumatic life events in a normal community-dwelling sample, higher rates of motor vehicle crashes were observed in African Americans than whites. However, when compared to African Americans, whites reported significantly higher lifetime rates of physical assault, disaster, and tragic deaths of others.[131]

In a study of 1361 female adolescents in California, Ohio and Maryland, the authors found that White females reported more interpersonal trauma (e.g. victimization of self/family member, physical assault) in the past year than African-American females.[132] In contrast, in an earlier study amongst older adults aged 65 and greater, African Americans reported more lifetime victimization by violent assault and intimidation compared to whites, whereas whites reported more lifetime victimization by property crimes, such as burglary, and vandalism.[133]

In another sample of young adults that included non-Hispanic whites, Cubans, non-Cuban Hispanics, and African- Americans, the authors found that African- Americans reported the highest rates of being shot or shot at and witnessing violence. By contrast, non-Hispanic

whites reported the highest rates of sexual molestation and physical abuse by a partner or parent.[134] These observations are consistent with findings from a community study of interpersonal violence as a specific traumatic event among 1,401 women, age 18–65 years, in Columbia, South Carolina that showed whites reported more physical violence events from current partners and more lifetime battering and emotional abuse in comparison to African-Americans.[135]

Theoretical models: Impact of stress on health

Further research is needed to identify the biological pathways by which psychosocial stressors affect health. Chronic exposure to stressors can lead to dysregulation across multiple physiological systems of the body, a framework called allostasis or the stress process model. Allostatic load is the idea that when chronic and /or excessive demands are placed on the body's regulatory system, these systems over time will exhibit wear and tear losing their ability to efficiently respond to stressors. The concept of allostatic load captures the cumulative burden of this physiological wear and tear that can increase the risk of disease, disability, and death.[136]

Racism threatens health when it produces physiological changes that are extensive, occur repeatedly, or take place during certain critical developmental periods. It makes the lives of the disadvantaged more and thus leads to negative mental and physical health consequences [137,138]. For example, evidence shows that the nocturnal blood pressure levels of African Americans who report encounters with discrimination fail to dip, that is, reach a normal low during sleep.[88,139,140] The biological pathway through which discrimination is thought to negatively impact physical well-being is the human stress response. At its core , this theory emphasizes the interaction

between exposures to psychosocial stressors and access to coping resources in the production of health and illness.[141]

The social stress theory is another theory that validates this research. It postulates that social sources of stress such as racism and other types of discrimination, can negatively impact a person's mental or physical health, through social comparisons.[142] These social stressors may impact the immune and other systems overtime, again through the bio-regulatory mechanisms involved in allostatic load.

Physical Disability- Race/Ethnicity Differences

Further research is needed to identify the biological pathways by which psychosocial stressors affect health. Chronic exposure to stressors can lead to dysregulation across multiple physiological systems of the body, a framework called allostasis or the stress process model. Allostatic load is the idea that when chronic and /or excessive demands are placed on the body's regulatory system, these systems over time will exhibit wear and tear losing their ability to efficiently respond to stressors. The concept of allostatic load captures the cumulative burden of this physiological wear and tear that can increase the risk of disease, disability, and death.[136]

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Heart disease

Heart disease is a major public health concern as it is the leading cause of death in the U.S.[1] In 2014, 27.6 million adults aged 18 or older were living with Heart disease, representing 11.5% of the adult population.[6] Since Heart disease can encompass various conditions such as high blood pressure, coronary heart disease, heart attack, stroke, heart failure, and angina, there are about 85.6 million American adults who have one or more types of heart disease, and 43.7 million of these are estimated to be aged 60 years or older.[7]

The cost of treating heart disease is also a substantial economic burden in the U. S. In the American Heart Association Statistical Update, it was estimated that the annual direct and indirect cost of cardiovascular disease and stroke in the U.S. was $316.6 billion in 2011-2012 based on data from the Medical Expenditure Panel Survey, National Center for Health Statistics, and Institute for Health and Aging.[7] Of the $316.6 billion, $116.9 billion were spent on adults greater than age 65.[7] Because of the health and economic burdens that occur with heart disease, it remains key condition that the Healthy People 2030 initiative hopes to address with a focus on prevention efforts and proving better treatment options.[149]

Type 2 Diabetes Mellitus

Type 2 diabetes is another growing public health concern in the United States. It is a leading cause of morbidity and was the seventh leading cause of death in 2014.[1] According to the Centers for Disease Control and Prevention (CDC), the number of adults diagnosed with diabetes aged 18 years or older has almost quadrupled from 5.5 million in 1980 to 21.9 million in 2014.[2] Recent data from the CDC's 2010–2012 National Health Interview Survey, 2009–2012 National Health and Nutrition Examination Survey, and 2012 U.S. Census data, estimated that about 1.7 million new diabetes cases were diagnosed in 2012 in adults 21 years or older, with 892,000 of these new cases occurring in adults aged 45-64 and 400,000 of these new cases occurring in adults aged 65 and older.[3]

The cost of treating Type 2 diabetes has also become an economic burden in the U.S. In 2012, it was estimated that $176 billion was spent in direct medical costs from medical goods and services and $69 billion was spent in indirect costs from reduced productivity at work and home, unemployment from chronic disability, lost work days, and even early death.[4] It was also estimated that medical expenses for people with diabetes is, on average, about 2.3 times higher than medical expenses for people without diabetes.[4]

Because of the increasing health and economic burdens that occur with diabetes, this condition remains a priority with the Healthy People 2030 initiative, with the goal of reducing diabetes cases, complications, and deaths.[149]

Cognitive Impairment

Cognitive impairment is a major public health and social issue due to increasingly aging populations around the world. In 2019, Alzheimer's disease and other forms of dementia ranked as the 7th leading cause of death among older adults globally[150], and 6th in the United States (USA).[151] The global prevalence of dementia is approximately 7% amongst individuals aged 65

and above.[152] In the USA, Alzheimer's disease is the most prevalent form of dementia, impacting about 6 million people. This number is projected to increase to 14 million people by 2060.[153] Cognitive decline contributes to diminished quality of life, loss of independence, decreased healthy life expectancy,[154,155] and elevated mortality in old age.[156,157] It is also costly as it leads to institutionalization and increases the need for social and healthcare services among those with impairment and their caregivers, such that a significant proportion of health care resources is spent caring for older people with the condition. [158-160] Cognitive impairment also hinders one's ability to work and play a role in retirement, particularly in the ever changing labor market which increasingly consists of jobs that require cognitive abilities and competence.[161] Conditions associated with cognitive impairment are also a priority for Healthy People 2030, with a focus on improving care and quality of life for people with Alzheimer's and other causes of dementia.[149]

Gaps in the Literature

Race, SES, heath relevant behaviors and toxic stress combine in complex ways to affect health outcomes. [162,163] Existing literature suggests that SES not only confounds the relationship between race and health, but part of the causal pathway that links race to health.[72] Studies have documented significant relationship between race/ ethnicity and SES in health outcomes across the life-course.[84] However, it is important to note that race/ethnicity related differences in health is not entirely explained by between-race differences in SES.[85] Among the implicated determinants include: variations in health relevant behaviors and disease prevention resources,[87] environmental conditions,[47,86] access to[39] and quality of healthcare interventions. [19] Specifically designed studies in nationally representative diverse cohort of Americans are needed to explicate the roles of these multiple, complex, and sometimes subtle relationships.

Stress occurs when the body responds to stimuli that threaten the maintenance of homeostasis, causing bodily or mental tension[90]. The stress response is mediated by both the nervous and endocrine systems[91] and results in increased activity of the sympathetic nervous system and increased secretion of adrenal hormones in response to adverse events.[92,93] The sympathetic nervous system secretes the cytokines, epinephrine and norepinephrine while the adrenal glands release glucocorticoids into the blood stream.[94] The effects of these cytokines and hormones usually include increased respirations, heart rate, blood pressure, and overall oxygen consumption.[95] In most situations, the physiological changes associated with these stressors are designed to be adaptive, temporary and in typical situations the body returns to its baseline state when the stressor is removed. [96] Depending on the nature, duration and severity of stress, physiologic maladaptation may occur particularly with higher frequency and severity of occurrence exceeding the ability of individuals to cope.[92,97]

Furthermore, psychosocial stress can lead to dysregulation of the hypothalamus-pituitary-adrenal (HPA) axis, which is the driver of the stress response, and the subsequent development of diseases such as type 2 diabetes, cardiovascular disease, and other inflammation-related conditions, and, in turn, physical disability. This could serve as an important mechanism driving disparities in physical disability outcomes. However, in order to better address these health disparities, it is necessary to contextualize the occurrence of more downstream risk factors and identify the upstream or "fundamental causes" of these risks and associated negative health outcomes.[123] One particular psychosocial factor that has been established as an indicator of health across a variety of contexts is SES.[162] For example, the stress of financial instability as well as the environmental insults that can result from living in under resourced neighborhoods can cause HPA axis dysregulation. Depending on the chronicity of socioeconomic hardship,

health problems may be exacerbated. Therefore, SES may not only initiate underlying disease through HPA axis dysregulation but may also foster progression or exacerbation of this into physical disability. Research farther suggests that reported stress symptoms such as anxiety, sleep disturbances, and lack of energy are associated with an increased risk for developing ADLs and IADLs.[163] The long-term effects of toxic stressors on age-associated diseases requires further elucidation.[34]

Additionally, studies generally show that stressful events are more frequent among Blacks and other minority groups relative to Whites, but the literature is quite variable.[132] Moreover, with the literature's emphasis on acute life events, the range of stressors examined is limited. With few exceptions most studies of racial differences in stress exposure compare the distribution of stressors among Blacks versus Whites, to the exclusion of Hispanics. This is problematic because Hispanics are now the largest minority population, are disproportionately poor, and experience high levels of stressors related to acculturation, job hazards, poverty, and legalizing their status.[162,164]

Furthermore, most of the earlier studies performed have been cross-sectional and were conducted over a small geographical area e.g., county. This is a longitudinal and utilize a nationally representative sample which is another strength of the study.

Public Health Significance

While the diversity of the American population is one of the country's greatest assets, one of its greatest challenges however is reducing the profound disparity in health outcomes of its racial and ethnic minority, rural, low-income, and other underserved populations. Increasing QOL, neurocognitive function later in life and mobilizing knowledge to eliminate racial

disparities in health disparities are important public health goals directly informed by our research. Policies and interventions that address the macro-level structural contexts – including variations by race within the United States, that shape exposure to a broad range of stressors may offer promising avenues towards improving health for all segments of the population.[60] This dissertation will inform prevention efforts that focus on strategies to decrease exposure to stressors and increase resources to cope with stressors for vulnerable populations.

There's also a need to increase participation by minority populations in clinical and health services research as drivers of disease and other outcomes may differ between populations.

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CHAPTER 3

GENERAL MATERIALS AND METHODS

This chapter provides a general description of the dataset, measures, and statistical analysis plans that used in the three studies of this dissertation. This was a secondary data analysis of participants enrolled in the Health and Retirement Study (HRS).

Design of the Health and Retirement Study

Initiated in 1992, the HRS is a longitudinal panel study representative of the non-institutionalized US population over the age of 50 years old. Data collection includes both age-eligible adults and their spouses/partners, regardless of age. This study was motivated by the need to understand life changes experienced by midlife adults as they entered into retirement and followed throughout old age. Birth cohorts are added every six years. The current HRS study includes the original HRS cohort, the Asset and Health Dynamics among the Oldest-Old (AHEAD), which were merged in 1998; the children of the Depression (CODA) and War Baby (WB) cohorts which were added in 1998, the Early Baby Boomers in 2004, the Mid Baby Boomers (MBB) in 2010, and the Late Baby Boomers in 2016.

By creating a large-scale dataset encompassing multiple aspects of midlife and older adults' lives, researchers across multiple fields could easily access information to address unanswered questions important for policy change. The HRS provides a plethora of demographic, psychosocial, health status, employment and financial information, and biomarker data collected every two years from eligible participants. On average, a total of 20,000

individuals participate in data collection each wave and are followed until death, with average subsequent wave response rates over 90%. The selection of participants represents the scope of diversity of midlife and older US adults and is a strength of the HRS.

HRS Sampling Procedures

The target population of the HRS is all non-institutionalized (at study entry) adults in the contiguous United States who are over the age of 50 years old. The household is the observational unit, which must include at least one age-eligible adult. The HRS utilizes a multi-stage area probability sample design. First, probability of being selected into the study begins with selection of both metropolitan statistical areas (MSAs) and non-MSA counties. Next, these areas of broken down into smaller segments. Then, all housing units within these segments are identified and a pre-specified number of these units are randomly selected from which to obtain individual age-eligible possible participants[1].

One goal of the HRS is to increase research on racial/ethnic minority midlife and older adults, thus improving researchers' ability to assess health disparities and their antecedents. This is achieved through oversampling in some communities. Sampling procedures were created to increase the number of black and Hispanic participants by selecting residential areas comprised of greater than 10% black households. For Hispanics, residential areas with at least 10% being Hispanic households, with households in the West and Southwest US targeted to increase the probability of identifying such areas.

To account for this complex sampling design, weight variables are included in each data file to ensure proper estimates are obtained from statistical analyses and that results are able to be generalized to the overall target population. Without these variables, researchers run the risk of

producing estimate variances that are too small and confidence intervals that are too narrow. Analyses of HRS data should include three variables to adjust for any biased estimates. A stratum variable indicates the sampling unit from the primary stage of participant selection (i.e., MSAs and non-MSAs), and a cluster variable accounts for the second stage of selection. Lastly, a respondent weight variable accounts for the probability of individuals being selected in the sample. As will be discussed in more detail in the following sections, the HRS contains multiple data files. These are the Core Survey measures (FAT files), the Tracker file which includes some demographic information as well as survey weight variables, and the RAND file which contains imputed SES variables.

Data Collection

This dissertation utilized a longitudinal cohort design approach including survey data from the Core Interview (2006, 2008, 2010, 2012, 2014 and 2016 waves), and Leave-Behind Psychosocial Survey (2006, 2008, 2010, 2012, 2014 and 2016 waves). Survey questions asked in the Core Interview are assessed of every participant at each wave, either by telephone or face-to-face interview. However, half the sample was assigned to randomly complete the psychosocial Leave-Behind module in each wave, so if one half completed the module in 2006, the other half did so in 2008.[2] The Leave-Behind questionnaire is self-administered after completion of in-person Core Interviews and participants are asked to mail their completed questionnaires back to HRS staff. The response rate of those face-to-face interview participants who were given the Leave-Behind questionnaire is about 90%. Spanish language versions of all questionnaires are available for participants who are not comfortable with using English to reduce the risk of obtaining misinformation.

Individual data files separated by topic area (e.g., physical health, psychosocial measures) for each wave of data collection are available for download for registered HRS users. The HRS also includes a Tracker file that includes demographic variables for every participant at every wave, including age, gender, race, Hispanic ethnicity, and education. Additionally, sampling weight variables are obtained from this data file. The Tracker file is updated after each wave of data collection. The RAND Center for the Study of Aging created RAND HRS data files in order to increase accessibility to researchers. A significant portion of variables have been compiled across all waves of data with more user-friendly naming schemes since variable names changed across waves for some variables. The RAND files are particularly useful when analyzing variables longitudinally. RAND has also created socioeconomic status variables (e.g., years of schooling, household income) that include imputations for missing data. This is helpful to maintain enough sample size for statistical analyses.

Data Protections and Ethics

Individual data files can be obtained from the HRS website after registering as a user. Most data files are available for public use because personal identifiers are removed from the final data files. Users are given a unique password in order to access all data files from their HRS data account. Participant consent is obtained even in the case of telephone interviews, though written consent is obtained for the collection of blood or saliva for biomarker assays. Approval for the HRS has been obtained from the University of Michigan Institutional Review Board. All data used in this study were de-identified anonymized data, hence ethical review and approval were waived for this study.

Analytic Strategy by Aim

Specific Aim 1: Role of toxic stress and stress resilience in explaining racial / ethnic differences in change in Quality of life (QOL) among US adults with Heart Disease (HD) and/ Type 2 Diabetes (T2DM).

Brief background: The goal of this study was to evaluate the impact of toxic stress/ resilience on disease progression. We modeled self-reported Quality of life (QOL) a surrogate of disease progression. We investigated racial group differences in changes in QOL among a nationally representative sample of middle-aged and older US-born non-Hispanic white, non-Hispanic black and Hispanic adults.

Study design: We used a longitudinal cohort study to address this aim. Longitudinal studies are studies in which the outcome variable is repeatedly measured in the same individual on several different occasions. In longitudinal studies, the observations of one individual over time are not independent of each other, and therefore require special statistical techniques which consider the fact that repeated observations of each individual are correlated.

The main advantage of a longitudinal study is that the individual development of a certain outcome over time can be studied. This makes it a powerful design for assessing incidence, that is, the number of new cases of a condition in a specified time interval. In addition, the individual development of a certain outcome variable can be related to the individual development of other variables. Longitudinal studies are also useful in assessing stability of a given characteristic over time. This is especially important when multiple measurements are taken from an individual over time. However, longitudinal studies are expensive to carry out, time consuming, and difficult to analyze. Analyses were limited to non-Hispanic white, non-Hispanic black, and Hispanic participants. Other racial/ethnic groups were excluded because of small sample sizes.

Inclusion and Exclusion criteria: The analysis included HRS2006 through HRS 2014 waves of data. We excluded any deaths prior to this 2006, prevalent cases of diseases other than HD and T2DM, individuals with age less than 51 at baseline, as wed as well as those with no stress/ resilience measures or QOL measures.

Research questions: We investigated (1) whether there are racial disparities in QOL given presence of HD / T2DM, (2) whether toxic stress/resiliency measures are independent predictors of QOL, and (3) whether toxic stress/resiliency measures modify the relationship between race/ethnicity and QOL in American adults. We hypothesized that there will be racial/ ethnic differences in QOL in aging US adults 65 years and older with prevalent HD/T2DM. We further hypothesized that individuals experiencing higher levels of toxic stress and lower resilience -promoting factors will report lower QOL.

Measures

Main exposures: Race/Ethnicity, Toxic stressors, and Resilience measures

The primary determinants in this study were race/ethnicity, measures of toxic stress and stress resilience. Race categorized as Black, White, or Hispanic was assessed by self-report. Respondents were classified as white or black if they indicated that they considered themselves, respectively, as primarily "white or Caucasian" or "black or African American" and did not report any Hispanic/Latino ethnicity. Individuals were be classified as Hispanic if they reported that they considered themselves to be "Hispanic or Latino."

Several indicators of toxic stress were measured including life-course stressors, recent stress, cumulative stressors, ongoing chronic stressors, experiences of everyday discrimination, major experiences of lifetime discrimination, experiences of chronic work discrimination. Traumatic life events such as , gun violence, death of a child, spouse/child addictions, victim of

abuse, experiences of major fire, or natural disaster) and stressful life events (e.g., long-term unemployment, job loss, home burglarized) were measured as counts of the events respondents reported experiencing (Figure 3.1). Cumulative stressors were a summation of recent and life course stressors.

Perceived everyday discrimination is comprised of six items that are considered to be "character assaults" and tend to occur on a daily basis. Examples include being treated with less courtesy or respect, receiving poorer service at restaurants, not being thought of as smart, being thought of as dangerous, and being threatened or harassed (Figure 3.2).[3] Values of perceived everyday discrimination reflected the sum of Likert scores across the six items, 1 ("almost always") to 6 ("never"). The measures of major lifetime discrimination reflect the sum of major events that respondents reported experiencing. Such events include being unfairly fired or denied a promotion, unfairly treated by the police, or unfairly denied a bank loan (Figure 3.3). Seven events, in total, were considered (range = 0-7) and were deemed "major" events because they tend to interfere with one's socioeconomic mobility, life chances, and well-being.[3] Experiences of chronic work discrimination included six items designed to assess chronic discrimination experienced at work (Figure 3.4), and these were asked in working participants. The variables were scored per guidelines in the psychosocial Leave-Behind module for each domain of stress.

Similarly, we defined resilience across several domains/ indicators such as personal mastery (control), self-efficacy, importance of religion and social support. Personal mastery represents one's perception of his or her ability to achieve goals. The measure includes statements such as "I can do just about anything really set my mind to" and "what happens to me in the future mostly depends on me". Perceived constraints represent one's perception of barriers

that limit the achievement of goals. Items in this measure include statements such as "What happens in my life is often beyond my control" (Figure 3.5).

Outcome: Quality of Life (QOL)

Quality of life (QOL) was measured using two variables namely self-rated health (SRH) and change in self-rated health. ''Self rated health '' is collected with Likert responses to the question: "Would you say your health is excellent, very good, good, fair, or poor?" The second question which assesses change in self-rated health is, "compared with your health when we talked with you in the previous wave, would you say that your health is better now, about the same, or worse?"

Potential confounders: We controlled for several other potential confounders variables including sex, age (in years) education (less than twelve years, twelve years, thirteen to fifteen years, sixteen plus years), retirement status, marital status, lifestyle factors e.g., cigarette smoking, consumption of alcohol, and health factors such as BMI, and presence of comorbid conditions.

Statistical analysis: We implemented descriptive analyses to estimate means (with standard deviation) for continuous variables in the total sample and by race/ethnicity. For categorical variables, chi-square (X^2) tests were used to examine differences by race/ ethnicity. We estimated the percentages of each response of the stress/ resilience measures in the total sample and by race/ ethnicity. Bivariate analyses determined crude associations for each outcome with the predictors, potential confounders, and socio demographic factors. Factors with a p-value < 0.2 were further evaluated in multivariable models as candidate confounders. We examined independent effects of race on self-rated health, as well as any ensuing modifying effects after the addition of stressors. Regression models using generalized estimating equations

(GEEs) controlling for age, gender, SES, multiple chronic conditions, were performed to evaluate racial disparity in the different types of stressors and resilience indicators of interest. The results were presented as odds ratios (ORs) and 95% confidence intervals (CIs). A p-value less than 0.05 was considered statistically significant. All analyses were performed with SAS software, version 9.4 (SAS Institute, Cary, NC). To avoid repetitions, common variables across the three aims are listed only in aim 1.

Specific Aim 2a): To determine the correlates of dementia (diagnosed at any age) in a representative sample of US adults enrolled in the HRS.

Brief background: This was a cross-sectional analysis of participants in the 2014 wave of HRS data. The importance of dementia as a leading cause of death has risen prominently. Yet, dementia is distinctive among the leading causes of death as the only endpoint for which there is a limited understanding of associated risk factors. This is perhaps because dementia is an acquired syndrome, with multiple possible causes, rather than a specific disease itself.

Measures

Main exposures: Toxic stress and resilience

As with aim 1) the primary exposures in this study were race/ethnicity, measures of toxic stress and resilience.

Outcome: Cognitive function

The HRS assesses cognitive function with a 35-point scale that includes: an immediate recall test of 10 words to measure memory. The same words are used in a delayed recall after about 5 minutes of intermediate tasks. The cognitive battery also includes a serial seven subtraction test to measure working memory; a counting backwards test to measure speed of mental processing; an object naming test to measure knowledge and language; and recall of the

date, the president, and the vice-president to measure orientation.[4,5] Respondents are also evaluated on another question asking "how would you rate your memory at the present time? Would you say it is excellent, very good, good, fair or poor?" By HRS design, the cognitive measures were completed when respondents first entered the study, regardless of their age. However, these questions are administered at subsequent waves if the respondents clock 65 years or at older ages.[6] Respondents are farther asked whether they had ever been diagnosed with dementia or memory-related problems. For those who were unable to respond due to physical or cognitive problems, a proxy informant is asked to rate the respondent's memory, judgment, organization of time, in a shorter questionnaire which is also used to assess dementia.

Statistical analysis: We summarized respondent characteristics for the 2014 HRS wave. We implemented descriptive analyses to estimate means (with standard deviation) for continuous variables in the total sample and by race/ethnicity. For categorical variables, X^2 tests were used to examine differences by race/ ethnicity. We estimated the percentages of each response of the stress/ resilience measures in the total sample and by race/ ethnicity. Bivariate analyses were implemented to determine crude associations for each outcome with the predictors, potential confounders, and socio demographic factors. Bivariate associations were used to determine racial differences in the characteristics assessed. Factors with a p-value < 0.2 were further evaluated in multivariable models as candidate confounders.

Specific Aim 2b): To evaluate Toxic stress / resilience as risk factors in neurocognitive decline.

Brief background: Cognitive decline and dementia are a growing social and public health concern among older adults. Alzheimer's disease is the most prevalent form of dementia in the United States, impacting about 6 million people. This number is projected to increase, as

the population of older adults is projected to grow from 13% to 20% by the year 2030 according to the US Census Bureau (2010). Cognitive functioning is a key indicator of overall individual health in aging studies. Together with physical decline, decline in cognitive functioning is an important predictor for loss of independence, institutionalization and death in the older population.[7,8] Cognitive functioning is also likely to impact one's ability to work and play a role in retirement, particularly in the modern labor market which increasingly consists of jobs that require cognitive abilities and competence. The objective of this study was to determine the impact of toxic stress or stress resilience on cognitive functioning in older Americans, and its demographic and socioeconomic predictors, using a nationally representative cohort serially tested for cognitive performance.

Research questions: In this third study, we asked the following research questions; (1) Among Americans without evidence of cognitive impairment in the 2006 wave of HRS, what is the relationship between toxic stress / resiliency and onset of cognitive decline? If so, (2) is the relationship between toxic stress/resiliency and incident cognitive decline modified by race/ethnicity? We hypothesized that individuals with higher levels of toxic stress and low resilience scores will be at higher risk for onset of cognitive decline.

Measures

Main exposures: Toxic stress and resilience

As with aim 1) the primary exposures in this study were measures of toxic stress and resilience.

Outcome: Onset of cognitive decline

The main outcome was onset of cognitive decline due to dementia defined with a new diagnosis of dementia and time to a new diagnosis. Respondents are asked, "Has a doctor ever told you that you have dementia or memory-related problems?" For those who were unable to

respond due to physical or cognitive problems, a proxy informant is asked to rate the respondent's memory, judgment, organization of time, in a shorter questionnaire which is also used to assess dementia.

Statistical analysis: We presented descriptive statistics for each of the cognitive and stress measures. We estimated means (with standard deviation) for continuous variables in the total sample and X^2 tests for categorical variables. Bivariate analyses were implemented to determine crude associations for each outcome with the predictors, potential confounders, and socio demographic factors. Bivariate associations determined racial differences in the characteristics assessed. Factors with a p-value < 0.2 were further evaluated in multivariable models as candidate confounders. Cox proportional hazards models and Kaplan-Meier curves were used for analyzing incidence of cognitive decline in a ten-year period.

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Figures

Figure 3.1. Life course and recent stress events asked in the HRS Psychosocial Questionnaire

Events That Occurred During Life (Life course Stress):
1. Has a child of yours ever died? **2. Have you ever been in a major fire, flood, earthquake, or other natural disaster?**
3. Have you ever fired a weapon in combat or been fired upon in combat?
4. Has your spouse, partner, or child ever been addicted to drugs or alcohol?
5. Were you the victim of a serious physical attack or assault?
6. Did you ever have a life-threatening illness or accident?
7. Did your spouse or a child of yours ever have a life- threatening illness or accident?
8. Before you were 18 years old, did you have to do a year of school over again?
9. Before you were 18 years old, did either of your parents drink or use drugs so often that it caused problems in the family?
10. Before you were 18 years old, were you ever physically abused by either of your parents? **11. Before you were 18 years old, were you ever in trouble with the police?**
Events That Occurred in the Last Five Years (Recent Stress):
1. Have you involuntarily lost a job for reasons other than retirement at any point in the past five years?
2. Have you been unemployed and looking for work for longer than months at some point in the past five years?
3. Was anyone else in your household unemployed and looking for work for longer than 3 months in the past 5 years?
4. Have you moved to a worse residence or neighborhood in the past five years?
5. Were you robbed or did you have your home burglarized in the past five years?
6. Have you been the victim of fraud in the past five years?

Figure 3.2. Questions on everyday discrimination asked in the HRS Psychosocial Questionnaire

Experiences of Everyday Discrimination

In your day-to day life how often have any of the following things happened to you?

1. You are treated with less courtesy and respect than other people.
2. You receive poorer service than other people at restaurants or stores.
3. People act as if they think you are not smart.
4. People act as if they are afraid of you.
5. You are threatened or harassed.
6. You receive poorer service or treatment than other people from doctors or hospitals.

Figure 3.3. Questions on major experiences of lifetime discrimination asked in the HRS Psychosocial Questionnaire

Major experiences of lifetime discrimination

For each of the following events, please indicate whether the event occurred at any point in your life.

If the event did happen, please indicate the year in which it happened most recently.

1. At any time in your life, have you ever been unfairly dismissed from a job?
2. For unfair reasons, have you been hired for a job?
3. Have you ever been unfairly denied a promotion?
4. Have you ever been unfairly prevented from moving into a neighborhood because the landlord or a realtor refused to sell or rent you a house or apartment?
5. Have you ever been unfairly denied a bank loan?
6. Have you ever been unfairly stopped, searched, questioned, physically threatened, or abused by the police?
7. Have you ever been unfairly denied health care or treatment?

Figure 3.4. Questions on chronic work discrimination asked in the HRS Psychosocial Questionnaire

Chronic work discrimination

Here are some situations that can arise at work. Please tell me how often you have experienced them during the LAST 12 months.

1. How often are you unfairly given the tasks at work that no one else wants to do?
2. How often are you watched more closely than others?
3. How often are you bothered by your supervisor or co-workers making slurs or jokes about women or racial or ethnic groups?
4. How often do you feel that you have to work twice as hard as others at work?
5. How often do you feel that you are ignored or not taken seriously by your boss?
6. How often have you been unfairly humiliated in front of others at work?

Figure 3.5. Perceived constraints and Mastery items in the HRS Psychosocial Questionnaire

A. Perceived Constraints

HELPLESS IN DEALING WITH PROBLEM	I often feel helpless in dealing with the problems of life.	*Responses* 1 = STRONGLY DISAGREE 2 = SOMEWHAT DISAGREE 3 = SLIGHTLY DISAGREE 4 = SLIGHTLY AGREE 5 = SOMEWHAT AGREE 6 = STRONGLY AGREE
OTHERS DETERMINE WHAT I CAN/NOT DO	Other people determine most of what I can and cannot do.	
LIFE IS BEYOND MY CONTROL	What happens in my life is often beyond my control.	
LITTLE CONTROL OVER THINGS	I have little control over the things that happen to me.	
NO WAY I CAN SOLVE MY PROBLEMS	There is really no way I can solve the problems I have.	

B. Personal Mastery

DO ANYTHING I SET MY MIND TO	I can do just about anything I really set my mind to.	*Responses* 1 = STRONGLY DISAGREE 2 = SOMEWHAT DISAGREE 3 = SLIGHTLY DISAGREE 4 = SLIGHTLY AGREE 5 = SOMEWHAT AGREE 6 = STRONGLY AGREE
USUALLY FIND A WAY TO SUCCEED	When I really want to do something, I usually find a way to succeed at it.	
GET WHAT I WANT IS IN MY OWN HANDS	Whether or not I am able to get what I want is in my own hands.	
THE FUTURE DEPENDS ON ME	What happens to me in the future mostly depends on me.	
DO THINGS THAT I WANT TO DO	I can do the things that I want to do.	

CHAPTER 4

CHANGE IN QUALITY OF LIFE OVER EIGHT YEARS IN A NATIONALLY REPRESENTATIVE SAMPLE OF US ADULTS WITH HEART DISEASE AND TYPE 2 DIABETES: MINORITY RACE AND TOXIC STRESS AS KEY SOCIAL DETERMINANTS[1]

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[1]Nkwata, A. K., Song, X., Zhang, M., & Ezeamama, A. E. (2020). *BMC public health*, *20*, 1-12. Reprinted here with permission of the publisher.

Abstract

Background: Toxic stress (TS), minority race and their interaction are evaluated as determinants of change in quality of life (QOL) over eight years follow-up in a nationally representative sample of United States (US) adults (≥50 years old) with heart disease (HD) and/or type-2 diabetes (T2DM) diagnosed by 2006 as part of the Health and Retirement Study (HRS).

Methods: Recent and life-course stress plus experiences of lifetime discrimination were measured every two years using the stressful life experiences questionnaire. QOL was assessed by participant self-rated health (SRH) and operationally defined as improved, unchanged, or declined in current year versus two years prior. Repeated measures multinomial logistic regression using generalized estimating equations (GEEs) was implemented to estimate race-, TS and their interaction- related odds of worse SRH from 2006-2014. Odds ratios (OR) and 95% confidence intervals (CIs) were calculated with adjustment for time, age, sex, and socio-economic status.

Results: 3,904 adults with HD/T2DM, mean age 71.1±9.3 years old, 80.9%, 14.7% and 4.4% that respectively self-identified as Caucasian, African-American and Other race, were included. Over the eight-year follow-up, the odds of worse SRH for African-American and Other race were respectively 1.46 (95% CI: 1.25–1.70) and 1.43 (95% CI: 1.10–1.86) times higher relative to Caucasians. Relative to older Americans that reported ≥2 lifetime discrimination events, the odds of poor SRH was respectively 33% (OR=0.67, 95% CI: 0.50–0.89) and 17% (OR=0.83, 95% CI: 0.59–1.17) lower for those that reported none vs one lifetime discrimination experience. Furthermore, the relationship of life-course stress to SRH decline over eight years varied by race (time*stress*race, p=0.1173). Specifically, increasing life-course stress predicted

worse QOL among Caucasians (p=0.0063) and among African-American (p=0.0820) but not among Other race (p=0.9943).

Conclusion: Toxic stress and minority race are social determinants of deterioration in QOL among older Americans with chronic diseases (HD/T2DM). The types and prevalence of toxic stressors varied by race/ethnicity. Policy interventions to address root causes of TS while targeted at proximate drivers of TS by race/ethnicity represent a viable strategy for mitigating racial disparities in overall wellbeing and improving QOL in all aging Americans regardless of race.

Keywords: Toxic stress, Minority race, Quality of Life, Older Americans, Health disparities

Background

The population of adults at least 65 years old is steadily growing in the United States (US) and around the world.[1,2] As of 2015 in the US, an estimated 15% (45.1 million) Americans were at least 65 years old. By the year 2050, nearly one in four Americans (approximately 83.7 million) will be at least 65 years old [1,3] – a demographic shift expected to result in considerable burden for public health systems, medical and social services, and family caregiving demands.[4,5] Chronic disease prevalence and incidence – including joint diagnoses with multiple chronic conditions, are expected to rise with cancers, diabetes and heart diseases driving health care consumption and associated costs.[6] Chronic diseases lower the quality of life (QOL) for older adults and are leading drivers of disability and death in the US and around the world.[7,8] Although the overall life-expectancy is increasing in all racial groups, notable racial disparity in life expectancy persists among US adults. [9] Furthermore, increase in life-expectancy is not accompanied by corresponding increase in years of life lived without a major health condition or healthy life expectancy (HLE) in all racial groups.[10,11] Hence, the US National Institutes of Aging (NIA) is encouraging scientific research on understanding modifiable determinants of reduction in HLE among older Americans.[12] Additionally, elimination of racial disparities in health remains an important public health challenge and a top priority of the Healthy People 2020 program of the U.S. Department of Health and Human Services. Empirically informed progress towards mitigating racial disparities in the US requires an understanding of the etiologic relevance of modifiable social determinants such as psychosocial stress .[13]

Well established mechanisms and theoretical frameworks, including the Stress Process Model (SPM) [14,15] link psychosocial stress - i.e., poverty, discrimination, racism, neglect, child abuse among other socially determined factors typically beyond the control of individuals - to

adverse physical health outcomes in human populations.[15,16] These psychosocial stressors, when prolonged and combined with limited adaptive coping at the individual level, constitute toxic stress (TS).[17] The nature of TS may evolve over the life-course [18] and manifest as negative emotional disorders like depression and anxiety, anger or hostility and external stressors resulting from repeated exposure to stressful conditions.[19] A hallmark manifestation of TS is induction of abnormal physiological responses leading to the body's failure to fully recover from physiologic and psychosocial adversities.[20] An understanding of the contribution of TS to accelerated QOL decline in older Americans with recently diagnosed chronic disease remains unknown. This research includes adults with type 2 diabetes mellitus (T2DM) and heart disease (HD) because these chronic conditions are among the leading causes of mortality among older adults in the US.[21] These middle age and older Americans with metabolic chronic disease represent a sensitive sub-group to investigate the health impact of psychosocial stress.

This research was further grounded in the stress process framework. Briefly, the SPM outlines three hypotheses: (a) social context shapes exposure to stressors and access to available coping resources, (b) stressors in turn negatively affect health, and (c) social and personal resources positively influence health, both directly and indirectly, by reducing the negative effects of toxic stress experiences in populations.[22] The extent to which SPM model adequately captures the psychosocial mechanisms underlying health among different racial groups in particular remains unclear because investigations in multi-ethnic US samples have been rare. A common limitation of this literature has been the implicit, tenuous assumption that relationships between psychosocial factors and health are similar across social groups.[23,24] Such an assumption does not take into account the drastic differences in experiences and social realities faced by those located at varying intersections of race and gender hierarchies.[25] To address this limitation,

we examined psychosocial stress in a multi-ethnic sample and conducted additional analyses within strata of racial groups to understand possible variations in toxic stress and relationship with wellbeing.

This longitudinal analysis used nationally representative US data from the Health and Retirement Study (HRS) during 2006 to 2014 and was designed to assess the relationship of psychosocial determinants measured at baseline (various domains of TS) to worsening SRH over 8 years among the insured older (i.e. 50+ years) US adults with recent diagnoses of either Type 2 Diabetes Mellitus (T2DM) or Heart Disease (HD). We hypothesized that there would be racial differences in QOL declines and that individuals experiencing higher levels of TS will have lower QOL over 8 years. Hence variations in deterioration of wellbeing during follow-up were examined with race and toxic stress as primary determinants. Specific additional analyses investigated interactions between race and TS in relationship to QOL change.

Methods

Study Population

This was a prospective cohort study from a nationally representative sample of older Americans followed as part of the Health and Retirement Study (HRS) from 2006 to 2014. Details on the HRS design and implementation have been extensively described elsewhere.[26,27] For the purposes of this analysis, our sample included insured adults at least 50 years old in the year 2006 who were diagnosed with T2DM and/or HD no earlier than the year 2004 and with available data on QOL and TS measures. We excluded uninsured persons, all diagnoses of HD/T2DM prior to HRS 2000, individuals <50 years old and those lacking TS or QOL measures. Exclusion of persons without health insurance was deemed necessary, because health outcomes, TS and access to health services were likely to be fundamentally different in this sub-

group. Participants were interviewed every 2 years and asked about physical health and functioning, cognitive functioning, health insurance, health care expenses, employment, and financial information such as income, assets, and pension plans. [26,27] Our analysis period is restricted to 2006 through 2014 as psychosocial Leave-Behind questionnaires from which TS measures are determined were first administered in 2006.[28]

Measures

Primary Determinants: Race/ethnicity and Toxic Stress

Race/ethnicity was self-reported and categorized as non-Hispanic Black/African American (AA), non-Hispanic White/ Caucasian (White) or Other race, i.e., Hispanic or Latino [26,27]. Toxic stress (TS) was assessed across several domains and included: recent stressors, life-course stressors, and experiences of racial discrimination.[28] Life-course stressors were determined per response to 11 questions that capture stressful life events at any point in a respondent's life time, including loss of a child, being in a major fire, flood, earthquake, or other natural disaster, life threatening illness or major accident.[28] Recent stressors are six items that capture major stressful life events that occurred in the last 5 years namely involuntary job loss, prolonged unemployment, being robbed or burglarized, moved to a worse neighborhood, or being a victim of fraud.[28] Cumulative stress is a summation of recent stressors and life-course stressors.

Experiences of discrimination were also evaluated as a dimension of toxic stress, and these included questions asked on experiences of everyday discrimination, major experiences of lifetime discrimination and experiences of chronic work discrimination. Measures of everyday discrimination are six questions designed to tap into the hassles and chronic stress associated with perceived everyday discrimination. Major experiences of lifetime discrimination are seven

questions that capture major experiences of unfair treatment at any point in one's lifetime. Experiences of chronic work discrimination are designed to assess chronic discrimination experienced at work. These questions are only asked of respondents who are currently working and are not required for those study participants that are retired. In this set of measures, participants are asked to rate how often some stressful experiences/ situations arose at work during the last 12 months.[28]

We analyzed each type of stress as a continuous variable where scores ranged from a minimum of zero to a theoretic maximum of 17 for cumulative stressors, 0–11 for life-course stress, and 0–6 for recent stress. For experiences of discrimination, the theoretic score ranged from 0-6 for measures of everyday discrimination, 0-7 for major experiences of lifetime discrimination, and 0-6 for experiences of chronic work discrimination.

We also analyzed each type of stress as categories based on the distribution of stress events. Cumulative stress categories and life-course stress categories included zero events (reference), one, two, and three or more events. Recent stress categories included zero events (reference), one, and two or more events. Similarly, measures of everyday, chronic work, and lifetime discrimination each included categories for zero events (reference), one, and two or more events.

Outcome Measure: Quality of Life (QOL)

QOL was defined per self-rated health (SRH) and self-reported in response to the question, "How would you rate your current health? Five Likert scale response options ranged from: excellent (highest), very good, good, fair, to poor (lowest). For analytic purposes, three ordinal QOL levels were defined as: poor (poor/fair), good, or excellent (i.e. very good or excellent) SRH.

Covariates

Age was assessed by self-reported date of birth and modeled categorically in 5-year increments. Other covariates were biological sex, self-reported years of education completed, marital status and behavioral risk factors such as BMI, smoking status, and current alcohol use.

Data Analysis

We implemented descriptive analyses to estimate means (with standard deviation) for continuous variables in the total sample and by race/ethnicity. For categorical variables, T – and X^2 tests were used to examine differences by race/ ethnicity. We estimated percentages of each response of the stress measures in the total sample and by race/ ethnicity. Bivariate analyses were additionally performed to determine crude associations for each outcome with the predictors, potential confounders, and socio-demographic factors. Bivariate associations were used to determine racial differences in the characteristics assessed. Factors with a p-value < 0.2 were further evaluated in multivariable models as candidate confounders.

To determine race-related and psychosocial status-related differences (and 95% confidence intervals) in SRH declines, we implemented repeated measures analyses for multinomial responses using generalized estimating equations (GEEs) controlling for age, sex, social economic status, marital status, BMI, smoking status, and alcohol use at baseline. To accommodate correlation between repeated measures within respondents, we assumed an independent working correlation structure and modeled the odds of declining SRH (poor to good to excellent). Thus, the odds of QOL decline were determined in relation to baseline psychosocial predictors. Time was included as a class variable with values ranging from 1, 2, 3 and 4 representing study years 2008, 2010, 2012, and 2014 respectively. A set of unadjusted

regression models were built to quantify independent effects of race (regression model included race, time, and their interaction) and TS (regression models included TS, time, and their interaction) on four measures of QOL per respondent between 2008 and 2014. In addition to TS, race and their interactions with one another, the baseline levels of the following confounders established considering the literature and bivariate analyses were adjusted for in multivariable models: age, sex, education, and marital status. Other extraneous factors adjusted for in the models included BMI, cigarette use and alcohol consumption. Odds ratios (ORs) and 95% confidence intervals (CIs) calculated from multivariable models at alpha = 0.05. P-values for interaction effects were set at $p < 0.10$ because the power of statistical tests for higher order terms is generally lower than for first-order terms.[29,30] All analyses were performed with SAS software, version 9.4 (SAS Institute, Cary, NC).

Results

Baseline characteristics

A total of 6,296 individuals with HD, T2DM or both conditions were identified for inclusion in the study at baseline**.** The baseline combined two waves of data (HRS 2006 and HRS 2008) because psychosocial questionnaires were randomly administered to half the sample in each wave. For instance, a participant who received the Psychosocial leave behind (PLB) questionnaire in 2006, had a second administration of the questionnaire in 2010, while a participant who received it in 2008, was scheduled again in 2012. Of these 103 (1.6%) were excluded with a diabetes diagnosis prior to the year 2000, 58 (0.9%) were younger than 50 years old, 675 (10.7%) lacked health insurance information, 1,324 (21%) lacked stress data at baseline and 232 (3.6%) had no data on outcome measures. 3,904 (65.7%) unique individuals with recent T2DM, HD or both chronic conditions were identified for analysis in the study (Figure 4.1).

Their baseline demographic characteristics by race are listed in Table 1. In brief, 3,159 (80.9%) participants were Caucasian, 574 (14.7%) were African American, and 171 (04.4%) were classified as Other race. Overall, the mean (SD) age of the participants was 70.9 (±9.3) years old, 2,009 (51%) were females, 2,469 (63%) were married, 1,934 (49.6%) were diabetic, 2,525 (64.7%) had a diagnosis of heart disease (HD). However, Caucasians were on average 3 and 5 years older than African Americans and Other race: 71.6 (±9.1) vs 68.6 (±8.7) and 66.6 (±9.2) years, respectively.

Overall median recent stressors were 0 (IQR: 0,0), life-course stressors 2 (IQR: 1.0, 3.0), cumulative stressors 2.0 (IQR: 1.0, 3.0), experiences of daily discrimination 1 (IQR: 0,1) major experiences of lifetime discrimination 0 (IQR: 0, 1) and experiences of chronic work discrimination 0 (IQR: 0,0).

Additional baseline characteristics are reported in Supplementary Tables 4.1-4.5 showing the distributions of toxic stress questions at baseline by race for each domain of toxic stress assessed.

Association of race on change in QOL

Race-ethnicity was an independent, strong, and time-invariant determinant of change in SRH in this sample after adjusting for the following covariates at baseline, education, sex, age, BMI, smoking status, alcohol use and marital status. Specifically, African Americans and Other race had 46% (OR 1.46, 95% CI: 1.25, 1.70) and 43% (OR 1.43, 95% CI: 1.10, 1.86) higher odds of poorer SRH respectively relative to older Caucasian Americans. The association between race/ethnicity and patient reported SRH change was stable over 8 years of follow-up (time*race, p=0.6575), thus time-averaged associations are provided. SRH change over time was similar in African Americans and Other race (Table 4.2).

Association of toxic stress domains on SRH declines

Major experiences of lifetime discrimination were strongly associated with higher odds for SRH change over time (p=0.095). Regardless of time interval, having none vs two or more major experiences of lifetime discrimination was associated with 33% lower odds of poorer SRH (OR 0.67, 95% CI: 0.50, 0.89). Similarly, having one vs two or more major experiences of lifetime discrimination was associated with 17% lower odds of SRH change, although this was not statistically significant (OR 0.83, 95% CI: 0.60, 1.17). A dose-dependent decrease in likelihood of poorer SRH was observed. Experiences of everyday and chronic work discrimination were not associated with poorer SRH (Table 4.2).

Recent stress-related changes in SRH over 8 years follow-up varied by race (race*time*stress, p=0.0809). Among older Caucasians, the association between recent stress and poorer SRH did not vary over time (time*stress, p=0.1286) and there was no significant association between experiences of none or one vs. two recent stressors in any study interval. Among older African Americans, however, the association between having none or one vs two or more recent stressors strengthened over time (and marginally significant in 2012) to become more protective for SRH declines (time*stress, p=0.033). Among older Americans of Other race, there was no significant association between having none or one vs two or more recent stressors on SRH declines over time (time*stress, p=0.5895) (Table 4.3).

Life-course stress-related changes in SRH varied over time and by race (time*stress*race, p=0.1173). The protective association between having none or one or two vs three or more life-course stressors and SRH declines strengthened over time becoming significant at study end across all dose-dependent categories (time *stress, p=0.1227). Amongst older Caucasians, life-course stressors were associated with decreased odds of SRH change over time (p=0.0063). The

protective association of having none or one or two vs three or more life-course stressors on SRH change was significant at baseline and stayed stable throughout the study period (time*stress, p=0.6654). Among older African Americans, the association between life-course stressors and change in SRH did not vary over time (time*stress, p=0.3159). However, the protective association of none vs three or more life-course stressors grew over time becoming significant at two study intervals during follow up. Among older Americans of Other race, the association between having none or one or two vs three or more life-course stressors strengthened over time to become more protective for SRH declines by study end (time*stress, p=0.0204) (Table 4.3).

Cumulative stress related declines in SRH varied over time and by race (time*stress*race, p=0.0282). The protective association of having none or one or two vs three or more life-course stressors on SRH declines increased over time and was strongest at the end of study. Amongst older Caucasians, cumulative stressors were associated with decreased odds of SRH declines over time (p=0.0091). The protective association of having none or one or two vs three or more cumulative stressors on SRH declines was significant at baseline and stayed stable throughout the study period.

Among older African Americans, the association between cumulative stressors and poorer SRH did not vary over time (time*stress, p=0.1424). However, the association between the experience of none or one vs three or more cumulative stressors strengthened over time becoming significant at two study intervals during follow up. Among older Americans of Other race, the association between having none or one or two vs three or more cumulative stressors varied over time (time*stress, p=0.0973). Of note, having one vs three cumulative stressors was associated with 193% higher odds for SRH declines in the second time interval (OR: 2.93, 95%CI: 1.22, 7.08) (Table 4.3).

Discussion

In this representative sample of vulnerable older Americans of average age 71+ years and with comorbid T2DM and/or HD at enrollment, SRH declined significantly as a function of aging and existing morbidity over the eight-year follow-up. Furthermore, we evaluated the heterogeneous impact of cumulative toxic stress by race/ ethnicity- a novel feature. In line with our hypothesis, higher TS predicted faster QOL decline in Whites and African Americans. Above and beyond the expected impact of time and comorbid disease, race, and TS-dependent differences in SRH declines were evident after adjusting for education, sex, age, BMI, smoking status, alcohol use and marital status. In line with our hypothesis, increasing numbers of life-course stressors, cumulative stressors, and major experiences of lifetime discrimination were associated with poorer SRH over time. These findings were consistent with prior research which showed increasing levels of TS to be a strong predictor of incident T2DM.[31] Our study, however, further showed that among persons with HD and T2DM, higher TS levels is associated with more rapid QOL decline. Experiences of every day discrimination were marginally predictive of poorer SRH. Recent stressors, experiences of chronic work discrimination, however, were not associated with change in SRH.

We also found higher odds of QOL decline for minority races vs. Caucasian Americans. These findings corroborate those from another study that explored how acculturation characteristics, social class, marital status, and chronic illness mediate or moderate differences in non-specific psychological distress for eight racial/ethnic populations in the US. The authors found that non-White populations had variable baseline differences in psychological distress compared to Whites; however, this variation was not connected to health outcomes, a gap that our study informs.[32] Our findings also corroborate those by Ste4rnthal and colleagues, who

found a higher prevalence and greater clustering of high stress scores in African Americans than in Caucasians. They also found comparable stress scores between American-born and African Americans, and similar scores between foreign-born Hispanics and Caucasians. In their study, multiple stressors were associated with poor physical and mental health outcomes.[33]

With regards to the effect of stressors on health, our findings are consistent with extant literature on racial disparities in health outcomes in the US.[34,35] Of note, literature on stress exposure has typically focused on acute life events, thus limiting the range of stressors examined.[36,37] Furthermore, with a few exceptions, most studies on racial differences in stress exposure compare distributions of stressors among Blacks versus Whites, to the exclusion of Hispanics. This is problematic because Hispanics who are now the largest minority population, are over represented in the lower socioeconomic stratum, and experience high levels of stressors related to acculturation, job hazards, poverty, and legal residency/citizenship status.[38,39] In addition, results from past research on race-related variations in stress domains have been variable. [24] Majority of past research that compared levels of distress between African Americans and Caucasian Americans found similar levels of psychological distress between the two groups.[40-42] The finding in this sample that overall levels of toxic stress is similar across racial groups is consistent with these prior reports. [40,41]

However, the potential heterogeneity by race in types of stressors and their adverse health effects on health within older US adults as implemented herein is novel. For example, regardless of race, high lifetime discrimination was associated with lower QOL, but participant-reported experience of any or multiple experiences of lifetime discrimination was highest among African Americans, followed by Other race and lowest in Caucasian Americans. This finding is consistent with prior reports linking the experience of discrimination with negative health effects

and poor work-place productivity.[43-46] Relative to Caucasian Americans, individuals of minority race are more likely to live in neighborhoods with concentrated disadvantages – a factor that partly explains the higher prevalence of stress exposure among African Americans and Hispanics relative to Caucasians.[47] Due to segregation, the conditions under which African Americans and Hispanics live are far worse than those of the rest of the population. For those residing in areas of concentrated disadvantage, with poor physical and social conditions such as extreme poverty and unemployment, pollution, deteriorating housing and violence, multiple stressful encounters may be the norm.[33,37] Also, minorities have for a long time been socially and economically deprived, exposed to toxic substances and hazardous working conditions, experienced more physical and mental trauma, unequal law enforcement and protection via the court system, lived in areas with food deserts, and limited access to adequate medical care among other things.[48] Addressing these and other extenuating factors would improve QOL among African Americans. Data from our study suggests benefits of policy interventions that reduce TS psychosocial stress among African Americans could result in long-lasting progressively protective effects over time. Of note, we specifically evaluated whether our study results were consistent with the intersectionality theory of race/stress effects on QOL – i.e. that inequities in QOL by race were mediated by experiences through discrimination and psychosocial stress.[49] This theory was not confirmed as our results show that minority race/ethnicity was a stable time-invariant predictor of worse QOL over eight years of follow-up. Higher levels of psychosocial stress were an independent determinant of wellbeing regardless of race. However, the salient indicator of psychosocial stress in relationship to change in QOL varied across racial groups (Supplementary Table 4.6).

Although subjective self-reported exposure (toxic stressors) and outcome (SRH) measures are the gold standard for these assessments, patient-reported measures are inherently variable and thus a limitation of this research. Specific elements of design including collection of these data using standardized and validated questionnaires, with known psychometric properties assure that these subjective measures are consistently quantified in the study base. Further, toxic stress scores have been defined as the sum of equally weighted individual questions which assumes that all stressful events have the same weight for the individual. This assumption may over-simplify more complicated phenomena; however, our empirical goal was to analyze cumulative stress within the ACES (adverse childhood experiences) framework and relate these to health outcomes. Because stress perception is self -reported and ultimately subjective relative to the individual, the negative valence of any one factor is unlikely to be the same across our entire sample. Hence, we considered equal weighting of factors to be a reasonable strategy for quantifying cumulative stress and this is approach has precedence in previous reports by our research group and others.[31,50,51]

This study features key strengths that should increase confidence in the reported findings. Specifically, we implemented a large prospective cohort study of older Americans with metabolic chronic disease where each participant had four repeated measures over eight years of follow-up. Hence, our design permitted evaluation of change in QOL in relation to toxic stress measures and we employed rigorous analytic techniques that controlled for several potential confounding factors. Lastly, we studied toxic stressors holistically by evaluating them across several dimensions; recent, life-course stressors and experiences of racial discrimination and thus substantially contribute to an understanding of the potentially modifiable role of various forms of toxic stress on change in QOL in a diverse sample of older Americans.

Conclusion

The present study evaluated TS and minority race as determinants of quality of life (QOL) decline in a nationally representative sample of ≥50 years old United States (US) adults with heart disease (HD) and/or type-2 diabetes (T2DM). Among older Americans with HD and T2DM, minority race and higher TS levels are social determinants of decline in wellbeing. Our findings are important given that we live in a race-conscious society in which racism still abounds on multiple levels, including institutionalized, personally mediated, and internalized, each of which can have negative impacts on health.[52] Our results provide empirical evidence that social, economic and health policies that address structural inequities in social experiences that shape exposure to a broad range of environmental stressors are likely to translate to improved wellbeing in a broad section of older US adults.[33] For example, social policies may be targeted accordingly to reduce community level TS known to vary along racial lines in the US such as: experiences with law enforcement with expected onward benefit for reducing race-related disparities in wellbeing observed in this representative sample of US adults.

Abbreviations

TS: Toxic Stress; QOL: Quality of Life; US: United States of America; HD: Heart Diseases; T2DM: Type 2 Diabetes Mellitus; HRS: Health and Retirement Study; AA: African American; NIA: National Institutes of Aging; SSA: Social Security Administration; HLE: Healthy Life Expectancy; SRH: Self-rated Health; SPM: Stress Process Model

Declarations

Ethics approval and consent to participate: This was a secondary data analysis on anonymized data; hence, informed consent was waived. The HRS is conducted under the University of Michigan and sponsored by the National Institute on Aging and the Social Security

Administration. The study has been approved by the University of Michigan Institutional Review Board.

Consent for publication: Not applicable.

Competing Interests: The authors declare that they have no competing interests.

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Availability of data and materials: The data that support the findings of this study are publicly available as HRS public release data files which can be accessed at https://hrs.isr.umich.edu/data-products/access-to-public-data.

Author Contributions: AKN and AEE conceived the study concept and design. AKN analyzed, interpreted data, and wrote the manuscript and revisions. XS, MZ and AEE contributed to data interpretation, manuscript critique and revision for intellectually important content. All authors reviewed drafts of the manuscript, provided suggestions for refinement, and were involved in the final approval of the version for peer-review.

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Tables and Figures

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Table 4.1: Socio-demographic characteristics of study participants, by race at baseline					
	All Races (N=3904)	**White (N=3159)**	**Black (A/A) (N=574)**	**Other (N=171)**	
Characteristic	**N (%)**	**N (%)**	**N (%)**	**N (%)**	**p-value**
Age mean (SD)	70.9 (9.3)	71.6 (9.1)	68.6 (8.7)	66.5 (9.2)	< 0.0001
Female sex	2009 (51.5)	1548 (49.0)	373 (65.0)	88 (51.5)	< 0.0001
Marital Status					
Married/ partnered	2469 (63.2)	2086 (66.0)	278 (48.4)	105 (61.4)	<0.0001
Separated/Divorced	442 (11.3)	312 (09.9)	109 (19.0)	21 (12.3)	
Widowed	904 (23.2)	701 (22.2)	164 (28.6)	39 (22.8)	
Never married	89 (02.3)	60 (01.9)	23 (04.0)	06 (03.5)	
Education					
Less than High School/GED	1150 (29.5)	831 (26.3)	243 (42.3)	76 (44.4)	<0.0001
High-school graduate	1247 (31.9)	1052 (33.3)	166 (28.9)	29 (17.0)	
Some college and above	1507 (38.6)	1276 (40.4)	165 (27.8)	66 (38.6)	
Disease conditions					
Diabetes	1934 (49.6)	1440 (45.6)	387 (67.4)	107 (62.6)	< 0.0001
Heart Disease	2525 (64.7)	2155 (68.2)	286 (49.8)	84 (49.1)	<0.0001
Diabetes & Heart Disease	649 (16.9)	516 (16.6)	108 (19.2)	25 (15.4)	0.001
Behavioral factors					
Ever smoked	2363 (60.9)	1925 (61.3)	341 (60.0)	97 (57.4)	0.5366
Current alcohol use	1773 (45.4)	1540 (48.8)	175 (30.5)	58 (33.9)	<0.0001
Life-course stressors					
0 events	734 (19.2)	567 (18.3)	129 (23.3)	38 (23.0)	0.0524
1 event	1041 (27.2)	857 (27.6)	144 (26.0)	40 (24.2)	
2 events	888 (23.2)	737 (23.8)	121 (21.8)	30 (18.2)	
3+ events	1157 (30.3)	940 (30.3)	160 (28.9)	57 (34.6)	
Recent stressors					
0 events	3209 (82.2)	2641 (83.6)	443 (77.2)	125 (73.1)	<0. 0001
1 event	533 (13.7)	398 (12.6)	105 (18.3)	30 (17.5)	
2+ events	162 (04.1)	120 (03.8)	26 (04.5)	16 (09.4)	
Cumulative stressors					
0 events	662 (17.3)	518 (16.7)	111 (20.0)	33 (20.0)	0.2315
1 event	937 (24.5)	769 (24.8)	133 (24.0)	35 (21.2)	
2 events	878 (23.0)	731 (23.6)	115 (20.8)	32 (19.4)	
3+ events	1343 (35.1)	1083 (34.9)	195 (35.2)	65 (39.4)	
Lifetime Discrimination					

0 events	2694 (70.0)	2236 (71.6)	348 (62.0)	110 (65.1)	< 0.0001
1 event	689 (17.9)	559 (17.9)	94 (16.8)	36 (21.3)	
2+ events	468 (12.1)	326 (10.5)	119 (21.2)	23 (13.6)	
Everyday Discrimination					
0 events	1742 (45.0)	1429 (45.6)	238 (41.9)	75 (44.4)	0.2252
1 event	1133 (29.3)	914 (29.2)	164 (28.9)	55 (32.5)	
2+ events	994 (25.7)	789 (25.2)	166 (29.2)	39 (23.1)	
Chronic work Discrimination					
0 events	764 (84.9)	600 (85.7)	119 (81.5)	45 (83.3)	0.4782
1+ events	136 (15.1)	100 (14.3)	27 (18.5)	09 (16.7)	
Self-rated health					
Excellent	865 (22.2)	758 (24.0)	81 (14.1)	26 (15.2)	<0.0001
Good	1384 (35.4)	1161 (36.8)	171 (29.8)	52 (30.4)	
Poor	1653 (42.4)	1238 (39.2)	322 (56.1)	93 (54.4)	

Table 4.2: Time-averaged effects of baseline toxic stressors on SRH-declines reported by HRS study participants over the eight-year follow-up.

		Odds Ratio (95% CI)	**p-Value Race**	**p-Value T*Race**
Race	Black/AA vs White/Caucasian	**1.46 (1.25, 1.70)**	< 0.0001	0.6575
	Other vs White/Caucasian	**1.43 (1.10, 1.86)**		
	Black/AA vs Other	1.02 (0.76, 1.37)		
Toxic stressor types	**Intensity of stressor**		**p-Value Stress**	**p-Value T*Stress**
Everyday Discrimination	0 vs 2+ Day discrimination	0.92 (0.71, 1.18)	0.8484	0.1960
	1 vs 2+ Day discrimination	0.95 (0.73, 1.25)		
Lifetime Discrimination	0 vs 2+ Lifetime discrimination	**0.67 (0.50, 0.89)**	0.0111	0.0950
	1 vs 2+ Lifetime discrimination	0.83 (0.59, 1.17)		
Chronic work discrimination	0 vs 1+ Work discrimination	0.95(0.51, 1.78)	0.8948	0.4059

*Notes: CI=confidence interval. Odds ratios in bold are statistically significant. Models adjusted for race, age, sex, education, marital status, BMI, cigarette use, alcohol consumption and interaction terms for race*time, stress*time as well as three -way terms for race*stress*time.*

Table 4.3: Toxic stressors as a determinant of Decline in Self-Rated Health (QOL) over 8 years in the Overall Sample and Within Race/Ethnicity Stratum								
		2008	**2010**	**2012**	**2014**	**Stress**	**Time*Stress**	**Race*Time*Stress**
Toxic Stress Domain		**Odds Ratio (95% CI)**	**Odds Ratio (95% CI)**	**Odds Ratio (95% CI)**	**Odds Ratio (95% CI)**	**P-value**	**P-value**	**P-value**
Recent Stressors	**Entire Sample Regardless of Race**							
	0 vs 2+ Recent stressors	1.04 (0.68, 1.60)	1.08 (0.67, 1.74)	0.74 (0.44, 1.26)	0.68 (0.37, 1.23)	0.7799	0.359	**0.0809**
	1 vs 2+ Recent stressors	1.14 (0.70, 1.88)	0.99 (0.57, 1.73)	0.66 (0.37, 1.18)	0.73 (0.37, 1.42)			
	Among Older White Americans							
	0 vs 2+ Recent stressors	0.76 (0.53, 1.09)	0.94 (0.65, 1.35)	1.03 (0.70, 1.53)	0.95 (0.63, 1.43)	0.5461	0.1286	n/a
	1 vs 2+ Recent stressors	0.97 (0.66, 1.43)	0.99 (0.66, 1.49)	1.01 (0.65, 1.56)	1.07 (0.67, 1.69)			
	Among Older African Americans							
	0 vs 2+ Recent stressors	1.11 (0.51, 2.42)	0.87 (0.36, 2.08)	**0.38 (0.15, 0.99)**	0.42 (0.14, 1.23)	0.4727	**0.033**	n/a
	1 vs 2+ Recent stressors	0.77 (0.34, 1.79)	0.79 (0.31, 2.02)	0.40 (0.15, 1.10)	0.56 (0.18, 1.77)			
	Among Older Other race							
	0 vs 2+ Recent stressors	1.34 (0.51, 3.51)	1.55 (0.52, 4.57)	1.02 (0.30, 3.49)	0.81 (0.21, 3.16)	0.6733	0.5895	n/a
	1 vs 2+ Recent stressors	2.00 (062, 6.43)	1.26 (0.34, 4.65)	0.70 (0.18, 2.82)	0.64 (0.13, 3.11)			
Life-course stressors	**Entire Sample Regardless of Race**							
	0 vs 3+ life-course stressors	0.81 (0.59, 1.12)	0.79 (0.55 1.12)	0.77 (0.53, 1.12)	**0.62 (0.42, 0.92)**	0.1863	**0.1227**	**0.1173**
	1 vs 3+ life-course stressors	**0.67 (0.49, 0.92)**	0.97 (0.69, 1.35)	0.94 (0.67, 1.32)	**0.69 (0.48, 0.99)**			
	2 vs 3+ life-course stressors	0.87 (0.62, 1.22)	0.95 (0.67, 1.36)	0.84 (0.57, 1.19)	**0.63 (0.42, 0.95)**			
	Among Older White Americans							
	0 vs 3+ life-course stressors	**0.76 (0.62, 0.92)**	**0.78 (0.64, 0.97)**	**0.73 (0.58, 0.91)**	0.86 (0.68, 1.10)	**0.0063**	0.6654	n/a
	1 vs 3+ life-course stressors	**0.72 (0.61, 0.87)**	**0.79 (0.66, 0.96)**	**0.71 (0.58, 0.87)**	0.85 (0.68, 1.09)			
	2 vs 3+ life-course stressors	**0.80 (0.66, 0.96)**	0.92 (0.76, 1.12)	0.86 (0.69, 1.07)	0.98 (0.78, 1.24)			
	Among Older African Americans							
	0 vs 3+ life-course stressors	0.88 (0.56, 1.42)	0.69 (0.43, 1.12)	**0.48 (0.29, 0.79)**	**0.47 (0.27, 0.83)**	0.0828	0.3159	n/a
	1 vs 3+ life-course stressors	0.75 (0.46, 1.20)	0.72 (0.45, 1.15)	0.73 (0.44, 1.20)	0.59 (0.33, 1.04)			

	2 vs 3+ life-course stressors	0.72 (0.45, 1.14)	0.83 (0.51, 1.36)	0.80 (0.47, 1.35)	0.72 (0.41, 1.26)			
	Among Older Other race							
	0 vs 3+ life-course stressors	0.80 (0.35, 1.83)	0.90 (0.35, 2.27)	1.24 (0.46, 3.33)	0.59 (0.22, 1.61)	0.9943	0.0204	n/a
	1 vs 3+ life-course stressors	0.55 (0.25, 1.23)	1.58 (0.67, 3.75)	1.58 (0.66, 3.75)	0.66 (0.27, 1.65)			
	2 vs 3+ life-course stressors	1.15 (0.48, 2.77)	1.12 (0.44, 2.86)	0.83 (0.33, 2.04)	0.36 (0.12, 1.04)			
Cumulative stressors	**Entire Sample Regardless of Race**							
	0 vs 3+ Cumulative stressors	0.83 (0.60, 1.15)	0.76 (0.54, 1.08)	0.75 (0.51, 1.11)	0.68 (0.45, 1.01)	0.361	**0.1035**	**0.0282**
	1 vs 3+ Cumulative stressors	0.77 (0.56, 1.07)	1.24 (0.89, 1.74)	1.06 (0.74, 1.51)	0.86 (0.59, 1.24)			
	2 vs 3+ Cumulative stressors	0.95 (0.69, 1.32)	1.03 (0.73, 1.46)	0.85 (0.61, 1.19)	0.83 (0.56, 1.23)			
	Among Older White Americans							
	0 vs 3+ Cumulative stressors	**0.73 (0.60, 0.89)**	**0.79 (0.64, 0.98)**	**0.78 (0.62, 0.98)**	0.82 (0.65, 1.05)	**0.0091**	0.8348	n/a
	1 vs 3+ Cumulative stressors	**0.74 (0.62, 0.88)**	**0.79 (0.66, 0.96)**	**0.76 (0.62, 0.92)**	0.89 (0.71, 1.11)			
	2 vs 3+ Cumulative stressors	**0.83 (0.70, 0.99)**	0.94 (0.78, 1.14)	0.92 (0.74, 1.13)	0.98 (0.79, 1.23)			
	Among Older African Americans							
	0 vs 3+ Cumulative stressors	1.04 (0.65, 1.66)	0.69 (0.43, 1.11)	**0.44 (0.27, 0.74)**	**0.45 (0.26, 0.79)**	**0.0934**	**0.1424**	n/a
	1 vs 3+ Cumulative stressors	0.84 (0.53, 1.33)	0.83 (0.53, 1.31)	0.71 (0.43, 1.16)	**0.56 (0.32, 0.97)**			
	2 vs 3+ Cumulative stressors	1.04 (0.66, 1.63)	0.91 (0.56, 1.48)	0.76 (0.46, 1.26)	0.82 (0.46, 1.44)			
	Among Older Other race							
	0 vs 3+ Cumulative stressors	0.76 (0.33, 1.75)	0.82 (0.33, 2.02)	1.34 (0.54, 3.29)	0.83 (0.29, 2.33)	0.452	**0.0973**	n/a
	1 vs 3+ Cumulative stressors	0.75 (0.33, 1.72)	**2.93 (1.22, 7.08)**	2.23 (0.90, 5.55)	1.27 (0.51, 3.20)			
	2 vs 3+ Cumulative stressors	1.00 (0.43, 2.33)	1.28 (0.52, 3.17)	0.89 (0.38, 2.08)	0.72 (0.26, 1.98)			

*Notes: CI=confidence interval. Odds Ratios in bold are statistically significant. Models adjusted for race, age, sex, education, marital status, BMI, cigarette use, alcohol consumption and interaction terms for race*time, stress*time as well as three -way terms for race*stress*time.*

Supplementary Tables

The following supplementary tables 4.1-4.5 show the distribution of our toxic stress questions at baseline by race. Questions are in their raw form before scores that are used in the analyses are derived. Scores were derived per guidelines in the HRS Psychosocial Leave Behind questionnaire (https://hrs.isr.umich.edu/sites/default/files/biblio/HRS%202006-2016%20SAQ%20Documentation_07.06.17.pdf).

Supplementary Table 4.1: Distribution of Everyday discrimination items at baseline by race

Experiences of Day to day discrimination	All Races (N=3904) N (%)	White (N=3159) N (%)	Black (A/A) (N=574) N (%)	Other (N=171) N (%)	p-value
1. You are treated with less courtesy and respect than other people.					< 0.0001
Never	1747 (45.4)	1404 (45.0)	261 (43.4)	82 (48.8)	
Less than once a year	790 (20.5)	689 (22.1)	72 (12.8)	29 (17.3)	
A few times a year	782 (20.3)	644 (20.7)	113 (20.1)	25 (14.9)	
A few times a month	281 (07.3)	211 (06.8)	55 (09.8)	15 (08.9)	
At least once a week	144 (03.7)	99 (03.2)	37 (06.6)	08 (04.8)	
Almost every day	103 (02.7)	69 (02.2)	25 (04.4)	09 (05.4)	
2. You receive poorer service than other people at restaurants or stores.					< 0.0001
Never	2297 (59.7)	1871 (60.0)	323 (57.5)	103 (62.0)	
Less than once a year	826 (21.5)	700 (22.4)	93 (16.6)	33 (19.9)	
A few times a year	500 (13.0)	394 (12.6)	90 (16.0)	16 (09.6)	
A few times a month	145 (03.8)	101 (03.2)	36 (06.4)	08 (04.8)	
At least once a week	54 (01.4)	38 (01.2)	15 (02.7)	01 (0.6)	
Almost every day	26 (0.7)	16 (0.5)	05 (0.9)	05 (03.0)	
3. People act as if they think you are not smart.					< 0.0001
Never	2216 (57.7)	1800 (57.9)	315 (56.0)	101 (59.8)	
Less than once a year	694 (18.1)	603 (19.4)	69 (12.3)	22 (13.0)	
A few times a year	552 (14.4)	437 (14.1)	94 (16.7)	21 (12.4)	

A few times a month	195 (05.1)	143 (04.6)	41 (07.3)	11 (06.5)	
At least once a week	102 (02.7)	74 (02.4)	22 (03.9)	06 (03.6)	
Almost every day	82 (02.1)	52 (01.7)	22 (03.9)	08 (04.7)	
4. People act as if they are afraid of you.					0.005
Never	3049 (79.1)	2476 (79.4)	444 (78.9)	129 (76.8)	
Less than once a year	387 (10.0)	328 (10.5)	43 (07.6)	16 (09.5)	
A few times a year	248 (06.4)	200 (06.4)	37 (06.6)	11 (06.5)	
A few times a month	91 (02.4)	66 (02.1)	19 (03.4)	06 (03.6)	
At least once a week	46 (01.2)	33 (01.0)	11 (02.0)	02 (01.2)	
Almost every day	29 (0.7)	16 (0.5)	09 (01.6)	04 (02.4)	
5. You are threatened or harassed.					0.005
Never	3161 (82.1)	2554 (81.9)	466 (82.9)	141 (83.9)	
Less than once a year	423 (11.0)	366 (11.7)	49 (08.7)	08 (04.8)	
A few times a year	171 (04.4)	131 (04.2)	28 (05.0)	12 (07.1)	
A few times a month	49 (01.3)	34 (01.1)	09 (01.6)	06 (03.6)	
At least once a week	28 (0.7)	20 (0.6)	07 (01.2)	01 (0.6)	
Almost every day	17 (0.4)	14 (0.4)	03 (0.5)	0 (0)	
6. You receive poorer service or treatment than other people from doctors or hospitals*					0.001
Never	1516 (80.1)	1238 (80.5)	209 (78.3)	69 (79.3)	
Less than once a year	219 (11.6)	183 (11.9)	29 (10.9)	07 (08.0)	
A few times a year	107 (05.7)	88 (05.7)	14 (05.2)	05 (05.8)	
A few times a month	25 (01.3)	11 (0.7)	10 (03.8)	04 (04.6)	
At least once a week	14 (0.7)	09 (0.6)	03 (1.1)	02 (02.3)	
Almost every day	11 (0.6)	09 (0.6)	02 (0.7)	0 (0)	

Note: Baseline stress measures combined the HRS waves 2006 and 2008 since the PLB questionnaires were randomly administered to half the sample in each wave. *=Question asked beginning in HRS 2008; score was rescaled for HRS 2006 to make it easy to compare data between 2006 and 2008.

Supplementary Table 4.2: Distribution of Lifetime discrimination items at baseline by race					
Experiences of Lifetime discrimination	**All Races (N=3904)** **N (%)**	**White (N=3159)** **N (%)**	**Black (A/A) (N=574)** **N (%)**	**Other (N=171)** **N (%)**	**p-value**
1. At any time in your life, have you ever been unfairly dismissed from a job?					0.8508
No	3214 (83.5)	2600 (83.4)	471 (84.3)	143 (84.1)	
Yes	634 (16.5)	519 (16.6)	88 (15.7)	27 (15.9)	
2. For unfair reasons, have you been hired for a job?					0.0003
No	3494 (91.3)	2863 (92.1)	480 (87.0)	151 (90.4)	
Yes	332 (08.7)	244 (07.9)	72 (13.0)	16 (09.6)	
3. Have you ever been unfairly denied a promotion?					< 0.0001
No	3388 (88.9)	2790 (90.1)	454 (82.7)	144 (86.2)	
Yes	423 (11.1)	305 (09.9)	95 (17.3)	23 (13.8)	
4. Have you ever been unfairly prevented from moving into a neighborhood because the landlord or a realtor refused to sell or rent you a house or apartment?					< 0.0001
No	3742 (97.1)	3076 (98.4)	508 (91.2)	158 (93.5)	
Yes	110 (02.9)	50 (01.6)	49 (08.8)	11 (06.5)	
5. Have you ever been unfairly denied a bank loan?					< 0.0001
No	3633 (94.5)	2995 (96.0)	481 (86.7)	157 (92.9)	
Yes	210 (05.5)	124 (04.0)	74 (13.3)	12 (07.1)	
6. Have you ever been unfairly stopped, searched, questioned, physically threatened, or abused by the police?					< 0.0001
No	3655 (94.8)	3015 (96.4)	488 (87.6)	152 (89.4)	
Yes	199 (05.2)	112 (03.6)	69 (12.4)	18 (10.6)	
7. Have you ever been unfairly denied health care or treatment? *					0.0003
No	1821 (96.8)	1494 (97.3)	241 (92.7)	86 (98.9)	
Yes	61 (03.2)	41 (02.7)	19 (07.3)	01 (01.1)	

Note: Baseline stress measures combined the HRS waves 2006 and 2008 since the PLB questionnaires were randomly administered to half the sample in each wave. *= Question asked beginning in HRS 2008; score was rescaled for HRS 2006 to make it easy to compare data between 2006 and 2008.

Supplementary Table 4.3: Distribution of Chronic work discrimination items at baseline by race					
Experiences of Chronic work discrimination	**All Races (N=3904)** N (%)	**White (N=3159)** N (%)	**Black (A/A) (N=574)** N (%)	**Other (N=171)** N (%)	**p-value**
1. How often are you unfairly given the tasks at work that no one else wants to do?					0.4457
Never	499 (55.9)	382 (55.00)	86 (59.7)	31 (58.5)	
Less than once a year	116 (13.0)	97 (14.0)	14 (09.7)	05 (09.5)	
A few times a year	137 (15.4)	109 (15.7)	22 (15.3)	06 (11.3)	
A few times a month	66 (07.4)	51 (07.3)	10 (06.9)	05 (09.4)	
At least once a week	48 (05.4)	36 (05.2)	06 (04.2)	06 (11.3)	
Almost every day	26 (02.9)	20 (02.9)	06 (04.2)	00 (0)	
2. How often are you watched more closely than others?					0.3088
Never	615 (69.3)	489 (70.7)	91 (64.1)	35 (64.8)	
Less than once a year	102 (11.5)	84 (12.1)	13 (09.1)	05 (09.3)	
A few times a year	65 (07.3)	47 (06.8)	13 (09.1)	05 (09.3)	
A few times a month	42 (04.7)	31 (04.5)	09 (06.3)	02 (03.7)	
At least once a week	25 (02.8)	16 (02.3)	06 (04.2)	03 (05.6)	
Almost every day	39 (04.4)	25 (03.6)	10 (07.0)	04 (07.4)	
3. How often are you bothered by your supervisor or co-workers making slurs or jokes about women or racial or ethnic groups?					0.2077
Never	696 (78.9)	550 (79.8)	108 (77.1)	38 (71.7)	
Less than once a year	76 (08.6)	59 (08.6)	12 (08.6)	05 (09.4)	
A few times a year	54 (06.1)	41 (06.0)	07 (05.0)	06 (11.3)	
A few times a month	26 (03.0)	21 (03.0)	04 (02.9)	01 (01.9)	
At least once a week	18 (02.0)	13 (01.9)	04 (02.9)	01 (01.9)	
Almost every day	12 (01.4)	05 (0.7)	05 (03.6)	02 (03.8)	
4. How often do you feel that you have to work twice as hard as others at work?					0.3442
Never	564 (63.2)	447 (64.3)	86 (60.1)	31 (57.4)	
Less than once a year	48 (05.4)	36 (05.2)	07 (04.9)	05 (09.3)	
A few times a year	104 (11.7)	83 (11.9)	18 (12.6)	03 (05.6)	
A few times a month	59 (06.6)	46 (06.6)	08 (05.6)	05 (09.3)	
At least once a week	50 (05.6)	36 (05.2)	08 (05.6)	06 (11.1)	
Almost every day	67 (07.5)	47 (06.8)	16 (11.2)	04 (07.4)	
5. How often do you feel that you are ignored or not taken seriously by your boss?					0.9606
Never	575 (64.8)	445 (64.5)	94 (65.7)	36 (66.7)	
Less than once a year	99 (11.2)	79 (11.4)	13 (09.1)	07 (13.0)	

A few times a year	103 (11.6)	82 (11.9)	15 (10.5)	06 (11.1)	
A few times a month	48 (05.4)	37 (05.4)	08 (05.6)	03 (05.6)	
At least once a week	20 (02.2)	16 (02.3)	03 (02.1)	01 (01.8)	
Almost every day	42 (04.7)	31 (04.5)	10 (07.0)	01 (01.8)	
6. How often have you been unfairly humiliated in front of others at work?					0.2840
Never	702 (79.0)	547 (79.0)	110 (76.9)	45 (83.3)	
Less than once a year	103 (11.6)	85 (12.3)	13 (09.1)	05 (09.3)	
A few times a year	45 (05.1)	30 (04.3)	11 (07.7)	04 (07.4)	
A few times a month	21 (02.4)	16 (02.3)	05 (03.5)	00 (0)	
At least once a week	11 (01.2)	10 (01.4)	01 (0.7)	00 (0)	
Almost every day	07 (0.8)	04 (0.6)	03 (02.1)	00 (0)	

Note: Baseline stress measures combined the HRS waves 2006 and 2008 since the PLB questionnaires were randomly administered to half the sample in each wave.

Supplementary Table 4.4: Distribution of Life course items at baseline by race

Life course stress questions	**All Races (N=3904)** N (%)	**White (N=3159)** N (%)	**Black (A/A) (N=574)** N (%)	**Other (N=171)** N (%)	**p-value**
1.Has a child of yours ever died?					<0.0001
No	3013 (78.3)	2523 (80.8)	364 (65.2)	126 (74.6)	
Yes	836 (21.7)	599 (19.2)	194 (34.8)	43 (25.4)	
2.Have you ever been in a major fire, flood, earthquake, or other natural disaster					0.7987
No	3064 (79.5)	2478 (79.3)	450 (80.5)	136 (80.0)	
Yes	790 (20.5)	647 (20.7)	109 (19.5)	34 (20.0)	
3.Have you ever fired a weapon in combat or been fired upon in combat?					0.0096
No	3488 (90.3)	2807 (89.6)	523 (93.6)	158 (92.4)	
Yes	374 (09.7)	325 (10.4)	36 (06.4)	13 (07.6)	
4.Has your spouse, partner, or child ever been addicted to drugs or alcohol?					0.0235
No	3078 (80.3)	2516 (81.0)	440 (78.6)	122 (73.0)	
Yes	756 (19.7)	591 (19.0)	120 (21.4)	45 (27.0)	
5.Were you the victim of a serious physical attack or assault in your life?					0.0002
No	3588 (93.0)	2929 (93.7)	512 (91.6)	147 (86.0)	

Yes	268 (07.0)	197 (06.3)	47 (08.4)	24 (14.0)	
6.Did you ever have a life-threatening illness or accident?					< 0.0001
No	2364 (61.7)	1864 (60.0)	391 (70.1)	109 (63.7)	
Yes	1469 (38.3)	1240 (40.0)	167 (29.9)	62 (36.3)	
7.Did your spouse or a child of yours ever have a life- threatening illness or accident?					0.0215
No	2570 (67.4)	2055 (66.4)	395 (71.6)	120 (72.3)	
Yes	1245 (32.6)	1042 (33.6)	157 (28.4)	46 (27.7)	
8.Before you were 18 years old, did you have to do a year of school over again?					0.2285
No	3243 (83.7)	2610 (83.2)	488 (85.8)	145 (85.8)	
Yes	633 (16.3)	528 (16.8)	81 (14.2)	24 (14.2)	
9.Before you were 18 years old, did either of your parents drink or use drugs so often that it caused problems in the family?					0.0495
No	3315 (85.7)	2673 (85.2)	503 (88.9)	139 (83.2)	
Yes	554 (14.3)	463 (14.8)	63 (11.1)	28 (16.8)	
10.Before you were 18 years old, were you ever physically abused by either of your parents?					0.2914
No	3627 (93.6)	2929 (93.3)	540 (95.0)	158 (94.0)	
Yes	247 (06.4)	209 (06.7)	28 (05.0)	10 (06.0)	
11.Before you were 18 years old, were you ever in trouble with the police? *					0.2752
No	1816 (95.4)	1480 (95.6)	256 (95.9)	80 (92.0)	
Yes	87 (04.6)	69 (04.4)	11 (04.1)	07 (08.0)	

Notes: Baseline stress measures combined the HRS waves 2006 and 2008 since the PLB questionnaires were randomly administered to half the sample in each wave. *= Question asked beginning in HRS 2008; score was rescaled for HRS 2006 to make it easy to compare data between 2006 and 2008.

Supplementary Table 4.5: Distribution of recent stress items at baseline by race

Recent stress question	**All Races (N=3904)** **N (%)**	**White (N=3159)** **N (%)**	**Black (A/A) (N=574)** **N (%)**	**Other (N=171)** **N (%)**	**p-value**
1.Have you involuntarily lost a job for reasons other than retirement at any point in the past five years?					0.7511
No	3724 (95.8)	3013 (95.7)	549 (96.3)	162 (95.3)	

Yes	165 (04.2)	136 (04.3)	21 (03.7)	08 (04.7)	
2.Have you been unemployed and looking for work for longer than 3 months at some point in the past five years?					0.2393
No	3746 (96.3)	3041 (96.6)	543 (95.3)	162 (95.3)	
Yes	143 (03.7)	108 (03.4)	27 (04.7)	08 (04.7)	
3.Was anyone else in your household unemployed and looking for work for longer than 3 months in the past 5 years?					< 0.0001
No	3638 (93.7)	2980 (94.8)	515 (90.5)	143 (84.6)	
Yes	244 (06.3)	164 (05.2)	54 (09.5)	26 (15.4)	
4.Have you moved to a worse residence or neighborhood in the past five years?					0.8781
No	3816 (98.0)	3091 (98.0)	558 (97.7)	167 (97.7)	
Yes	80 (02.0)	62 (02.0)	13 (02.3)	04 (02.3)	
5.Were you robbed, or did you have your home burglarized in the past five years?					0.0002
No	3709 (95.4)	3024 (96.0)	531 (93.3)	154 (90.6)	
Yes	180 (04.6)	126 (04.0)	38 (06.7)	16 (09.4)	
6.Have you been the victim of fraud in the past five years?*					0.3362
No	1811 (95.2)	1478 (95.4)	252 (94.7)	81 (92.0)	
Yes	92 (04.8)	71 (04.6)	14 (05.3)	07 (08.0)	

Notes: Baseline stress measures combined the HRS waves 2006 and 2008 since the PLB questionnaires were randomly administered to half the sample in each wave. *= Question asked beginning in HRS 2008; score was rescaled for HRS 2006 to make it easy to compare data between 2006 and 2008.

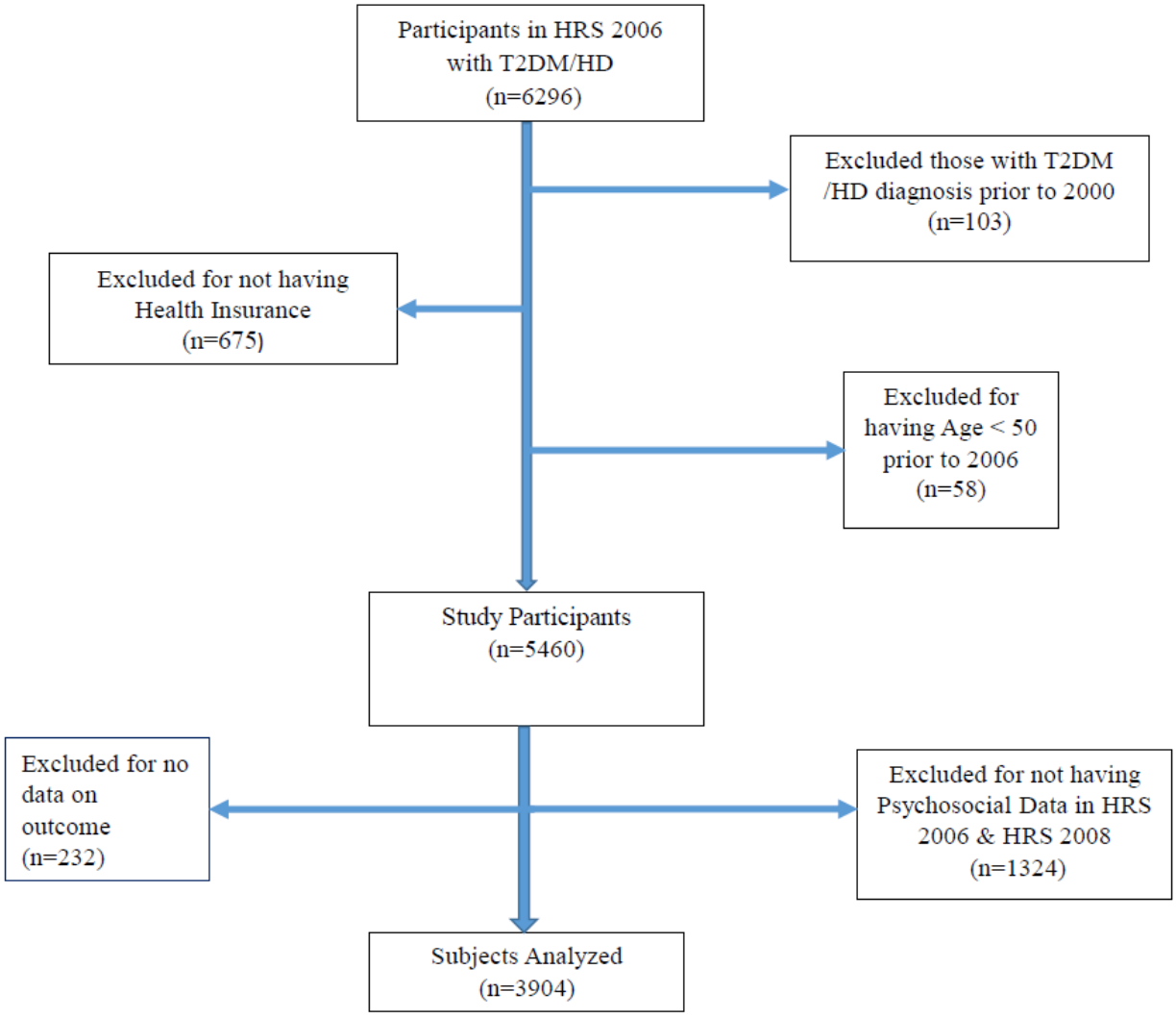
Mediation analysis

Additionally, we conducted a mediation analysis and found that the effect of race is not mediated by toxic stressors (Supplementary Table 4.6). This suggests that race and our measures of toxic stress are independent predictors of QOL declines and therefore no evidence of intersectionality in our findings.

Supplementary Table 4.6: Mediation analysis on impact of toxic stressors association between race and SRH declines.						
	Toxic stressor		**OR (95% CI)**	**p-Value Stressor**	**p-Value T*Stressor**	**Proportion due to TS**
Race	**None**	Black/AA vs White/Caucasian	**1.459 (1.252, 1.702)**	< 0.0001	0.6575	
		Other vs White/Caucasian	**1.429 (1.095, 1.864)**			
		Black/AA vs Other	1.021 (0.762, 1.370)			
Race	**Life course stressors**	Black/AA vs White/Caucasian	**1.464 (1.252, 1.710)**	< 0.0001	0.8762	0%
		Other vs White/Caucasian	**1.432 (1.093, 1.877)**			0%
		Black/AA vs Other	1.022 (0.758, 1.378)			0%
Race	**Recent stressors**	Black/AA vs White/Caucasian	**1.456 (1.249, 1.698)**	0.487	0.3133	0%
		Other vs White/Caucasian	**1.422 (1.089, 1.857)**			0%
		Black/AA vs Other	1.024 (0.763, 1.375)			0%
Race	**Lifetime discrimination**	Black/AA vs White/Caucasian	**1.377 (1.179, 1.609)**	< 0.0001	0.1087	6%
		Other vs White/Caucasian	**1.379 (1.055, 1.804)**			3%
		Black/AA vs Other	0.998 (0.742, 1.342)			2%
Race	**Everyday discrimination**	Black/AA vs White/Caucasian	1.463 (1.253, 1.707)	0.0052	0.7197	0%
		Other vs White/Caucasian	1.450 (1.107, 1.899)			-1%
		Black/AA vs Other	1.009 (0.749, 1.359)			1%
Note: Proportion due to TS for effect of Race= $((OR_{Race}-OR_{TS})/ OR_{Race}) *100$						

Figures

Figure 4.1: Selection of study participants from HRS 2006



CHAPTER 5

MINORITY RACE AND LOW RESILIENCE PROMOTING FACTORS PREDICT SUSTAINED QUALITY OF LIFE (QOL) DEFICITS AMONG OLDER ADULTS WITH CHRONIC DISEASE-A PROSPECTIVE COHORT STUDY[1]

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Abstract

Objective: Resilience-promoting factors (RPF), minority race and their interaction with each other, are evaluated as determinants of quality of life (QOL) decline in a nationally representative sample of ≥50 years old United States (US) adults with heart disease (HD) and/or type-2 diabetes (T2DM) diagnosed by 2006 with follow up from 2008-2014 as part of the Health and Retirement Study (HRS).

Methods: Social support, global and domain-specific mastery, and perceived constraints were measured every two years using the psychosocial leave behind questionnaire. QOL was assessed by participant self-rated health (SRH) and operationally defined as improved, unchanged, or declined in current year vs two years prior. Repeated measures multinomial regression using generalized estimating equations (GEEs) approach related race, RPF and their interaction to SRH declines over eight years. Odds ratios (OR) and 95% confidence intervals (CIs) were calculated with adjustment for time, age, sex, and socio-economic status.

Results: 3932 adults average age 71.1±9.3 years - including 80.9%, 14.7% and 4.4% that respectively self-identified as Caucasian, African American (AA) and Other race, were enrolled. Low global mastery was associated with 127% (OR 2.27, 95% CI: 1.83, 2.81) higher odds of QOL declines over 8 years. QOL declines related to Negative social support (NSS) from children varied by race over 8 years (race*time*NSS-children, p=0.0824). Among older Caucasians, low NSS was strongly associated with decreased odds of QOL declines over time ($p < 0.0001$). Among older African Americans, and non-White, non-African Americans, there was no significant association between low vs high NSS on change in QOL over time.

Interpretation/Conclusion: Resilience-promoting factors and minority race are social determinants of QOL decline in older Americans with comorbid HD/T2DM. The types and prevalence of RPF vary according to race/ethnicity in the US. Policy interventions to enhance resiliency represent a

viable strategy for mitigating racial disparities in overall wellbeing and improving health outcomes in all aging Americans regardless of race.

Keywords: Resilience-promoting factors, Minority race, Quality of Life, Older Americans, Health disparities

Introduction

A large and compelling body of evidence has identified psychosocial factors such as social support, loneliness, marital status, bereavement, social status, social disruption, work environments, and social integration as crucial determinants that shape both health and life span in human populations [1-5]. This evidence does not deny that medical care influences health; rather, it indicates that medical care is not the only influence on health and suggests that the effects of medical care may be more limited than commonly thought, particularly in determining who becomes sick or injured in the first place [6].

Numerous studies have also consistently documented racial disparities across numerous health outcomes, [7,8] even among young people [9]. Compared to members of other racial groups, African Americans experience aging-related chronic diseases earlier in life, at greater severity, and with more serious disease-related consequences [9]. According to life course and developmental perspectives, disproportionate disease risk among African Americans can be traced to systematic disadvantage and social inequities, starting at conception, and continuing throughout childhood and adolescence [10,11]. The health risk inequities that African Americans experience undoubtedly arise from more than class disadvantage. Psychosocial stressors that disproportionately impact African Americans have been proposed as a mechanism that increases their vulnerability to poor health. Consistent with this reasoning, an emerging line of research has focused on racial discrimination, a qualitatively unique source of psychosocial stress that African Americans face.[12]

Stress research has provided evidence that resources such as personal mastery, self-esteem, optimism, life satisfaction, and social support can buffer the negative impact of stress on

health [13]. Collectively known as measures of resilience, these resources comprise individual and contextual factors that help individuals to adapt to and overcome adverse experiences.[14] A sense of control or personal mastery is a generalized belief that most circumstances in one's life are under one's personal control and not due to chance, fate or the actions of other people [15] . High self-esteem is a perception of oneself as a good, valued, and competent person. Social support refers to emotional, informational, or practical assistance from significant others such as family members, friends, or co-workers [16]. This support may be received from others or simply perceived to be available when needed. All these resources augment individuals' abilities to cope with stressful demands. Mastery and self-esteem encourage active attempts at problem-solving, and perceived social support, especially perceived emotional support diminishes stress-induced psychological distress and physiological arousal [17,18]. A stronger sense of personal mastery (control) has been associated with better self-reported physical and mental health, lower risk of heart disease and diabetes, better chronic disease outcomes, and lower mortality. Lower status, disadvantaged groups (women, minorities, unmarried persons, working class and poor individuals) generally have lower levels of these coping resources,[18 19] implying that they are doubly at risk of developing ill health and mental health problems. Acute and chronic stressors are concentrated in the very groups that are deficient in these stress-buffering assets.

Worth noting, racial disparities in the prevalence and incidence of many chronic conditions are not new. However, the proximate mechanisms of racial disparities – including their potential mediators/moderators, for various health outcomes are poorly understood. Additionally, common among older adults with HD/T2DM is declining health-related quality of life (QOL) that comes with disease progression and as risk for limitations increase. QOL

involves mental, physical, and social aspects, and is defined as the individual's perceptions of his or her mental, physical, and social capabilities, and how he or she is impacted by a chronic condition over time.

This study is grounded in the socio-ecological framework which stipulates that the social, physical and cultural aspects of an environment have a cumulative effect on the health of individuals [20,21], and that resilience comprises various individual and contextual factors that facilitate well-being when experiencing stress [22]. The socio-ecological approach considers interactions among three key areas- individual factors (e.g, self-esteem, self-efficacy, and coping), contextual factors (e.g, their support systems, including support from family and friends), and the interactions within their environment, including their relationships, cultural identity, and the material resources available to them [22,23]. The concept of resilience in the health-related QOL of patients with T2DM/HD is important because it may influence how subjects manage their health and well-being.

Despite decades of research, our understanding of the factors responsible for racial differences in health is still limited. This hampers the development of effective strategies to mitigate health inequities. Farther more, the role of resilience mechanisms in moderating racial disparities is currently unknown. We therefore inform an existing knowledge gap by evaluating various domains of resilience measures, and changes in these indicators over eight years as potential mediators of chronic disease prevalence in a nationally representative sample of peri-retirement age US adults followed as part of the HRS from 2006-2014. This study specifically sought to investigate differences in measures of resiliency as key mediators of race-related differences in quality of life in an aging population of retired and semi-retired adults with heart

disease and/or diabetes. Thus, we hypothesized that those with lower scores on resilience factors will be more likely to report declines in QOL relative to those with higer scores.

Methods

Study Population and Analytic Sample

This is a longitudinal study of a nationally representative cohort of Americans 50 years and older with comorbid type-2 diabetes and/or heart disease enrolled in the Health and Retirement Survey (HRS) from 2006 to 2014. The HRS has been extensively described elsewhere [24]. Briefly, participants are interviewed using structured questionnaires every 2 years to document levels of psychosocial stress, physical health and functioning, cognitive functioning, health insurance, health care expenses, employment, and financial information such as income, assets, and pension plans. Because the psychosocial Leave-Behind questionnaires which provided measures of psychosocial stress/resiliency were first administered in 2006 HRS wave, the analysis period was limited to the eight years period between 2006 and 2014.[25]

The study base included insured adults ≥50 years old with physician diagnosed T2DM or HD within six years (in year 2000 and beyond) with at least baseline data on the exposure and primary outcomes. We excluded individuals with comorbid disease diagnosed prior to HRS 2000 to minimize variability in disease duration at baseline- a variable independently associated with change in QOL. We further excluded individuals without health insurance at enrolment as QOL outcomes are expected to differ substantially due to lack of access to medical care.

Measures

Main Exposures: Race/ethnicity, Resilience promoting factors

Race/ethnicity: The primary exposure in this study was race. Race was categorized as Black/African American (AA), White/ Caucasian (White) or Other /non-White non-African American and assessed by self-report. Respondents were classified as white or black if they considered themselves, respectively, as primarily "White or Caucasian" or "Black or African American" and did not report any Hispanic/Latino ethnicity. Individuals were classified as "Other race" if they reported that they considered themselves to be "Hispanic or Latino."

Resilience promoting factors: Resilience promoting factors (RPF) are coping resources assessed at individual and contextual level that buffer against physical/psychosocial stress and thus enhance well-being. The individual-level factors included: perceived constraints or lack of control, global personal mastery, and domain-specific control of one's health, social life and finances. Contextual factors included percieved social support from relationships.

Personal mastery measures one's perception of his or her ability to achieve goals. Included were five questions getting at one's resolve at engaging situations around them. Items include; 1) I can do just about anything that I set my mind to, 2) When I really want to do something, I usually find a way to succeed at it, 3)Whether I am able to get what I want is ni my own hands, 4) What happens to me in the future depends on me and 5) I can do the things that I want to do.

Perceived constraints on personal control were five items that capture how one perceives control of things going on around them. Items asked incude; 1) I often feel helpless in dealing with the problems of life, 2) Other people determine most of what I can and cannot do, 3)What

happens in my life is often beyond my control, 4) I have little control over the things that happen to me, and 5)There is really no way that I can solve the problems I have.

In both dimensions above, respondents were asked how much they agree or disagree with the items, and likert type responses provided where 1=Strongly disagree, 2=Somewhat disagree, 3=Slightly disagree, 4=Slightly agree, 5=Somewhat agree and 6=Strongly agree. Indices of global mastery and constraints were created by averaging the scores across the items in each construct.

Questions on social support assessed quality of support from key relationships. Included were four sets of seven items that examined the percieved support that respondents get from their spouses/partners, children, other family members and friends. For each relationship category, there are three positively worded items - positive social support (PSS) and four negatively worded items - negative social support (NSS). PSS questions included; 1) How much do they understand the way you feel about things? 2) How much can you rely on them if you have a serious problem? 3) How much can you open up to them if you need to talk about your worries? NSS questions included; 1) How often do they make too many demands on you? 2) How much do they criticize you? 3) How much do they let you down when you're counting on them? And 4) How much do they get on your nerves? Responses to the above were graded on a scale of 1-4 where 1= a lot and 4=Not at all, and were reverse-coded to create scores of positive and negative social support for each relationship category. We farther created additional constructs to sum up responses on from immediate family (spouses and children), extended family (friends and other family members), and all four relationship groups (spouses, children, other family members and friends). These were created for both the positive and negative social support domains.

Three single item measures of domain-specific control for health, social life and finances were also assessed. Respondents were asked, “using a scale of 0-10 where, 0 means no control at all and 10 means very much control, how would you rate the amount of control you have over (health, social life or finances) these days?” For purposes of analysis, resilience constructs above were as high or low.

We analyzed each RPF score first as a continuous variable and farther dichotomized them as high vs low based on the mean distribution of each factor. For the purposes of analysis, categorical variables were used.

Outcome: Quality of life (QOL)

Quality of life (QOL) was defined as self-rated health (SRH) measured every two years in response to the question: “Would you say your health is excellent, very good, good, fair, or poor?” For analytic purposes, three ordinal QOL levels were defined as: poor (fair/poor), good, or excellent (i.e. very good or excellent) SRH.

Covariates

Age was established via self-reported date of birth and analyzed categorically in five-year increments. Other covariates included: biological sex, self-reported years of education completed, marital status, body mass index (BMI) and behavioral risk factors such as smoking status and alcohol consumption.

Data Analysis

We implemented descriptive analyses in the overall sample and by race/ethnicity. For continuous and categorical variables respectively means (with standard deviation) and frequency (with percent) were estimated. Hypothesis testing for potential difference in factors by

race/ethnicity was implemented using t-tests for continuous variables and Chi-square tests for categorical covariates. Bivariate analyses were additionally performed to estimate crude associations between each variable and change in SRH. Bivariate associations were also used to determine racial differences in the characteristics assessed. Factors with a p-value < 0.2 from bivariate analyses were further evaluated in multivariable models as candidate confounders.

To determine race-related and psychosocial status-related differences (and 95% confidence intervals) in SRH declines, we implemented repeated measures analyses for multinomial outcomes using SAS PROC GEE adjusted for baseline for age, sex, social economic status, marital status, BMI, smoking status, and alcohol use at baseline. We assumed a multinomial distribution with an independent working correlation structure to account for repeated assessments of the outcome within participants. From this model, the odds of worse/poorer SRH during follow-up was determined in relation to baseline psychosocial predictors. A time indicator with values 1, 2, 3 and 4 was constructed, representing the intervals between the study years 2008, 2010, 2012, and 2014. We first ran an unadjusted model which included race, time, and the race* time interaction. We ran additional unadjusted models each including a measure of toxic stress at baseline, time, and the stress * time interaction. Then, from the literature and preliminary analyses we controlled for the following variables in adjusted models: age, resilience domain, sex, education, race, marital status, BMI, cigarette use and alcohol consumption and interaction terms for race* time, resilience*time as well as three-way terms for race * resilience*time. Regression models estimated the odds (odds ratios and corresponding 95% confidence intervals (CI) of SRH decline during follow-up in relation to primary determinants – race and measures of resiliency at alpha=0.05. For analyses of interaction

between race/ethnicity and resiliency measures where statistical tests are generally underpowered, $p < 0.10$ was used to determine presence of possible interaction .[26,27] In that case, analyses were conducted within stratum of race. All analyses were performed with SAS software, version 9.4 (SAS Institute, Cary, NC).

Results

Baseline characteristics

6,296 individuals were identified for inclusion in the study at baseline. The baseline combines two waves of data (HRS 2006 and HRS 2008) because psychosocial questionnaires were randomly administered to half the sample in each wave. For instance, a participant who received the psychosocial leave behind (PLB) questionnaire in 2006, had a second administration of the questionnaire in 2010, while a participant who received it in 2008, was scheduled again for 2012. Of these 103 (1.6%) were excluded with a diabetes diagnosis prior to the year 2000, 58 (0.9%) were less than 50 years old, 675 (10.7%) lacked health insurance, 1324(21%) lacked stress/ resilience data at baseline and 206 (3.3%) lacked QOL measures. 3932 (62.4%) unique individuals with recent diabetes (T2DM), recent heart disease (HD) or both conditions were identified for analysis in the study.

Their baseline demographic characteristics stratified by race are listed in Table 5.1. Briefly, 3,172 (80.7%) participants were Caucasian, 584 (14.8%) were African American, while 176 (04.5%) were classified as Other race. Overall, the mean (SD) age of the participants was 70.9 (±9.3) years old, 2,025 (51%) were females, 2,485 (63%) were married, 1956 (49.8%) were diabetic, 2,538 (64.7%) had a diagnosis of Heart disease (HD). Within this sample, self-rated health (SRH) relative to two years prior declined over time (Table 5.2).

Association of race with SRH declines

Regardless of study interval, race-ethnicity was an independent and strong determinant of change in SRH in this sample. After adjusting for baseline education, sex, age, BMI, smoking status, alcohol use and marital status the odds of SRH decline was 46% (OR 1.46, 95% CI: 1.25, 1.70) higher for African Americans and 43% (OR 1.43, 95% CI: 1.10, 1.86) higher for Other race relative to older Caucasian Americans. The observed association between race/ethnicity and patient reported SRH decline was stable over 8 years follow-up (time*race, p=0.6575) (Table 5.3).

Time averaged associations of Resilience measures on SRH declines

Among resilience domains personal mastery, perceived constraints, positive social support from the spouse/ partner were strong and time invariant predictors of SRH declines as well as having one's control over health, finances, and social life (Table 5.3). Low personal mastery was associated with 127% (OR 2.27, 95% CI: 1.83, 2.81) higher odds of SRH declines relative to having high mastery. Having low control over social life was associated with 114% (OR 2.14, 95% CI: 1.74, 2.63) higher odds of SRH declines relative to having higher control. Similarly, having a low sense of control over one's finances was associated with 84% (OR 1.84, 95% CI: 1.50, 2.24) higher odds of SRH declines relative to having a high sense of financial control. Low positive social support (PSS) was associated with higher odds of SRH declines relative to higher PSS for the following groups; from partner/ spouse 30% (OR 1.30, 95% CI: 1.01, 1.68), other family members 30% (OR 1.30, 95% CI: 1.03, 1.64), immediate family (spouses and children combined) 40% (OR 1.40, 95% CI:1.12, 1.74) and all relationship groups combined 35% (OR 1.35, 95% CI: 1.10, 1.65).

Time varying associations of Resilience domains on SRH declines

Declines in SRH over 8 years of follow up related to PSS from friends varied by race (race*time*PSS, p=0.0932, Table 5.4). Among older Caucasians, the association between PSS from friends and change in SRH did not vary over time (time*PSS, p=0.6761) and there was no significant association between experiencing low or high PSS. Among older African Americans, low PSS was associated with increased odds of SRH declines over time (p=0.0314). The association between having low PSS on change in SRH was weakly significant at baseline and stayed stable throughout the study period (time*PSS, p=0.5032). Among older non-White non-African Americans, the association between having low PSS on change in SRH varied over time (time*PSS, p=0.0339).

Declines in SRH over 8 years of follow up related to NSS from children varied over time and by race (race*time*NSS-children, p=0.0824). Among older Caucasians, low NSS was strongly associated with decreased odds of SRH declines over time (p <0.0001). The protective effect of having low vs high NSS from children on change in SRH stayed stable throughout the study period (time*NSS-children, p=0.4032). Among older African Americans, the protective effect of low vs high NSS from children on SRH declines did not vary over time (time*NSS-children, p=0.8456) and there was no significant association between experiencing low or high NSS on SRH declines. Among older non-White, non-African Americans, there was no significant association between having low vs high NSS on change in SRH over time (Table 5.4).

Declines in SRH over 8 years of follow up related to NSS from other family members varied over time and farther by race (race*time*NSS-other family, p=0.0357). Among older

Caucasians, low NSS from other family members was strongly associated with decreased odds of SRH declines over time ($p < 0.0001$). The protective effect of having low vs high NSS from other family on change in SRH stayed stable throughout the study period (time*NSS-other family, $p=0.9753$). Among older African Americans, low NSS from other family members was strongly associated with decreased odds of SRH declines over time ($p= 0.0263$). The protective effect of low vs high NSS from other family members on SRH declines varied over time and was strongest and significant at baseline and at study end (time*NSS-other family, $p=0.0289$). Among older non-White, non-African Americans, there was no significant association between having low vs high NSS on change in SRH over time (time*NSS-other family, $p=0.3889$).

Declines in SRH over 8 years of follow up related to NSS from immediate family members (children and spouses) varied by race (race*time*NSS-immediate family, $p=0.0186$). Among older Caucasians, low NSS from immediate family members was strongly associated with decreased odds of SRH declines over time ($p =0.0055$). The protective effect of having low vs high NSS from immediate family on change in SRH increased during follow up and weakened by study end (time*NSS-immediate family, $p=0.082$). Among older African Americans, association between low NSS from immediate family and change in SRH varied over time and was protective at baseline and at study end (time*NSS-immediate family, $p=0.0384$). Among older non-White, non-African Americans, there was no significant association between having low vs high NSS on change in SRH over time (Table 5.4).

Furthermore, declines in SRH over 8 years related to NSS from all support groups combined, varied over time and by race (race*time*NSS-all groups, $p=0.0052$). Among older Caucasians, low NSS from all support groups was associated with decreased odds of SRH

declines over time (p = 0.0185). The protective effect of having low vs high NSS from all support groups on change in SRH increased during follow up. Among older African Americans, the protective effect of low vs high NSS from all support groups on SRH declines varied over time (time*NSS- all groups, p=0.010) and was weakly significant at baseline. Among older non-White, non-African Americans, having low NSS from all support groups was associated with change in SRH over time (p= 0.05) with the association being protective at baseline but not during follow up.

Discussion

This study sought to examine differences in resilience-promoting factors (RPF) as key mediators of race-related differences in quality of life (QOL) declines over 8 years in a sample of peri-retired or retired adults 50 years old and above with a chronic debilitating disease. We found that individuals who reported having higher levels of RPF were less likely to experience declines in self-rated health, and this was consistent with our hypothesis. Among resilience domains, personal mastery, positive social support from the spouse/ partner were strong predictors of SRH declines over time as well as having one's control over health, finances, and social life.

Our findings are consistent with literature that says mastery is associated with perceived wellness despite living with a chronic debilitating disease. In a study to identify resilience factors important in patients with chronic obstructive pulmonary disease (COPD), a high HRQOL was found in subjects who had high levels of self-esteem, self-efficacy, good coping, relationships, and positive views of supported pulmonary rehabilitation programs [28]. Similarly, our findings corroborate those of Ward, based on analyses of the 2006 HRS. In their study, people with higher mastery were less likely to report fair/poor health [29]. In another study that examined

whether higher levels of RPF were associated with lower healthcare use, the authors found that individuals that reported having high levels of domain-specific health and financial mastery were less likely to have fewer doctor visits and were less likely to be hospitalized in the prior 2 years [13].

With regards to social support, our findings across the various domains corroborate previous research that shows that impact of social networks on health, disease progression and mortality among older adults [30-33]. However, these studies were limited to clinical samples, community samples or international populations and were not nationally representative. However, In another study of over 3400 older American adults, the authors found that having social support is associated with good self-rated health (SRH) [34].

We farther found that race was a strong independent predictor of declines in SRH declines over time. This finding was consistent with prior research that we performed looking at the effects of toxic stressors on quality of life declines in the same population [35]. Our results can also be interpreted in the context of racism as racism in America still persists at multiple levels, including interpersonal, environmental, institutional, and cultural [36-38]. Racial discrimination combined with other environmental stressors contribute to the biological pathways leading to disease and death in minority populations. Studies have shown how slavery, residential segregation, poverty, violence, lack of access to healthcare and educational opportunities contribute to the adverse health effects among African-Americans [39-42]. In another study, African Americans reporting experiences with racism exhibited higher blood pressure than those who did not [43].

Our research also corroborates research findings on racial differences in psychological distress- on mental health issues. Most of this has been attributed to differences in social class/SES imbalances. In one study, the authors found a negative interaction between race and class: with racial differences in psychological distress being most pronounced at the lowest socioeconomic levels,[44] and poverty being more damaging to blacks than whites. Stress-by-race interactions, however, were not examined in this study [45]. However, the potential heterogeneity by race across various domains of RPF and their adverse health effects on health within older US adults as implemented herein is novel. For instance, regardless of race, lower levels of negative social support from children or other family were associated with higher QOL, but this was more the case in Caucasian, and not in African Americans, or Other race and lowest in Caucasian Americans. This could be partly due to minority populations tend to live in areas of concentrated disadvantage, wiping out the beneficial effects of social support.

Given that our study participants are older and suffering from either chronic HD, T2DM or both, we provide farther evidence on the ways toxic effects of racism as a stressor drive the disproportionate rates of chronic disease observed in minority populations, notably in African Americans, and Hispanics. Strengths of our study included the fact that we examined the impact of multiple domains / measures of resilience on quality of life outcomes over time, all of which confirmed our hypothesis. We additionally examined racial differences in QOL deficits between various racial groups. Most other studies published estimated disease burden for African Americans compared with whites, not including other minority groups.

Although this study highlighted some important findings, it had a few limitations that need to be considered when interpreting the results. First, this study relied on data that were

obtained by using self-reported questionnaires, which are a subjective measure and is based on the individual's perspective. As a result, the answers provided in the questionnaires may not objectively reflect the real experiences or severity of subjects who are undergoing extreme difficulties. The validity of these findings could be strengthened by adding biomarker data for analysis. Second, this being a secondary data analysis, we tried to answer our questions using data that may not have been originally collected to answer them.

Understanding the role of resilience measures is critical to the establishment of efforts aimed at reducing racial disparities in health. We should endeavor to address health disparities because such inequities are inconsistent with the values of American society and addressing them also is an issue of social justice. Besides that, harmful health behaviors lend themselves to and continue to be perpetuated by lingering inequalities. The racial disparities observed in resilience levels in this study should be understood in the context of persistent inequities in societal institutions and relations that still silently plague American culture.

Conclusion

The present study evaluated measures of resilience and minority race as determinants of quality of life (QOL) decline in a nationally representative sample of ≥50 years old United States (US) adults with heart disease (HD) and/or type-2 diabetes (T2DM). Among older Americans with HD and T2DM, minority race and lower levels of RPF are social determinants of decline in wellbeing. We demonstrated, using various measures, that having lower levels of resilience promoting factors predicted sustained QOL declines in this population, whereas higher levels of resilience promoting factors were associated with decreased odds of QOL declines. Our findings are important given that we live in a race-conscious society in which racism still

abounds on multiple levels, including institutionalized, personally mediated, and internalized, each of which can have negative impacts on health.[37] Resilience promoting factors- both innate and social resources are a salient feature of optimal QOL as they provide buffers to the avalanche of toxic stressors and hence social interventions that enhance them should be implemented especially in minority populations.

Abbreviations

RPF: Resilience promoting factors, Indicators; QOL: Quality of Life; US: United States of America; HD: Heart Diseases; T2DM: Type 2 Diabetes; HRS: Health and Retirement Study; SRH: Self-rated Health; AA: African American; BMI: Body Mass Index; PSS: Positive Social Support; NSS: Negative Social Support

Declarations

Ethics approval and consent to participate: This was a secondary data analysis on anonymized data; hence, informed consent was waived. The HRS is conducted under the University of Michigan and sponsored by the National Institute on Aging and the Social Security Administration. The study has been approved by the University of Michigan Institutional Review Board.

Consent for publication: Not applicable.

Competing Interests: The authors declare that they have no competing interests.

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Availability of data and materials: The data that support the findings of this study are publicly available as HRS public release data files which can be accessed at https://hrs.isr.umich.edu/data-products/access-to-public-data.

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Table 5.1: Baseline characteristics of the study participants by Race					
	All Races (N=3932)	**White (N=3172)**	**Black (A/A) (N=584)**	**Other (N=176)**	
Characteristic	**N (%)**	**N (%)**	**N (%)**	**N (%)**	**p-value**
Age mean (SD)	70.9 (9.2)	71.6 (9.1)	68.6 (8.7)	66.5 (9.2)	< 0.0001
Female sex	2025 (51.5)	1557 (49.1)	378 (64.7)	90 (51.1)	< 0.0001
Marital Status					
Married/ partnered	2485 (63.2)	2096 (66.1)	281 (48.1)	108 (61.4)	<0.0001
Separated/Divorced	437 (11.1)	308 (09.7)	109 (18.7)	20 (11.4)	
Widowed	916 (23.3)	704 (22.2)	171 (29.3)	41 (23.3)	
Never married	94 (02.4)	64 (02.0)	23 (03.9)	07 (03.9)	
Education					
Less than High School/GED	1161 (29.5)	833 (26.3)	248 (42.5)	80 (45.5)	<0.0001
High-school graduate	1253 (31.9)	1055 (33.3)	168 (28.8)	30 (17.0)	
Some college and above	1518 (38.6)	1284 (40.5)	168 (28.8)	66 (37.5)	
BMI					
< 18.5 kg/m^2 (Underweight)	39 (01.0)	34 (01.1)	03 (0.5)	2 (01.1)	<0.0001
18.5-24 kg/m^2 (Normal weight)	891 (22.8)	763 (24.2)	90 (15.5)	38 (21.7)	
25-29 kg/m^2 (Overweight)	1493 (38.2)	1251 (39.7)	182 (31.3)	60 (34.3)	
≥30 kg/m^2 (Obese)	1482 (38.0)	1100 (34.9)	307 (52.8)	75 (42.9)	
Disease conditions					
Diabetes	1956 (49.8)	1451 (45.8)	395 (67.7)	110 (62.5)	< 0.0001
Heart Disease	2538 (64.6)	2160 (68.1)	293 (50.2)	85 (48.3)	<0.0001
Diabetes & Heart Disease	659 (16.9)	521 (16.6)	113 (19.2)	25 (15.4)	0.001
Behavioral factors					
Ever smoked	2372 (60.7)	1931 (61.2)	344 (59.5)	97 (55.7)	0.2877
Current alcohol use	1779 (45.3)	1542 (48.6)	179 (30.7)	58 (33.0)	<0.0001
Measures of resiliency					
Perceived mastery					
Low mastery	1499 (38.1)	1205 (38.0)	237 (40.6)	57 (32.4)	0.1369
High mastery	2433 (61.9)	1967 (62.0)	347 (59.4)	119 (67.6)	
Perceived constraints					
Low constraints	2277 (58.3)	1870 (59.3)	303 (52.4)	104 (59.4)	0.0088
High constraints	1632 (41.7)	1286 (40.8)	275 (47.6)	71 (40.6)	
Positive Social support domains					
Spouse/partner					
Low social support	1070 (42.4)	855 (40.7)	160 (50.6)	55 (51.4)	0.0006
High social support	1452 (57.6)	1244 (59.3)	156 (49.4)	52 (48.6)	

Children					
Low social support	1930 (53.7)	1585 (54.4)	266 (50.3)	79 (51.3)	0.1741
High social support	1664 (46.3)	1326 (45.6)	263 (49.7)	75 (48.7)	
Other family					
Low social support	2588 (71.0)	2147 (73.0)	338 (62.5)	103 (62.8)	< 0.0001
High social support	1059 (29.0)	795 (27.0)	203 (37.5)	61 (37.2)	
Friends					
Low social support	2500 (70.0)	2082 (71.9)	307 (59.3)	111 (70.2)	< 0.0001
High social support	1072 (30.0)	814 (28.1)	211 (40.7)	47 (29.8)	
All Relationship groups combined					
Low social support	3187 (81.4)	2570 (81.3)	469 (80.9)	148 (85.1)	0.4345
High social support	727 (18.6)	590 (18.7)	111 (19.1)	26 (14.9)	
Negative Social support domains					
Spouse/partner					
Low social support	491 (19.5)	418 (19.9)	60 (19.0)	13 (12.3)	0.1473
High social support	2029 (80.5)	1680 (80.1)	256 (81.0)	93 (87.7)	
Children					
Low social support	1364 (38.0)	1152 (39.6)	157 (29.7)	55 (35.0)	< 0.0001
High social support	2230 (62.0)	1757 (60.4)	371 (70.3)	102 (65.0)	
Other family					
Low social support	1764 (48.4)	1504 (51.2)	188 (34.8)	72 (44.2)	< 0.0001
High social support	1878 (51.6)	1434 (48.8)	353 (65.2)	91 (55.8)	
Friends					
Low social support	2029 (56.8)	1720 (59.4)	233 (45.0)	76 (48.1)	< 0.0001
High social support	1541 (43.2)	1174 (40.6)	285 (55.0)	82 (51.9)	
All Relationship groups combined					
Low social support	1772 (45.3)	1461 (46.2)	238 (41.0)	73 (42.0)	0.0460
High social support	2142 (54.7)	1699 (53.8)	342 (59.0)	101 (58.0)	
Domain-specific control of:					
Health					
Low control	2037 (52.9)	1673 (53.7)	286 (50.8)	78 (45.6)	0.0643
High control	1811 (47.1)	1441 (46.3)	277 (49.2)	93 (54.4)	
Social Life					
Low control	1496 (41.1)	1183 (40.3)	245 (45.5)	68 (41.2)	0.0733
High control	2145 (58.9)	1755 (59.7)	293 (54.5)	97 (58.2)	
Finances					
Low control	1644 (42.3)	1333 (42.4)	237 (41.5)	74 (43.3)	0.8900
High control	2240 (57.7)	1809 (57.6)	334 (58.5)	97 (56.7)	
Self-rated health					
Excellent	872 (22.2)	763 (24.0)	83 (14.2)	26 (14.8)	<0.0001
Good	1391 (35.3)	1163 (36.7)	174 (29.8)	54 (30.7)	
Poor	1669 (42.5)	1246 (39.3)	327 (56.0)	96 (54.5)	

Table 5.2: Change in Self-Rated Health (SRH) among the Study participants Relative to 2 Years prior				
Change in SRH	**2008 (baseline)**	**2010**	**2012**	**2014**
	N (%)	N (%)	N (%)	N (%)
Improved	798 (20.3)	821 (20.9)	606 (15.4)	487 (12.4)
No Change	2077 (52.8)	1756 (44.7)	1569 (39.9)	1383 (35.2)
Worse	1057 (26.9)	796 (20.2)	798 (20.3)	680 (17.3)

Table 5.3: Time-averaged effects of resilience factors on SRH declines over 8 years			
Race	**Time averaged OR (95% CI)**	**p-Value Race**	**p-Value Time*Race**
Black/AA vs White/Caucasian	**1.46 (1.25, 1.70)**	< 0.0001	0.6575
Other vs White/Caucasian	**1.43 (1.10, 1.86)**		
Black/AA vs Other	1.02 (0.76, 1.37)		
Resilience measures		**p-Value Resilience**	**p-Value Time*Resilience**
Perceived mastery			
Low vs High	**2.27 (1.83, 2.81)**	**< 0.0001**	0.2644
Perceived constraints			
Low vs High	**0.55 (0.44, 0.68)**	**< 0.0001**	0.3164
Positive Social support domains			
Spouse/partner*			
Low vs high positive social support	**1.30 (1.01, 1.68)**	**0.0483**	0.2423
Children			
Low vs high positive social support	1.09 (0.89, 1.33)	0.4279	0.2611
Other family			
Low vs high positive social support	**1.30 (1.03, 1.64)**	0.0277	0.7587
Immediate Family (Spouse & children)			
Low vs high positive social support	**1.40 (1.12, 1.74)**	**0.0031**	0.3992
Extended Family (Others & friends)			
Low vs high positive social support	1.19 (0.98, 1.46)	0.0799	0.7095
All Relationship groups combined			
Low vs high positive social support	**1.35 (1.10, 1.65)**	0.0044	0.2372
Negative Social support domains			
Spouse/partner*			
Low vs high negative social support	0.84 (0.65, 1.09)	0.1881	0.4410
Friends			

Low vs high negative social support	0.90 (0.73, 1.09)	0.2915	0.2341
Extended Family (Others & friends)			
Low vs high negative social support	0.98 (0.81, 1.20)	0.8580	0.1211
Domain-specific control			
Social Life			
Low vs High control of Social life	**2.14 (1.74, 2.63)**	**< 0.0001**	0.8943
Finances			
Low vs High control of finances	**1.84 (1.50, 2.24)**	**< 0.0001**	0.8862

CI=confidence interval. Odds Ratios in bold are statistically significant. Models adjusted for age, sex, education, race, marital status, BMI, cigarette use and alcohol consumption and interaction terms for race* time, resilience*time as well as three-way terms for race * resilience*time.

TABLE 5.4: BASELINE RESILIENCE FACTORS AND LIKELIHOOD OF DECLINE IN SELF-RATED HEALTH (QOL) OVER 8 YEARS IN THE OVERALL SAMPLE AND STRATIFIED BY RACE/ETHNICITY STRATUM

POSITIVE SOCIAL SUPPORT DOMAIN (PSS)		**2008**	**2010**	**2012**	**2014**	**p-value (Resilience)**	**p-value (Time* Resilience)**	**p-value (Race* Time* Resilience)**
FRIENDS		**Odds Ratio (95% CI)**	**Odds Ratio (95% CI)**	**Odds Ratio (95% CI)**	**Odds Ratio (95% CI)**			
ENTIRE SAMPLE REGARDLESS OF RACE	Low vs high PSS	1.39 (1.08-1.79)	1.10 (0.84, 1.46)	1.18 (0.88, 1.58)	1.05 (0.77, 1.42)	0.1603	0.1327	**0.0932**
AMONG OLDER WHITE AMERICANS	Low vs high PSS	1.06 (0.91, 1.24)	1.16 (0.98, 1.37)	1.14 (0.95, 1.36)	1.07 (0.88, 1.30)	0.1229	0.6761	n/a
AMONG OLDER AFRICAN AMERICANS	Low vs high PSS	1.35 (0.96, 1.92)	**1.57 (1.10, 2.25)**	1.27 (0.86, 1.87)	1.20 (0.79, 2.01)	**0.0314**	0.5032	n/a
AMONG OLDER NON-WHITE NON-AFRICAN AMERICANS	Low vs high PSS	1.86 (0.96, 3.59)	0.74 (0.36, 1.53)	1.14 (0.53, 2.41)	0.89 (0.40, 1.94)	0.7422	**0.0339**	n/a
NEGATIVE SOCIAL SUPPORT DOMAINS (NSS)								
CHILDREN								
ENTIRE SAMPLE REGARDLESS OF RACE	Low vs high NSS	0.82 (0.64, 1.06)	0.97 (0.74, 1.28)	1.13 (0.84, 1.50)	1.20 (0.88, 1.63)	0.8592	**0.0794**	**0.0824**
AMONG OLDER WHITE AMERICANS	Low vs high NSS	**0.78 (0.68, 0.90)**	**0.70 (0.60, 0.82)**	**0.73 (0.62, 0.86)**	**0.78 (0.66, 0.94)**	**<0.0001**	0.4032	n/a
AMONG OLDER AFRICAN AMERICANS	Low vs high NSS	0.86 (0.59, 1.25)	0.99 (0.67, 1.43)	1.07 (0.70, 1.62)	1.00 (063, 1.57)	0.3616	0.8546	n/a
AMONG OLDER NON-WHITE NON-AFRICAN AMERICANS	Low vs high NSS	0.83 (0.44, 1.58)	1.33 (0.65, 2.70)	1.83 (0.87, 3.86)	2.20 (0.99, 4.87)			n/a
OTHER FAMILY								
ENTIRE SAMPLE REGARDLESS OF RACE	Low vs high NSS	0.80 (0.63, 1.02)	1.14 (0.88, 1.48)	1.04 (0.79, 1.35)	0.95 (0.70, 1.28)	0.8091	**0.0455**	**0.0357**
AMONG OLDER WHITE AMERICANS	Low vs high NSS	**0.75 (0.66, 0.86)**	**0.77 (0.67, 0.89)**	**0.75 (0.64, 0.88)**	**0.76 (0.64, 0.90)**	**<0.0001**	0.9753	n/a
AMONG OLDER AFRICAN AMERICANS	Low vs high NSS	**0.69 (0.49, 0.99)**	1.12 (0.77, 1.62)	0.89 (0.60, 1.33)	**0.64 (0.41, 0.99)**	**0.0263**	**0.0289**	n/a

AMONG OLDER NON-WHITE NON-AFRICAN AMERICANS	Low vs high NSS	0.99 (0.54, 1.81)	1.72 (0.89, 3.34)	1.67 (0.86, 3.26)	1.77 (0.83, 3.79)	0.3552	0.3889	n/a
IMMEDIATE FAMILY (SPOUSE & CHILDREN)								
ENTIRE SAMPLE REGARDLESS OF RACE	Low vs high NSS	0.93 (0.72, 1.19)	1.10 (0.85, 1.43)	1.03 (0.79, 1.36)	1.04 (0.78, 1.39)	0.8218	0.5856	**0.0186**
AMONG OLDER WHITE AMERICANS	Low vs high NSS	0.90 (0.78, 1.05)	**0.83 (0.71, 0.97)**	**0.76 (0.64, 0.89)**	0.89 (0.74, 1.06)	**0.0055**	**0.0824**	n/a
AMONG OLDER AFRICAN AMERICANS	Low vs high NSS	0.76 (0.54, 1.08)	0.98 (0.68, 1.39)	1.23 (0.84, 1.81)	0.78 (0.51, 1.19)	0.7903	**0.0384**	n/a
AMONG OLDER NON-WHITE NON-AFRICAN AMERICANS	Low vs high NSS	1.16 (0.63, 2.16)	1.65 (0.85, 3.22)	1.19 (0.60, 2.36)	1.61 (0.78, 3.33)			n/a
ALL RELATIONSHIP CATEGORIES								
ENTIRE SAMPLE REGARDLESS OF RACE	Low vs high NSS	0.82 (0.65, 1.03)	1.09 (0.85, 1.41)	1.08 (0.83, 1.40)	1.04 (0.79, 1.38)	0.9918	**0.0576**	**0.0052**
AMONG OLDER WHITE AMERICANS	Low vs high NSS	0.90 (0.78, 1.04)	0.87 (0.75, 1.01)	**0.82 (0.70, 0.96)**	0.90 (0.76, 1.07)	**0.0185**	0.5888	n/a
AMONG OLDER AFRICAN AMERICANS	Low vs high NSS	**0.71 (0.51, 0.99)**	0.93 (0.66, 1.32)	1.18 (0.81, 1.72)	0.69 (0.46, 1.04)	0.3499	**0.01**	n/a
AMONG OLDER NON-WHITE NON-AFRICAN AMERICANS	Low vs high NSS	0.86 (0.48, 1.54)	1.61 (0.84, 3.09)	1.28 (0.66, 2.48)	1.82 (0.89, 3.72)	**0.050**	0.1643	n/a

CI=confidence interval. Odds Ratios in bold are statistically significant. Models adjusted for age, sex, education, race, marital status, BMI, cigarette use and alcohol consumption and interaction terms for race* time, resilience*time as well as three-way terms for race * resilience*time

CHAPTER 6

THE RELATIONSHIP OF RACE, PSYCHOSOCIAL STRESS AND RESILIENCY INDICATORS TO NEUROCOGNITIVE IMPAIRMENT AMONG OLDER AMERICANS ENROLLED IN THE HEALTH AND RETIREMENT SURVEY: A CROSS-SECTIONAL STUDY[1]

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Abstract

Background: Race/ethnicity, toxic stress (TS), resiliency promoting factors (RPFs) and their interactions were investigated in relationship to neurocognitive impairment (NI) in a nationally representative sample of adult Americans >=50 years enrolled in the Health and Retirement Study (HRS) between 2012 and 2014.

Methods: TS comprised experiences of everyday discrimination and chronic stressors, RPF included global and domain-specific mastery, social support measures. Race/ethnicity was self-reported as black, white, or Other. NI was operationally defined as self-reported physician diagnosis of Alzheimer's disease or dementia plus a total cognition score ≤10 on the modified TICS scale. Multivariable logistic regression models estimated race, TS, RPF associated odds ratios (ORs) and 95% confidence intervals (CIs) with adjustment for comorbidity, lifestyle, and socio-demographic confounders.

Results: Chronic stress (OR 1.31, 95%CI: 1.01, 1.70) and discrimination (OR 2.51, 95% CI: 1.75, 3.59) were associated with higher NI risk while high vs. low mastery (OR 0.61, 95%CI: 0.47, 0.77) was associated with lower NI risk. High vs. low mastery-associated lower NI risk was evident among adults that denied experiencing discrimination (OR 0.57, 95%CI: 0.44, 0.74) but not among those that reported experience of discrimination (OR 0.93, 95%CI: 0.47, 1.81). Relative to White/Other race, African American race was associated with NI risk but only in the sub-group that achieved high mastery (OR 1.83, 95%CI: 1.20, 2.80).

Conclusion: Among older US adults, everyday discrimination, chronic psychosocial stress, and low mastery were associated with worse cognition. The cognitive disadvantage for high mastery African American vs. White/Other race adults suggests that adverse social

experiences may overwhelm the cognitive benefit of high mastery in status-inconsistent individuals. Reduction of TS and implementing policies that disincentivize unequal treatment by race/ethnicity in social life and in health, justice and economic systems may promote successful cognitive aging in adult Americans.

Keywords: toxic stress; resilience promoting factors; everyday discrimination; neurocognitive impairment; minority race; older Americans

Introduction

As of 2014, an estimated 33% of the United States (US) population self-identified as a member of a racial or ethnic minority group.[1] By the year 2050, an estimated 50% of the US population will be represented by individuals of racial/ethnic minority background [2] such as Hispanic /Latino, Black/African American, Asian / Pacific Islander, and American Indian/Alaska natives.

Despite being a highly diverse country, few aspects of American life are free of racial tension that sometimes manifests as explicit racism- i.e., actions guided by the belief that members of one or more races are inferior to members of another race. In the US, racism benefits the political, economic, social and cultural interests of white Americans at the expense of racial and ethnic minority groups and takes three major forms: institutionalized, personally mediated and internalized racism.[3] Institutionalized racism is structurally maintained by policies that promote racial inequity in experiences and outcomes in the realm of politics, medicine and access to healthcare, housing, education, employment and criminal justice systems.[4,5] Personally mediated racism, on the other hand, refers to attitudes and beliefs about the inferiority of minority racial groups (prejudices) and differential treatment of people based on race (discrimination) which is directly experienced at the individual level. Internalized racism, as opposed to personally mediated racism which has an identifiable perpetrator, refers to the acceptance of negative socio-cultural beliefs about the intrinsic worth of one's own racial group.[6]

Experiences of racial discrimination by minority groups may impact physical and mental health outcomes directly through elevated risk of incarceration, physical injury, patterns of police brutality or death. Recent data on police-involved fatalities suggests that Black males are 3.2 -

3.5 times and Hispanic males 1.4-1.7 times more likely to be killed by law enforcement than White males in their life time.[7-9] More recently, several high profile cases of police killings of unarmed Black men and women in this country have drawn public attention to the use of lethal force by law enforcement.[10] There is also extensive social justice literature on disparities in the juvenile justice system making the classroom to prison pipeline that is systemically designed to maintain high percentage of African Americans and Hispanics in and out of jail/prison.[11-13] Less immediately dangerous but highly prevalent forms of racial discrimination such as micro-aggression, lack of respect or courtesy in the work place and minority status-related psychosocial stress have been associated with sub-optimal physical [14-16] and mental health outcomes.[17,18] High levels of psychosocial stressors that exceed coping resources – i.e. resilience-enhancing factors, manifest as toxic stress (TS). Individuals with sufficient coping resources are expected to demonstrate a resilient trajectory and maintain high levels of physical and mental functioning despite high levels of stress-related adversity.[19,20] Resilience promoting factors (RPF) may include personality traits such as high mastery or contextual resources such as social support that enable individuals to behaviorally resist or down-modulate adverse effects of stressful experiences.[21] Toxic stress has been associated with cognitive dysfunction in the domains of learning and memory.[22] Abundant literature documents black-white differences in neurocognitive aging [23-25] but specific investigation of toxic psychosocial stress as a potential mediator or moderator of racial differences in neurocognitive decline or cognitive reserve has not been done. Further still, although extensive research has demonstrated lifelong sequalae of adverse childhood experiences in older adults [26-28] little information is available regarding the potentially mitigating role of RPF as moderators of adverse neurocognitive aging.[29,30]

Conditions associated with neurocognitive impairment including Alzheimer's disease and other forms of dementia [31] are among the leading causes of death in the United States, with Alzheimer's disease ranking sixth.[32] The estimated prevalence of dementia among Americans older than 70 years of age in 2010 was 14.7% and is projected to rise with increased life expectancies.[33,34] Additionally, the social and economic costs of dementia among elderly Americans are rising, for instance, in 2010, the total monetary cost of dementia in the United States was estimated between $159 - $215 billion.[33] Despite this, we still have a limited understanding of associated risk factors for dementia.

Psychosocial factors such as stressful life experiences have been identified as a major concern in the etiology and treatment of depression. This research, grounded in the Stress Process Model (SPM), directly informs present gaps in the understanding of TS and RPF as potential mediators or moderators of racial differences in neurocognitive impairment. The SPM postulates that psychosocial resources may impact health directly or indirectly by buffering the negative impacts of stressors.[35] This study specifically examines whether TS and RPF are associated with neurocognitive impairment (NI) in a nationally representative sample of semi-retired and retired older American adults. The following specific hypotheses are tested: a) higher levels of TS and lower levels of RPF are associated with higher rates of neurocognitive impairment in older American adults, b) the relationship between race/ethnicity and NI varies according to levels of TS and RPF and c) respective relationships between TS, RPF and NI in older adults vary according to race ethnicity.

Methods

We conducted a cross-sectional secondary data analysis of older semi-retired or retired American Adults enrolled in the Health and Retirement Study (HRS) between 2012 and 2014. The HRS is an ongoing biennial study of U.S. adults aged 51 years and older that began in 1992 with the aim of improving our understanding of the social, economic, environmental, and behavioral factors associated with aging and the health of older adults. The study population includes a representative sample of about 20,000 Americans along with their spouses or partners who may be younger than 50 years.[36] Data combines two waves of HRS, that is, HRS 2012 and HRS 2014 as half the sample randomly received the psychosocial leave behind (PLB) questionnaire in each wave. Furthermore, modules that require only a one-time collection such as items on early life trauma, life course stressors, and relationships with parents were omitted from the PLB after 2014 as they have been asked multiple times and many new constructs added.[37] This analysis includes participants with TS, RPF and cognition measures.

Measures

Primary Determinants: Race/ethnicity, Toxic Stress and Resilience promoting factors

Race/ethnicity was self-reported and categorized as non-Hispanic Black/African American (AA), non-Hispanic White/ Caucasian (White) or Other race, i.e., Hispanic or Latino.[38] Briefly, TS was assessed across several domains and included: experiences of everyday discrimination, ongoing chronic stressors and perceived constraints on personal control.[37] Measures of everyday discrimination were six questions that tap into the hassles and chronic stress associated with perceived everyday discrimination and comprised “character assaults” that tend to occur daily. Ongoing chronic stressors included eight items that capture current and

ongoing problems that have lasted twelve months or longer. Perceived constraints on personal control were five items that capture a sense of lack of control of things going on around an individual. [37]

Resilience promoting factors (RPF) on the other hand included global mastery, domain-specific control of finances, health and social life, and measures of social support from spouses, children, relatives and friends. Global mastery included five questions getting at one's resolve at attaining goals. Domain-specific mastery of health, social life and finances was measured via a single-item measure assessing the amount of control for each aspect on a 10-point scale that ranged from ''no control at all'' to ''very much control'', with higher scores indicating greater domain-specific mastery. [37] Measures of social support included four sets of seven items that examined the level of social support received from spouses/partners, children, other family members and friends. For each relationship category were three positively worded items - positive social support (PSS) and four negatively worded items - negative social support (NSS). We created additional constructs to sum up social support responses from immediate family (spouses and children), extended family (friends and other family members), and all four relationship groups (spouses, children, other family members and friends).

Details regarding the items that constitute TS and RPF constructs as well as their scoring processes have been described elsewhere.[37] Additionally, for participants with one or two missing items, the score was rescaled to the theoretic maximum for each construct by taking the sum of the items present and dividing it by the number of items present. This quotient was then multiplied by the maximum number of items that could be present. This final number was then

rounded to a whole number. All combinations of missing items were accounted for when calculating a score for participants missing two items.

Other measures

Age was assessed by self-reported date of birth and was modeled categorically in 10-year increments. Other covariates included sex, years of education completed, marital status, access to health insurance, body mass index (BMI) and health habits, such as having ever smoked and current alcohol use. The following physician-diagnosed conditions were included in the analysis: high blood pressure, heart disease (HD), stroke, Type 2 Diabetes (T2DM), psychiatric disorders, cancer, arthritis, and lung disease. For the purposes of modeling, a comorbidity index was created to sum up individuals with comorbid HD, T2DM and stroke, as these conditions are considered important risk factors for neurocognitive impairment and have similar metabolic pathways.[39,40]

Outcome

Neurocognitive Impairment (NI) was defined as a composite score summing up those who reported a physician diagnosis of Dementia, Alzheimer's disease or had a total cognition score ≤ 10 on the cognitive functioning tests administered in the HRS. The HRS assesses cognitive function using the modified Telephone Interview for Cognitive Status (TICSm), a validated cognitive screening tool that has been widely used in population-based studies to evaluate cognition.[41,42] Briefly, individual cognitive functioning measures include immediate and delayed word recall, the serial 7s test, counting backwards, naming tasks such as date naming, and vocabulary questions. These measures are summed up into three summary indices; a total recall index for the immediate and delayed word recall tasks, a mental status index that sums

scores from counting, naming and vocabulary tasks, and a total cognition score that sums total recall and mental status indices.[43] Additionally, HRS participants are asked two questions- on physician diagnosis of Alzheimer's disease, and dementia, senility or any other serious memory impairment. Cognition data are collected from all participants each wave. For purposes of analysis, NI included those with a physician diagnosis of Alzheimer's disease, Dementia or had a total cognition score ≤ 10 from HRS 2014 data.

Data analysis

Race, TS, and RPF were analyzed as predictors in relation to presence of NI over two years. First, descriptive analyses determined the distribution of baseline TS, race, RPF, and frequency of NI over 2 years. Bivariate associations were implemented to determine crude associations for NI with race, TS, RPF, potential confounders and sociodemographic factors. Since both TS and RPF were analyzed as categorical variables, chi square tests were used to evaluate differences in proportion of NI. Factors with a p-value ≤0.2 were further evaluated in multivariable models as candidate confounders. Multivariable logistic regression models were used to estimate odds ratios (ORs) and 95% confidence intervals (CIs) with adjustment for candidate confounders such as age, sex, education, alcohol consumption, and comorbidity due to diabetes, heart diseases and stroke. A series of incremental nested models were implemented, beginning with crude models, followed by models with sociodemographic factors adjusted for, and models adjusting for sociodemographic factors as well as TS. The final models further adjusted for RPF. Additionally, separate regression models evaluated interaction between race/ethnicity and respective TS and RPF and the potential for interaction between TS and RPF. P-values for interaction effects were set at $p < 0.10$ because the power of statistical tests for

higher order terms is generally lower than for first-order terms.[44,45] When potential interactions were indicated, stratum specific results were presented. All results were adjusted for the complex sampling design of the HRS.[46] All analyses were implemented with SAS software, version 9.4 (SAS Institute, Cary, NC).

Results

Included were 6317 respondents interviewed between the years 2012 and 2014 and ranged in age from 55 and 104 years of age. The analytic sample included 83% non-Hispanic White, 13% Black/African American, and 4% Other race (includes Hispanics). Majority of the sample were female (60%), 62% were married/partnered, 46% had some college education or more, 50% had a cardiometabolic diagnosis (HD, T2DM, or stroke), and about 5% were neurocognitively impaired. Of note nearly half (49%) reported ≥ three comorbid conditions. (Table 6.1).

Across race groups, the proportions of individuals reporting TS varied significantly at baseline for experiences of everyday discrimination ($p < 0.0001$), chronic stressors ($p = 0.008$) and personal constraints ($p = 0.0009$) and were higher amongst minority groups. Similarly, the prevalence of NI was higher among minority groups relative to Whites ($p = 0.04$, Table 6.2). Sociodemographic factors, BMI, and lifestyle fac-tors measured at baseline by race are reported in Supplementary Table 6.1.

Race is not associated with cognitive impairment, but disparities persist according to level of mastery.

Unadjusted for confounding covariates, the odds of NI were 76% elevated (OR = 1.76, 95% CI: 1.21–2.56) Black vs. White Americans. However, this association was not robust to adjustment for socio-demographic confounders, comorbidity, and resiliency indicators (Table 6.3). However, race-related differences in risk of NI were dependent on the level of mastery among older Americans (mastery x race, $p = 0.027$; Figure 6.1). On one hand, among Americans with high mastery, African American race was associated with 100% increased odds of NI, relative to Caucasian race (OR = 2.00, 95% CI: 1.20–3.35), and with 76% increased odds of NI relative to Other race (OR = 1.76, 95% CI: 0.63–4.93), but the odds of NI was similar for those that identified as Other relative to Caucasian race (OR = 1.14, 95% CI: 0.42–3.07). On the other hand, among American adults with low mastery, race-related differences in odds of NI were absent. Specifically, African American race was on average associated with lower NI odds relative to Caucasian American race (OR = 0.72, 95% CI: 0.41–1.26) and Other race (OR = 0.43, 95% CI: 0.16–1.14) while Other vs. Caucasian race was associated with 68% higher NI odds (OR = 1.68, 95% CI: 0.68–4.13).

High Toxic Stress is associated with higher NI; relationship varies by mastery level and age

The odds of NI, was elevated for adults that reported high vs. low levels of chronic stress (OR = 1.88, 95% CI: 1.43–2.49), the experience of one or more vs. no everyday discrimination (OR = 4.05, 95% CI: 2.61–6.30) and having high vs. low perceived constraints (OR = 2.91, 95% CI: 2.03–4.17) in unadjusted models (Table 6.3). The magnitude of these associations was down modulated, but remained statistically robust, with sequential adjustment for socio-demographic

factors, lifestyle factors, comorbidity, and toxic stress (Model 3) and RPF (Model 4, Table 6.3). However, the magnitude of discrimination-related differences in risk of NI varied according to level of mastery (discrimination x mastery, $p = 0.0297$; Figure 6.1). Specifically, the experience of any vs. no discrimination was associated with twice the odds of NI (OR = 1.95, 95% CI: 1.09–3.46) among adults with low mastery and 5.4 times the odds of NI (OR = 5.42, 95% CI: 2.99–9.83) among adults with high mastery. Furthermore, low vs. high stress associated risk of NI varied according to age (chronic stress x age, $p = 0.022$; Figure 6.2) and with stress-related elevation of NI risk evident among older Americans aged ≤ 70 years (OR = 3.66, 95% CI: 1.84–7.27) but not among individuals aged 71–79 years (OR = 1.35, 95% CI: 0.85–2.16) or ≥ 80 years old (OR = 1.09, 95% CI: 0.75–1.67).

Low RPF is associated with higher NI Risk; relationship varies by race and the experience of discrimination

Low vs. high levels of RPF were consistently associated with higher odds of NI (OR = 1.93–2.40, 95% CI: 1.46–3.38) in unadjusted models. This association was down modulated with adjustment for confounding covariates but the odds of NI remained elevated for adults reporting low vs. high levels of perceived global and domain specific mastery (OR = 1.70–2.02, 95% CI: 1.31–2.85) and for individuals reporting low vs. high positive social support from key relationships (OR = 1.45, 95% CI: 0.95–2.21; Table 6.3). However, the relationship between global mastery and NI differed according to the race/ethnicity of older Americans (mastery x race, $p = 0.027$; Figure 6.3). Specifically, low vs. high mastery was associated with higher odds of NI among Whites (OR = 1.87, 95% CI: 1.36–2.58) and among Americans of Other race (OR = 2.76, 95% CI: 0.67–11.40) but not among Blacks (OR = 0.67, 95% CI: 0.35–1.28). Likewise,

low vs. high mastery was associated with 100% increase in odds of NI (OR = 2.01 95% CI: 1.51–2.68) among older Americans without the social experience of everyday discrimination but no relationship was evident between mastery and NI (OR = 0.72, 95% CI: 0.32–1.62) among Americans that reported one or more experiences of everyday discrimination.

Increasing age is associated with higher risk of NI; relationship varies by level of stress

Increasing age was also associated with higher odds of NI (OR = 1.36–4.73, 95% CI: 0.86–7.43) in unadjusted models. This association was down modulated with adjustment for confounders, but the odds of NI remained elevated for adults ≥ 80 years old compared to adults aged ≤ 70 years (OR = 4.34, 95% CI: 2.74–6.87; Supplementary Table 6.2). Of note, age-related differences in NI odds varied according to high vs. low chronic stress (chronic stress x age, p = 0.022; Figure 6.2). Specifically, among adults with low levels of chronic stress, the odds of NI was respectively twice (OR = 2.27, 95% CI: 1.23–4.19) and nearly eight (OR = 7.72, 95% CI: 4.28–13.91) times as high for adults 71–79 years and ≥80 years old compared to adults aged ≤70 years. Among older Americans with high chronic stress on the other hand, the odds of NI was comparable for adults 71–79 vs. ≤70 years old (OR = 0.84, 95% CI: 0.45–1.58), and was elevated but to a lower degree for adult Americans ≥80 vs. ≤70 years old (OR = 2.30, 95% CI: 1.22–4.34).

Other Factors associated with increased risk of NI

Among other factors, lower education status and having comorbid HD, T2DM or stroke were associated with increased risk of NI after controlling for TS, RPF and potential confounders, (Supplementary Table 6.2).

Discussion

In this population-based cohort study of 6317 older Americans, we found that higher levels of Toxic stress (TS) – i.e. toxic stress and discrimination, and lower levels of resilience indicators e.g., mastery, were associated with an increased risk for neurocognitive impairment (NI). Furthermore, we found novel empirical evidence that in the presence of discrimination (a toxic stressor), the benefit of high mastery for cognitive reserve is muted. These findings were consistent with our study hypothesis and align with prior research among adults with trauma that associated the presence of post-traumatic stress disorder (PTSD) with a greater NI risk.[47] These findings are also in line with previously reported higher perceived stress related to worse cognitive function and stress associated with more rapid cognitive decline in a community-based study of Black and White American adults.[48] Support for these associations is found in studies relating stress that occurred earlier in the life-course (i.e., childhood adversity or trauma exposure) with neuropsychiatric morbidity- specifically depression, anxiety [49] and adverse cognitive function in adulthood. [50] Furthermore, studies on rodents provide mechanistic insight underlying the findings of this large epidemiological study by demonstrating that psychological stress is associated with detectable cellular changes in regions of the hippocampus, decreased proliferation of neurons in the dentate gyrus, and with loss of hippocampal volume resulting in atrophy and cognitive deficits.[51-57]

We also confirm previous studies that have identified advanced chronologic age, [58] low educational attainment [24,59] and the presence of metabolic chronic disease [60-62] as important determinants of NI. In line with some [24,48] but not all prior studies, we found limited evidence of substantial race-related differences in rates of NI in this diverse sample of older American

adults. Data from this study suggests that the strength and consistency of psychosocial adversity-i.e. TS and RPF, associated NI risk was generally stronger than race-related differences in NI risk. While overall difference in NI risk by race was limited, our study expands the scope of knowledge pertaining to how disparate social experiences by race may accentuate disparity in cognitive function among older Americans because African-American vs. White or Other race-associated disadvantage in NI persisted among Americans that achieved higher levels of mastery. Of note, mastery is an indicator of intrinsic capacity for control, self-efficacy, competency or demonstrated effectiveness at achieving personal and social goals. Over-represented in the high end of mastery would be older Americans of higher socioeconomic status (education, occupation, income) and by extension, those with above average access to health care resources and the wherewithal to benefit from self-directed health agency to counteract a health risk.

High mastery status is expected to be neuro-protective regardless of race. Unlike older Americans of White or Other race, the expected benefit of achieving high mastery for cognitive reserve, is muted or absent for older African American adults in this study. This observation is similar to previously reported higher levels of allostasis for Black and Mexican Americans relative to White Americans with a college degree or higher, whereas allostasis was similar across race groups among adults with low educational achievement in same study.[63] Race is a well described social determinant of stress and overall wellbeing in the United States.[64-66] Prior data shows that Black Americans of higher educational status report high frequency of experienced micro-aggression and work-place discrimination and more frequently report being in jobs below their qualification level [67]. Both the nature and frequency of everyday discrimination varies according to race, with African Americans more frequently on the receiving end of the

most insidious forms of discrimination in occupational and social interactions – whether in healthcare, educational, financial, law enforcement and judicial systems.[67,68] Common experiences of discrimination related psychosocial stressors, such as receiving less respect, poorer services, being considered unintelligent, being perceived as threatening, not receiving benefit of the doubt and numerous other forms of adverse social experiences are more frequent among individuals of African American descent, [69-71] do not change substantially by objective mastery level and mediate higher risk of adverse physical, [69,72-75] and reproductive health outcomes.[76-78] Our data suggests that the differential amplification of psychosocial adversity-likely due to status inconsistency for high African Americans with high mastery, successfully overwhelms the expected neuroprotective benefit of mastery for high mastery African American relative to high mastery Americans of White or Other race.

The implementation of a large nationally representative study using rigorous analytic approaches adjusted for multiple confounders are an important strength of this study. An additional strength and novel contribution of the present study lies in the evaluation of multiple indicators of toxic stress and resiliency as proxies for social experiences that affect cognitive aging. Limitations of the present study include its cross-sectional design which limits causal inference due to potential for residual confounding by unmeasured factors and inability to infer temporal sequence. Further limitation lies in low statistical power to evaluate heterogeneity in relationship of social determinants to NI particularly within the stratum of Other race.

Conclusion

Maintaining cognitive reserve is crucial for promoting healthy life span and acceptable quality of life in advanced age.[79-81] This study provided empirical evidence that high psychosocial adversity and low levels of RPF are important social determinants of NI and impaired cognitive reserve in a diverse sample of older US adults. African American race was associated with cognitive disadvantage, but only in the status inconsistent context of high mastery. Regardless of race, the benefit of high mastery for cognitive reserve among older Americans was muted among those that reported experience of discrimination. Therefore, policy interventions that decrease psychosocial stress and opportunities that enhance social equity are needed to promote healthy cognitive aging regardless of race. However, specific social policies/interventions to mitigate psychosocial adversity associated cognitive impairment must be tailored by race to maximize its effectiveness.

Supplementary Materials: Page: 141

The following are available online at www.mdpi.com/xxx/s1

Table S1: Demographic characteristics of older American adults enrolled in the HRS 2012-14 sample by Race, Table S2: Other factors in relation to risk for Neurocognitive impairment among older adults from HRS 2012-14, and Table S3: The relationship between Race and Neurocognitive Impairment with or without adjustment for Toxic Stress or Resilience promoting factors.

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Informed Consent Statement: Not applicable

Data Availability Statement: Publicly available datasets were analyzed in this study. This data can be found here:https://hrs.isr.umich.edu/data-products/access-to-public-data

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Tables and Figures

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Table 6.1: Demographic characteristics of American adults enrolled in the HRS 2012-2014 sample by cognitive function status

Characteristic	All (*N* = 6317)	Normal (*N* = 6019)	Impaired (*N* = 298)	*p*-Value
	N (%)	*N* (%)	*N* (%)	
Age: mean (SD)	73.9 (6.7)	73.7 (6.5)	78.7 (8.1)	
Age categories (years)				<0.0001
≤70	2076 (32.9)	2025 (33.6)	51 (17.1)	
71–79	3055 (48.4)	2942 (48.9)	113 (37.9)	
>80	1186 (18.7)	1052 (17.5)	132 (45.0)	
Sex: Female	3764 (59.6)	3601 (59.8)	163 (54.7)	0.0782
Marital Status				0.0002
Never married	177 (02.8)	167 (02.8)	10 (03.3)	
Married/partnered	3910 (61.9)	3761 (62.5)	149 (50.0)	
Separated/Divorced	672 (10.6)	633 (10.5)	39 (13.1)	
Widowed	1558 (24.7)	1458 (24.2)	100 (33.6)	
Education				<0.0001
Less than High School/GED	1326 (21.0)	1203 (20.0)	123 (41.3)	
High-school graduate	2062 (32.6)	1979 (32.9)	83 (27.8)	
Some college and above	2927 (46.4)	2835 (47.1)	92 (30.9)	
Race				0.0414
White/Caucasian	5217 (82.6)	4987 (82.8)	230 (77.2)	
Black/AA	815 (12.9)	765 (12.7)	50 (16.8)	
Other	285 (04.5)	267 (04.4)	18 (06.0)	
Have Health Insurance	6081 (98.1)	5810 (98.1)	271 (97.1)	0.2474
Ever smoked	3459 (55.2)	3299 (55.2)	160 (54.2)	0.7745
Current alcohol use	3209 (50.8)	3120 (51.8)	89 (29.9)	<0.0001
No. of comorbidities ever had				<0.0001
None	424 (06.7)	410 (06.8)	14 (04.7)	
One	1096 (17.3)	1061 (17.6)	35 (11.7)	
Two	1719 (27.2)	1665 (27.7)	54 (18.1)	
Three or more	3077 (48.7)	2882 (47.9)	195 (65.4)	
Diagnosis of HD, T2DM or Stroke	3177 (50.2)	2973 (49.4)	204 (68.5)	<0.0001
Measures of Toxic Stress				
Chronic stressors				0.005
Low	4542 (71.9)	4349 (72.2)	193 (64.8)	
High	1775 (28.1)	1670 (27.8)	105 (35.2)	
Everyday discrimination				<0.0001
Zero	5888 (94.3)	5638 (94.8)	250 (84.5)	
One or more	357 (05.7)	311 (05.2)	46 (15.5)	
Perceived constraints				<0.0001
Low	4262 (67.8)	4122 (68.9)	140 (47.0)	
High	2021 (32.2)	1863 (31.1)	158 (53.0)	
Measures of resilience				
Personal mastery				<0.0001
Low	2206 (34.9)	2049 (34.0)	157 (52.7)	

High	4111 (65.1)	3970 (66.0)	141 (47.3)	
Control over Health				<0.0001
Low	2794 (45.6)	2624 (44.9)	170 (60.1)	
High	3329 (54.4)	3216 (55.1)	113 (39.9)	
Control over finances				<0.0001
Low	2375 (38.1)	2224 (37.4)	151 (51.7)	
High	3867 (61.9)	3726 (62.6)	141 (48.3)	
Control over social life				<0.0001
Low	1892 (30.3)	1748 (29.4)	144 (49.7)	
High	4345 (69.7)	4199 (70.6)	146 (50.3)	
Positive Social Support domains				
Immediate Family (Spouse & children)				0.0247
Low social support	2314 (38.6)	2188 (38.3)	126 (45.0)	
High social support	3678 (61.4)	3524 (61.7)	154 (55.2)	
Extended Family (Others & friends)				0.0095
Low social support	1473 (23.6)	1388 (23.3)	85 (30.0)	
High social support	4759 (76.4)	4561 (76.7)	198 (70.0)	
All Relationship groups combined				<0.0001
Low social support	841 (13.3)	772 (12.9)	69 (23.1)	
High social support	5462 (86.7)	5233 (87.1)	229 (76.9)	

Notes: SD = Standard Deviation. 02 missing education; 116 missing health insurance; 46 missing smoking status; 1 missing alcohol consumption; 72 missing measures of everyday discrimination; 34 missing perceived constraints; 194 missing information on control over health; 80 missing information on control over social life; 75 missing information on financial control; 325 missing information on positive social support from immediate family; 85 missing information on positive social support from extended family; 14 missing information on positive social support from all relationship groups combined.

Table 6.2: Distribution of Toxic Stress and Resilience promoting factors among American adults enrolled in the HRS 2012-2014 sample at baseline by Race

Characteristic	**All (*N* = 6317)**	**White/Caucasian (*N* = 5217)**	**Black/African American (*N* = 815)**	**Other (*N* = 285)**	
Dimensions of Toxic Stress	***N* (%)**	***N* (%)**		***N* (%)**	***p*-Value**
Chronic stressors					0.0084
Low	4542 (71.9)	3792 (72.7)	560 (68.7)	190 (66.7)	
High	1775 (28.1)	1425 (27.3)	255 (31.3)	95 (33.3)	
Everyday discrimination					<0.0001
Zero	5888 (94.3)	4925 (95.3)	716 (90.2)	247 (87.2)	
One or more	357 (5.8)	244 (4.7)	78 (9.8)	35 (12.8)	
Perceived constraints					0.0009
Low	4262 (67.8)	3538 (68.2)	561 (69.3)	163 (57.8)	
High	2021 (32.2)	1653 (31.8)	249 (30.7)	119 (42.2)	
Measures of resilience					
Personal mastery					0.9508
Low	2206 (34.9)	1820 (34.9)	288 (35.3)	98 (34.4)	
High	4111 (65.1)	3397 (65.1)	527 (64.7)	187 (65.6)	
Control over Health					0.2371
Low	2794 (45.6)	2330 (46.0)	351 (45.2)	113 (40.8)	
High	3329 (54.4)	2740 (54.0)	425 (54.8)	164 (50.2)	
Control over finances					0.1666
Low	2375 (38.1)	1989 (38.5)	280 (35.0)	106 (37.7)	

High	3867 (61.9)	3173 (61.5)	519 (65.0)	175 (62.3)	
Control over social life					0.0155
Low	1892 (30.3)	1594 (30.9)	207 (26.0)	91 (32.3)	
High	4345 (69.7)	3565 (69.1)	589 (74.0)	191 (67.7)	
Positive Social Support (All Relationship groups combined)					0.3237
Low social support	841 (13.3)	681 (13.1)	115 (14.2)	45 (15.8)	
High social support	5462 (86.7)	4525 (86.9)	697 (85.8)	240 (84.2)	
Neurocognitive impairment					0.0414
Normal	6019 (95.3)	4987 (95.6)	765 (93.9)	267 (93.7)	
Impaired	298 (4.7)	230 (4.4)	50 (6.1)	18 (6.3)	

Notes: 72 missing measures of everyday discrimination; 34 missing perceived constraints; 194 missing information on control over health; 80 missing information on control over social life; 75 missing information on financial control; 325 missing information on positive social support from immediate family; 85 missing information on positive social support from extended family; 14 missing information on positive social support from all relationship groups combined.

Table 6.3: Race, Toxic Stress and Resilience promoting factors in relation to risk for Neurocognitive impairment among older American adults enrolled in the HRS 2012-2014.

Variable	***n/N***	**Model 1 (Crude) ***	**Model 2 ɤ**	**Model 3 α**	**Model 4 †**
Race		**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**
Black (AA) vs. Caucasian	50/815	**1.76 (1.21, 2.56)**	1.33 (0.89, 1.99)	1.26 (0.82, 1.94)	1.32 (0.87, 2.00)
Other vs. Caucasian	18/285	**2.09 (1.18, 3.72)**	1.63 (0.95, 2.82)	1.45 (0.87, 2.43)	1.59 (0.93, 2.72)
Toxic stress indicators					
Everyday discrimination					
One or more experiences vs. None	46/357	**4.05 (2.61, 6.30)**		**3.31(2.12, 5.19)**	
Chronic stressors					
High vs. low chronic stress	105/1775	**1.88 (1.43, 2.49)**		**1.88 (1.42, 2.48)**	
Perceived constraints					
High vs. Low	158/2021	**2.91 (2.03, 4.17)**		**2.16 (1.52, 3.07)**	
Resilience indicators					
Perceived Mastery					
Low vs. High global mastery	157/2206	**2.38 (1.78, 3.20)**			**1.85 (1.38, 2.48)**
Positive social support from all groups					
Low vs. High	69/841	**1.89 (1.36, 2.62)**			1.45 (0.95, 2.21)
Domain-specific mastery					
Low vs. High control over health	170/2794	**2.04 (1.54, 2.70)**			**1.70 (1.31, 2.21)**
Low vs. High control over finances	151/2375	**1.93 (1.46, 2.57)**			**1.96 (1.44, 2.67)**
Low vs. High Social life	144/1892	**2.40 (1.70, 3.38)**			**2.02 (1.43, 2.85)**

Notes: OR (95% CI): Odds Ratios (95% Confidence Intervals); Bold indicates *p*-value < 0.05; * Model 1 are crude models. Models 2–4 are adjusted models. ɤ Model 2- adjusts for race and demographic factors, age, sex, education, alcohol consumption, smoking, BMI, and comorbidity due to Diabetes, Heart diseases and Stroke. α Model 3 adjusts for race and demographic factors, age, sex, education, alcohol consumption, smoking, BMI, and comorbidity due to Diabetes, Heart diseases and Stroke plus Toxic stress measures. † Model 4 adjusts for race and demographic factors, age, sex, education, alcohol consumption, smoking, BMI, and comorbidity due to Diabetes, Heart diseases and Stroke plus resilience indicators. Measures of toxic stress and indicators of resilience were not mutually adjusted for one another in any multivariable models.

Supplementary Tables

Supplementary Table 6.1: Demographic characteristics of older American adults enrolled in the HRS 2012-2014 sample by Race.

	All (N=6317)	White/ Caucasian (N=5217)	Black / African American (N=815)	Other (N=285)	
Characteristic	**N (%)**	**N (%)**	**N (%)**	**N (%)**	**p-value**
Age: mean(SD)	73.9 (6.7)	74.2 (6.7)	72.6 (6.3)	72.2 (6.0)	
Age categories (years)					< 0.0001
<=70	2076 (32.9)	1615 (31.0)	332 (40.7)	129 (45.3)	
71-79	3055 (48.4)	2555 (49.0)	382 (46.9)	118 (41.4)	
>80	1186 (18.8)	1047 (20.1)	101 (12.4)	38 (13.3)	
Sex					0.003
Female	3764 (59.6)	3077 (59.0)	528 (64.8)	159 (55.8)	
Marital Status					< 0.0001
Never married	177 (02.8)	113 (2.2)	48 (5.9)	16 (5.6)	
Married/ partnered	3910 (61.9)	3381 (64.8)	355 (43.6)	174 (61.0)	
Separated/Divorced	672 (10.6)	475 (9.1)	159 (19.5)	38 (13.3)	
Widowed	1558 (24.7)	1248 (23.9)	253 (31.0)	57 (20.0)	
Education					< 0.0001
Less than High School/GED	1326 (21.0)	961 (18.4)	255 (31.3)	110 (38.6)	
High-school graduate	2062 (32.6)	1751 (33.6)	255 (31.3)	56 (19.6)	
Some college and above	2927 (46.4)	2504 (48.0)	304 (37.4)	119 (41.8)	
Health Insurance					0.0003
Yes	6081 (98.1)	5033 (98.3)	783 (97.6)	265 (95.0)	
Ever smoked					0.6196
Yes	3459 (54.8)	2851 (54.6)	457 (56.1)	151 (53.0)	
Current alcohol use					< 0.0001
Yes	3209 (50.8)	2802 (53.7)	296 (36.3)	111 (38.9)	
No. of comorbidities ever had					< 0.0001
None	424 (06.7)	360 (6.9)	35 (4.3)	29 (10.2)	
One	1096 (17.3)	939 (18.0)	105 (12.9)	52 (18.2)	
Two	1719 (27.2)	1415 (27.1)	241 (29.6)	63 (22.1)	
Three or more	3077 (48.7)	2502 (48.0)	434 (53.2)	141 (49.5)	
Diagnosis of HD, T2DM or Stroke					< 0.0006
Yes	3177 (50.2)	2566 (49.2)	454 (55.7)	157 (55.1)	
Ever had High blood pressure					< 0.0001
Yes	4317 (68.5)	3443 (66.1)	678 (83.3)	196 (69.0)	
BMI					< 0.0001
BMI < 18.5 kg/m^2 (Underweight)	101 (1.6)	85 (1.6)	10 (1.2)	6 (2.1)	
BMI 18.5-24 kg/m^2 (Normal weight)	1736 (27.5)	1508 (28.9)	145 (17.8)	83 (29.1)	
BMI 25-29 kg/m^2 (Overweight)	2390 (37.8)	1976 (37.9)	305 (37.4)	109 (38.3)	
BMI ≥30 kg/m^2 (Obese)	2090 (33.1)	1648 (31.6)	355 (43.6)	87 (30.5)	

SD=Standard Deviation
Note: 02 missing education; 116 missing health insurance; 46 missing smoking status; 1 missing alcohol consumption; 14 missing High blood pressu

Supplementary Table 6.2: Other factors in relation to risk for Neurocognitive impairment among older adults from HRS 2012-2014.

Variable	n/N	Model 1 (Crude)*	Model 2[ɤ]	Model 3[α]	Model 4[†]
Age categories (years)		**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**
71-79 vs <=70	113/3055	**1.36 (0.86, 2.16)**	1.20 (0.76, 1.89)	1.25 (0.81, 1.95)	1.22 (0.78, 1.93)
>80 vs <=70	134/1186	**4.73 (3.01, 7.43)**	**4.0 (2.50, 6.50)**	**4.34 (2.74, 6.87)**	**3.82 (2.35, 6.21)**
Education					
Less than High School vs College and above	123/1326	**3.08 (2.22, 4.26)**	**2.07 (1.55, 2.78)**	**1.94 (1.43, 2.64)**	**2.04 (1.51, 2.75)**
High School vs College and above	83/2062	1.08 (0.75, 1.56)	0.86 (0.59, 1.24)	0.84 (0.58, 1.22)	0.85 (0.58, 1.24)
Marital Status					
Never married vs Married	10/177	1.81 (0.72, 4.54)	1.79 (0.71, 4.50)	1.64 (0.66, 4.05)	1.75 (0.69, 4.44)
Separated/divorced vs Married	39/672	**1.62 (1.10, 2.39)**	**1.65 (1.09, 2.49)**	**1.63 (1.09, 2.43)**	**1.67 (1.11, 2.51)**
Widowed vs Married	100/1558	**2.03 (1.42, 2.92)**	1.23 (0.81, 1.87)	1.23 (0.82, 1.84)	1.21 (0.80, 1.83)
Sex					
Male vs Female	135/2553	1.17 (0.91, 1.50)	**1.48 (1.13, 1.93)**	**1.44 (1.11, 1.87)**	**1.51 (1.17, 1.95)**
Body Mass Index					
Underweight vs normal	7/101	1.77 (0.81, 3.86)	1.59 (0.62, 4.07)	1.35 (0.42, 4.28)	1.48 (0.56, 3.93)
Overweight vs normal	106/2333	0.83 (0.58, 1.18)	0.86 (0.60, 1.22)	0.86 (0.61, 1.21)	0.85 (0.60,1.21)
Obese vs normal	89/2098	0.87 (0.59, 1.28)	0.89 (0.62, 1.29)	0.87 (0.60, 1.27)	0.88 (0.61, 1.27)
Alcohol consumption					
No vs Yes	209/3111	**2.59 (1.88, 3.57)**	**1.98 (1.43, 2.75)**	**1.97 (1.44, 2.69)**	**1.94 (1.40, 2.68)**
Cigarette smoking					
Yes vs No	161/3473	0.96 (0.76, 1.22)	0.96 (0.73, 1.27)	0.97 (0.73, 1.31)	0.94 (0.71, 1.25)
Health conditions					
Comorbid HD, Diabetes or Stroke					
Yes vs No	205/3183	**2.63 (1.84, 3.76)**	**2.04 (1.40, 2.98)**	**1.99 (1.37, 2.89)**	**1.98 (1.37, 2.86)**

Notes: Odds Ratios (95% Confidence Intervals); Bold indicates p-value<0.05.*Model 1 are crude models. Models 2-4 are adjusted models.
[ɤ] Model 2 adjusts for demographic factors, age, sex, race, education, alcohol consumption, smoking, BMI, and comorbidity due to Diabetes, Heart diseases and Stroke.
[α] Model 3 adjusts for demographic factors; age, sex, race, education, alcohol consumption, smoking, BMI and comorbidity due to Diabetes, Heart diseases and Stroke plus Toxic stress measures.
[†] Model 4 adjusts for demographic factors- age, sex, race, education, alcohol consumption, smoking, BMI and comorbidity due to Diabetes, Heart diseases plus Stroke and indicators of resilience.

Supplementary Table 6.3: The relationship between Race and Neurocognitive Impairment with or without adjustment for Toxic Stress or Resilience promoting factors.

			Model 1 (Crude)*	**Model 5‡**	
Characteristic	**Adjusted for**	**Association**	**OR (95% CI)**	**OR (95% CI)**	**p-value (Interaction)**
					Race*Discrimination
Race	Discrimination	Black (AA) vs Caucasian	**1.76 (1.21, 2.56)**	1.33 (0.74, 2.40)	0.3653
		Other vs Caucasian	**2.09 (1.18, 3.72)**	1.78 (0.89, 3.56)	
		Black (AA) vs Other	0.84 (0.42, 1.68)	0.75 (0.33, 1.69)	
					Race*Mastery
Race	Mastery	Black (AA) vs Caucasian	**1.76 (1.21, 2.56)**	1.20 (0.79, 1.82)	0.0272
		Other vs Caucasian	**2.09 (1.18, 3.72)**	1.38 (0.77, 2.47)	
		Black (AA) vs Other	0.84 (0.42, 1.68)	0.87 (0.44, 1.72)	
Other predictors					
					Discrimination*Mastery
Discrimination	Mastery	One or more experiences vs None	**4.05 (2.61, 6.30)**	**3.25 (2.14, 4.92)**	0.0297
					Mastery*Age
Mastery	Age	Low vs High global mastery	**2.38 (1.78, 3.20)**	**1.73 (1.28, 2.34)**	0.5851
					Discrimination*Age
Discrimination	Age	One or more experiences vs None	**4.05 (2.61, 6.30)**	**2.76 (1.87, 4.08)**	0.1379
					Chronic stress*Age
Chronic stress	Age	High vs low chronic stress	**1.88 (1.43, 2.49)**	**1.75 (1.28, 2.41)**	0.0218

Notes: OR (95%CI): Odds Ratios (95% Confidence Intervals); Bold indicates p-value<0.05; *Model 1 are crude models.
‡Models 5 adjust for race and demographic factors- age, sex, education, alcohol consumption, smoking, BMI, and comorbidity due to Diabetes, Heart diseases plus Stroke and resilience indicators. Interaction terms have been added as well.

Figures

Figure 6.1: Race and discrimination-related differences in risk of Neurocognitive Impairment vary within strata of mastery

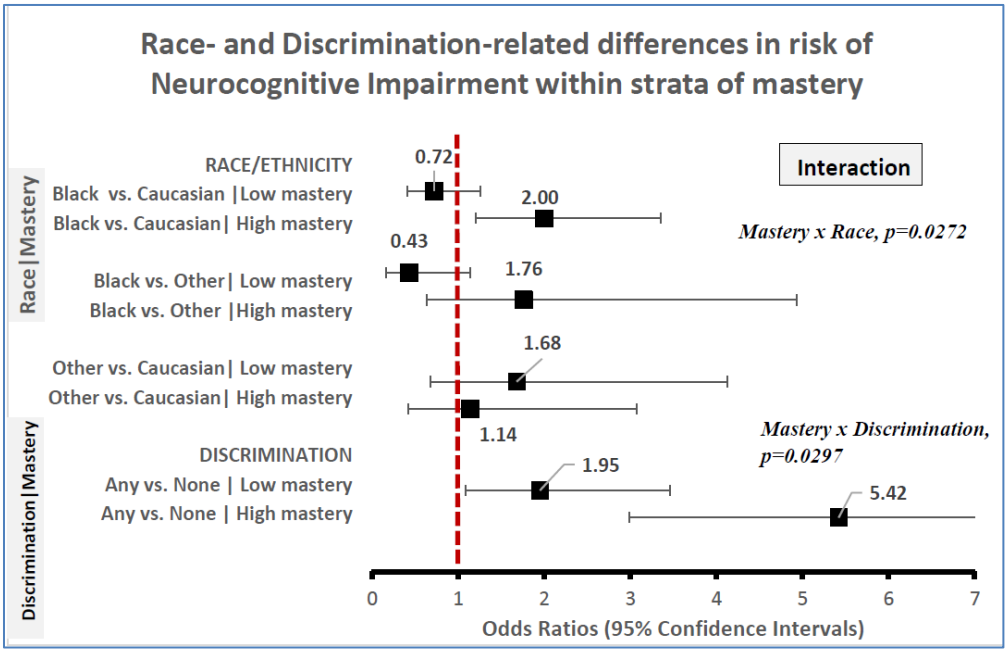


Figure 6.2. Heterogeneity in age and chronic stress-related associations for risk of Neurocognitive impairment

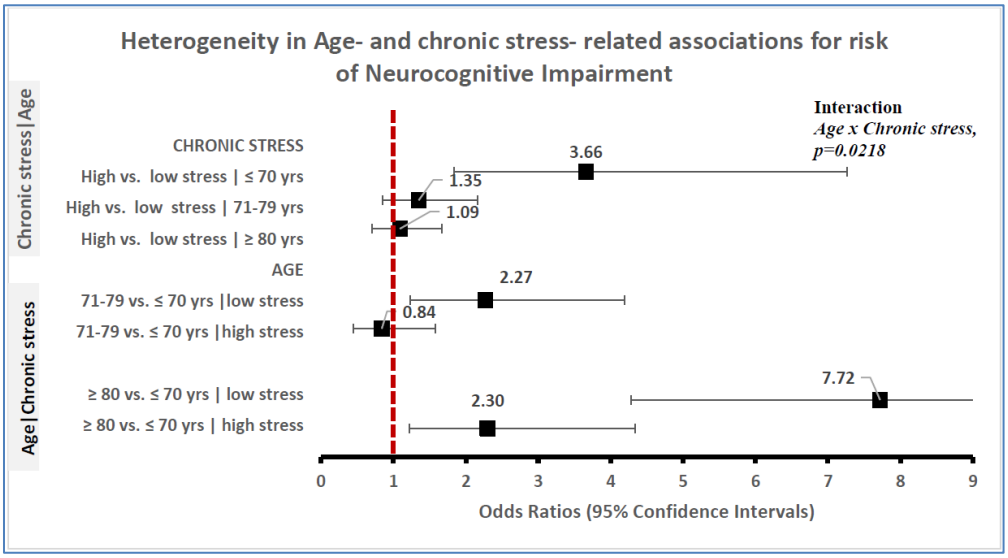
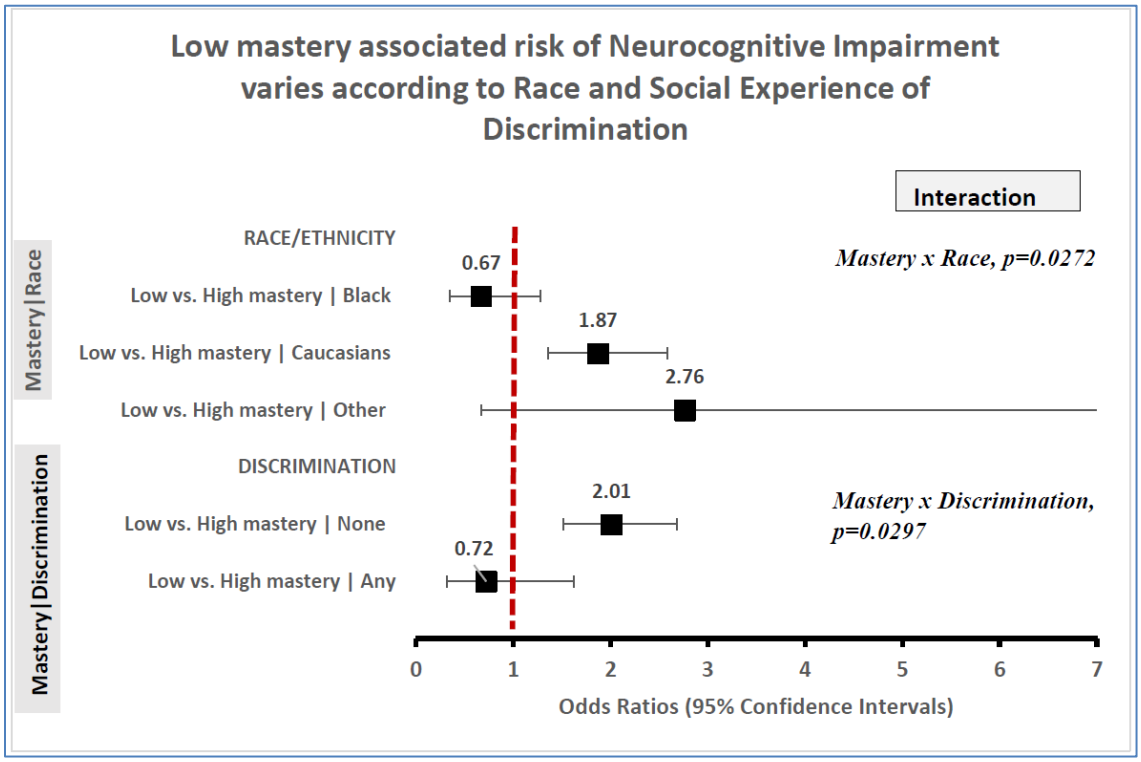


Figure 6.3. Low mastery associated risk of Neurocognitive impairment varies within strata of race, and social experience of discrimination



CHAPTER 7

PSYCHOSOCIAL DETERMINANTS OF ACCELERATED COGNITIVE DECLINE IN A NATIONALLY REPRESENTATIVE SAMPLE OF OLDER AMERICANS. DO RELATIONSHIPS BETWEEN TOXIC STRESS / RESILIENCE PROTECTING FACTORS VARY ACCORDING TO RACE / ETHNICITY?[1]

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Abstract

Background: Toxic stress (TS), resiliency promoting factors (RPFs) and their interactions were investigated in relationship to incident dementia in a nationally representative sample of adult Americans >=50 years enrolled in the Health and Retirement Study (HRS) between 2006 and 2016.

Methods: 6719 adults free of dementia were followed from 2006-2016 with biennial assessment of psychosocial factors and dementia diagnosis. TS comprised experiences of everyday discrimination and chronic stressors, RPF included global and domain-specific mastery, social support measures. Race/ethnicity was self-reported as black, white, or Other. Multivariable Cox proportional hazards regression models estimated TS, RPF race, associated hazard ratios (HRs) and 95% confidence intervals (CIs) with adjustment for comorbidity, lifestyle, and socio-demographic confounders.

Results: Chronic stress (HR 1.88, 95%CI: 1.30, 2.72) and everyday discrimination (HR 2.95, 95% CI: 1.95, 447) were strongly associated with incident while high vs. low mastery (HR 0.72, 95%CI: 0.53, 0.98) was associated with lower dementia risk. Discrimination-related risk of dementia varied according to education status: any vs no discrimination -among those with less than high school, (HR 1.94, 95% CI: 1.00, 3.79); amongst high school graduates, (HR 5.79, 95% CI: 2.75, 12.17), while among those with college and above, (HR 2.59, 95% CI: 1.56, 4.28). Relative to Whites, African American race was associated with incident dementia risk but only in the sub-group that achieved high mastery (HR 1.90, 95%CI: 1.22, 2.97).

Conclusion: Among older US adults, everyday discrimination, chronic psychosocial stress, and low mastery were associated with worse cognition. The cognitive disadvantage for

high mastery African American vs. White/Other race adults suggests that adverse social experiences may overwhelm the cognitive benefit of high mastery in status-inconsistent individuals. Reduction of TS and implementing policies that disincentivize unequal treatment by race/ethnicity in social life and in health, justice and economic systems may promote successful cognitive aging in adult Americans.

Key words: Toxic stress, resiliency promoting factors, incident dementia, everyday discrimination, older Americans

Introduction

Cognitive impairment is a major public health and social issue due to increasingly aging populations around the world. In 2019, Alzheimer's disease and other forms of dementia ranked as the 7th leading cause of death among older adults globally[1], and 6th in the United States (USA).[2] The global prevalence of dementia is approximately 7% amongst individuals aged 65 and above.[3] In the USA, Alzheimer's disease is the most prevalent form of dementia, impacting about 6 million people. This number is projected to increase to 14 million people by 2060.[4] Cognitive decline contributes to diminished quality of life, loss of independence, decreased healthy life expectancy,[5,6] and elevated mortality in old age.[7,8] It is also costly as it leads to institutionalization and increases the need for social and healthcare services among those with impairment and their caregivers, such that a significant proportion of health care resources is spent caring for older people with the condition. [9-11] Cognitive impairment also hinders one's ability to work and play a role in retirement, particularly in the ever-changing labor market which increasingly consists of jobs that require cognitive abilities and competence.[12]

The impact that toxic stress (TS) has on the development of cognitive impairment is still being evaluated. Studies of laboratory animals have shown that psychological stress can lead to cellular changes in regions of the hippocampus, decreased proliferation of neurons in the dentate gyrus, and loss of hippocampal volume resulting in atrophy and cognitive deficits.[13-15] In humans, early life stress (e.g., childhood adversity or trauma exposure) has been associated with enduring neuropsychiatric effects such as depression [16 17] and long term deficits in cognitive function.[18] Additionally, chronic stress in adults is associated with hormonal and inflammatory

indicators of accelerated aging [19], lower quality of life [20] as well as excess risk of cardiovascular morbidity and mortality, including increased stroke.[21-24]

While there's a large body of literature that shows the beneficial effects of resilience in the face of adversity,[25-27] research in this area is still evolving. In the past, most research was focused on children exposed to destructive early environments such as poverty and chronic maltreatment.[28,29] Recent studies are increasingly assessing coping mechanisms in adults. However, hardly any studies have assessed the joint effects of Toxic stress and Resilience promoting factors in the development of dementia.

This research is grounded in the allostatic theory. Adversity from chronic stress accelerates both physiological and psychological responses, thus inducing allostatic load leading to increased morbidity and mortality of chronic conditions such as dementias.[30] There is limited knowledge on the impact that Toxic stressors and resilience promoting factors have on the development of cognitive impairment in aging U.S. adults. The objective of this study is to determine the impact of toxic stress or resilience on cognitive functioning in older Americans, and its demographic and socioeconomic predictors, using a nationally representative cohort serially tested for cognitive performance. This study specifically seeks to investigate whether toxic stress and resilience promoting factors were associated with dementia incidence in a nationally representative sample of dementia-free adults followed longitudinally in the Health and Retirement Study (HRS). The following specific hypotheses were tested: (a) higher levels of TS and lower levels of RPF are associated with higher rates of cognitive impairment in older American adults, (b) race/ethnicity is associated with earlier onset of cognitive decline over 10

years, and (c) the relationship between race and earlier onset of cognitive decline varies according to levels of TS and RPF.

Methods

Study Population

This prospective cohort study used data from the 2006, 2008, 2010, 2012, 2014 and 2016 waves of the HRS. The HRS collects data biennially on health outcomes and expenses, psychosocial and lifestyle factors, employment, retirement, and finances in order to address issues related to aging Americans. The HRS surveys a representative sample of Americans over the age of 50 along with their spouses/partners who may be younger than 50 years old.[31]

Participants included in our study must have information on dementia status and psychosocial factors, that is stress and resilience measures. Psychosocial factors were initially collected in the 2006 and 2008 waves using the Psychosocial Leave-Behind (PLB) Participant Lifestyle Questionnaire, a survey used to collect data on psychosocial and lifestyle factors that is left with participants to mail back after an in-person interview. This survey was piloted and reviewed in a sample of about 4000 respondents before it was administered every two years beginning in 2006 to a random, rotating 50% of the sample who were selected to complete an in-person interview [32].

Two subsets of data were created and combined for analyses: 1) participants who were dementia-free in 2006 and had their first psychosocial measure in 2006 and 2) participants who were dementia-free in 2008 and had their first psychosocial measure in 2008. Participants were excluded for the following reasons: if date of birth unknown, missing more than two stress / resilience measures and having a diagnosis of a memory-related problem prior to 2006. The final sample size for analyses was 6719 (Figure 1).

Measures

Primary Determinants: Psychosocial factors

Assessment of Toxic Stress: The main exposures in this study were Toxic stress (TS) and resilience promoting factors (RPF). Briefly, TS was assessed across several domains and included: cumulative stressors, life course stressors, recent stressors, experiences of everyday discrimination, major experiences of lifetime discrimination, ongoing chronic stressors and perceived constraints on personal control.[32] Life-course stressors are 11 questions that capture stressful life events at any point in a respondent's life time, including loss of a child, being in a major fire, flood, earthquake, or other natural disaster, life threatening illness or major accident [32] Recent stressors are six items that capture major stressful life events that occurred in the last 5 years namely involuntary job loss, prolonged unemployment, being robbed or burglarized, moved to a worse neighborhood, or being a victim of fraud.[32] Cumulative stress is a summation of recent stressors and life-course stressors. Ongoing chronic stressors include eight items that capture current and ongoing problems that have lasted twelve months or longer such as health problems, difficulties at work, housing problems and financial strain. Measures of everyday discrimination are six questions that tap into the hassles and chronic stress associated with perceived everyday discrimination and comprised "character assaults" that tend to occur daily. Major experiences of lifetime discrimination are seven questions that capture major experiences of unfair treatment at any point in one's lifetime. Experiences of chronic work discrimination are designed to assess chronic discrimination experienced at work. These questions are only asked of respondents who are currently working and are not required for those study participants that are retired. In this set of measures, participants are asked to rate how often some stressful experiences/ situations arose at work during the last 12 months. Perceived constraints on

personal control were five items that capture a sense of lack of control of things going on around an individual. [32]

We analyzed each type of stress as a continuous variable where scores ranged from a minimum of zero to a theoretic maximum of 17 for cumulative stressors, 0–11 for life-course stress, and 0–6 for recent stress. For experiences of discrimination, the theoretic score ranged from 0-6 for measures of everyday discrimination, 0-7 for major experiences of lifetime discrimination, and 0-5 for experiences of chronic work discrimination. Finally, theoretic scores ranged from 1-8 for ongoing chronic stressors, and 1-6 for perceived constraints.

We farther analyzed each type of stress as categories based on the distribution of stress events. Cumulative stress categories and life-course stress categories included zero events (reference), one- two, and three or more events. Categories for recent stress, measures of everyday, chronic work, and lifetime discrimination included zero events (reference), and one or more events. However, ongoing chronic stressors and personal constraints were dichotomized as high vs low based on their mean distributions.

Assessment of Resilience: Resilience promoting factors (RPF) on the other hand included global mastery, domain-specific control of finances, health and social life, and measures of social support from spouses, children, relatives and friends. Global mastery included five questions getting at one's resolve at attaining goals. Domain-specific mastery of health, social life and finances was measured via a single-item measure assessing the amount of control for each aspect on a 10-point scale that ranged from ''no control at all'' to ''very much control'', with higher scores indicating greater domain-specific mastery. [32] Measures of social support included four sets of seven items that examined the level of social support

received from spouses/partners, children, other family members and friends. For each relationship category were three positively worded items - positive social support (PSS) and four negatively worded items - negative social support (NSS). We created additional constructs to sum up social support responses from immediate family (spouses and children), extended family (friends and other family members), and all four relationship groups (spouses, children, other family members and friends).

Details regarding the items that constitute TS and RPF constructs as well as their scoring processes have been described elsewhere.[32] Additionally, for participants with one or two missing items, the score was rescaled to the theoretic maximum for each construct by taking the sum of the items present and dividing it by the number of items present. This quotient was then multiplied by the maximum number of items that could be present. This final number was then rounded to a whole number. All combinations of missing items were accounted for when calculating a score for participants missing two items.

Other measures

Additional factors were measured at baseline and were included in the analyses based on review of the literature and what HRS collects. Socio-demographic factors included race, sex, retirement status, education level, and marital status. Lifestyle covariates included alcohol use, tobacco use, and moderate physical activity. BMI and comorbidities were also assessed. Comorbidities included the following physician-diagnosed conditions: high blood pressure, diabetes, stroke, lung problems (i.e. chronic bronchitis or emphysema), arthritis, psychiatric problems (i.e. emotional or nervous), and cancer. A comorbidity index was created where one point was given for each yes with a maximum total of seven.

Outcome: Assessment of Dementia

The main outcome was incident dementia defined with a new dementia diagnosis and time to a new diagnosis. A new dementia diagnosis was defined by a 'no' diagnosis in 2006 and a report of 'yes' in any of the subsequent years since the last interview based on the question, "Has a doctor ever told you that you have a memory-related disease?" In 2010, this question was changed to ask participants if they have ever been told they have Alzheimer's disease or dementia. Time to new dementia was defined as participant chronologic age in the first year a new dementia diagnosis was reported. Participants with a 'no' in all interviews were censored in the 2016 study year.

Statistical Analyses

Race, TS, and RPF were analyzed as predictors in relation to incidence of dementia over ten years. First, descriptive analyses determined the distribution of baseline TS, RPF, and race/ ethnicity. Bivariate associations were implemented to determine crude associations for TS, RPF, potential confounders and sociodemographic factors with race. Since both TS and RPF were analyzed as categorical variables, chi square tests were used to evaluate differences in proportions by race/ethnicity. Kaplan-Meier curves were generated for domains of stress/resilience and compared using the log-rank test. Factors with a p-value ≤ 0.2 were further evaluated in multivariable models as candidate confounders.

Cox proportional hazards regression models were used to evaluate the association between stress/ resilience parameters and incident dementia. Hazard ratios (HR) were generated and reported with 95% confidence intervals (CI). Proportional hazards assumptions were assessed by graphing log-log survival curves and examining Schoenfeld residuals. The following covariates were assessed as candidate confounders: race/ethnicity, sex, education

status, alcohol consumption, moderate physical activity, BMI, retirement status and comorbidity due to diabetes, heart diseases and stroke. A series of incremental nested models were implemented, beginning with crude models, followed by models with sociodemographic factors adjusted for, and models adjusting for sociodemographic factors as well as TS. The final models further adjusted for RPF. Measures of TS and RPF were not mutually adjusted for one another in any multivariable model. Additionally, separate Cox regression models evaluated interaction between race/ethnicity and respective TS and RPF and the potential for interaction between TS and RPF. P-values for interaction effects were set at $p < 0.10$ because the power of statistical tests for higher order terms is generally lower than for first-order terms.[33,34] All results were adjusted for the complex sampling design of the HRS.[35] All analyses were implemented with SAS software, version 9.4 (SAS Institute, Cary, NC).

Results

A total of 6719 unique individuals were included in this analysis. The analytic sample included 83.4 % non-Hispanic White, 13% Black/ African American and 4% Other race (includes Hispanics). Majority of the sample were female (63%), 70% were married/ partnered, 45% had some college education or more, 33% had a cardiometabolic diagnosis (HD, T2DM or stroke). Of note 27% reported ≥three comorbid conditions. There were 294 (4.4%) subjects who developed dementia over the ten-year follow-up period. Baseline psychosocial measures are provided by race (Table 7.1).

Across racial groups, the proportions of individuals reporting TS varied significantly at baseline for experiences of everyday discrimination ($p< 0.0001$), major experiences of lifetime discrimination ($p < 0.0001$), chronic stressors ($p= 0.0057$) and perceived constraints ($p=0.0013$)

and were higher amongst minority groups. The following RPFs varied significantly at baseline by race: control over health, PSS from spouses/ partners, children, other family members, friends, and all relationship groups combined. NSS from all domains assessed also varied by race at baseline (Table 7.1). Additional baseline data on the distribution of sociodemographic and lifestyle characteristics by race are reported in Supplementary Table 7.1.

Statistically significant associations were observed between high levels of the following TS domains and incident dementia: cumulative stress, experiences of everyday discrimination, perceived constraints and ongoing chronic stressors. The risk of developing dementia was 77% elevated (HR 1.77, 95% CI: 1.28, 2.46) for individuals who reported high levels of personal constraints vs low levels of constraints at baseline after adjusting for race, sex, retirement status, education, marital status, moderate physical activity, smoking, alcohol consumption, BMI and comorbidity due to Heart disease, Type 2 Diabetes and Stroke. Additionally, the risk of developing dementia was 86% higher (HR 1.86, 95% CI: 1.18, 2.92) amongst individuals that experienced increased constraints (Table 7.2).

Similarly, statistically significant associations were observed between the following RPF domains and incident dementia: global mastery, PSS- children, and domain-specific control of social life, health, and finances, NSS- children, NSS-other family members, NSS-all relationship groups combined. Higher levels of PSS from children was associated with 34% protection from the risk of dementia (HR 0.66, 95%CI: 0.51-0.85). On the contrary, The risk of developing dementia increased by 60% (HR 1.60, 95%CI: 1.10-2.33) amongst older Americans who reported high NSS from children compared to those with low NSS- children. Similar trends were observed in association of other NSS relationships with onset of dementia (Table 7.2).

Kaplan-Meier survival curves revealed that the development of dementia differed significantly by experiences of everyday discrimination and major experiences of lifetime discrimination. A trend of shorter dementia diagnosis free survival time was evident in those that reported one or more experiences of everyday discrimination (p<0.0001), and one or more major experiences of lifetime discrimination (p=0.0036, Figure 7.2).

Race is associated with incident dementia, and disparities persist according to level of mastery

Unadjusted for confounders, the risk of incident dementia was 63% higher in African Americans (HR 1.63, 95%CI: 1.20, 2.23) and 50% higher in Other race (HR 1.50, 95% CI: 0.81, 2.75) compared to Caucasians over 10 years. This association was down modulated in multivariable models, with the risk of developing dementia attenuated though remained statistically robust (HR 1.43, 95% CI: 1.03, 1.99) among African Americans relative to Caucasians (Table 7.2). We also found that African Americans advanced to dementia on average a year earlier than their Caucasian colleagues (78.8 vs 79.7 years respectively, data not shown). However, race-related differences in risk of incident dementia were dependent on the level of mastery amongst these older Americans (mastery* race, p=0.0075, Figure 7.3). Among African Americans, having high mastery was not associated with onset of dementia. However, among Caucasians, high mastery was associated with 28% protection from the risk of dementia (HR 0.72, 95% CI:0.54, 0.96). Among those with low mastery, there was no association between African Americans and Caucasians in risk of dementia. However, among those with high mastery, the risk of incident dementia was 90% higher in African Americans relative to Caucasians (HR 1.90, 95% CI:1.22, 2.97, Figure 7.3). Furthermore, among African Americans,

those with low mastery on average developed dementia 3 years faster than those with high mastery (76.4 vs 79.5 years respectively).

High Toxic Stress is associated with incident dementia; relationship varies by level of mastery

The risk of incident dementia increased by 38% (HR 1.38, 95%CI: 1.01-1.90) among adults who reported any compared to no cumulative stress events in unadjusted models The magnitude of this association was attenuated with adjustment for sociodemographic factors, lifestyle factors and comorbidity (Table 7.2). However, the relationship of cumulative stress to incident dementia varied according to levels of mastery (cumulative stress*mastery, p=0.0659). Among those with no events reported, there was no association of cumulative stress to incident dementia between those who had high vs low mastery. However, among those that reported any cumulative stress events, having high mastery was associated with 34% protection from risk of dementia (HR 0.66, 95% CI: 0.48, 0.91). Among those with low mastery, the risk of incident dementia was 81% elevated in those who experienced any vs no events (HR 1.81, 95%CI:1.07, 3.05). On the other hand, among those with high mastery, there was no relationship between cumulative stress and incident dementia between those who experienced any vs no events (Figure 7.4). Among those with low mastery, individuals experiencing any cumulative stress developed dementia on average 4 years earlier than those who did not (79.1 vs 83.0 years respectively). Whereas among those with high mastery, individuals experiencing any cumulative stress developed dementia on average 3 years earlier than those that did not (78.5 vs 81.4 years respectively).

High Toxic Stress is associated with incident dementia; relationship varies by level of education

Experiences of everyday discrimination were strongly associated with incident dementia in unadjusted models (HR 2.91, 95%CI: 2.01, 4.23). This association remained elevated with adjustment for confounding variables for older Americans reporting any vs no experiences of discrimination (HR 2.95, 95%CI: 1.95, 4.47). Additionally, the risk of developing dementia was 140% higher amongst individuals that experienced increased discrimination above baseline (HR 2.40, 95% CI: 1.22, 4.70, Table 7.2). However, the relationship of everyday discrimination to incident dementia varied according to education status (discrimination*education, p=0.0097). In the absence of discrimination, having less than high school was associated with 81% increased risk of dementia onset (HR 1.81, 95% CI: 1.15, 2,87) relative to High school graduates, and 54% increased risk relative to College and above (HR 1.54, 95% CI: 1.03, 2.29). On the other hand, in the presence of discrimination, there were was no association between education status and incident dementia in any of the categories assessed. Among those with less than high school, experiencing discrimination was associated with 94 % increased risk of dementia, (HR 1.94, 95% CI: 1.00, 3.79). Amongst high school graduates, the risk of incident dementia increased 479% in individuals with any vs no experiences of discrimination (HR 5.79, 95% CI: 2.75, 12.17). Similarly, among those with college and above, the risk of incident dementia increased 169% in older Americans with any vs no experiences of discrimination (HR 2.59, 95% CI: 1.56, 4.28, Figure 7.5). Additionally, among those with less than high school education, individuals experiencing discrimination developed dementia on average 2 years earlier than those who did not (76.1 vs 77.9 years respectively).

Other factors associated with incident dementia

Among other factors, cigarette smoking, alcohol consumption and retirement status and a physician diagnosis of a stroke each associated with increased risk of dementia onset after controlling for social demographic factors, lifestyle factors, toxic stress or resilience promoting factors (Supplementary Table 7.2).

Discussion

Our study examined a cohort of aging American adults who were dementia-free in 2006 and followed for ten years through 2016. Our results showed that high levels of toxic stressors including, everyday discrimination, ongoing chronic stressors and perceived constraints at baseline were associated with an increased risk of developing dementia when measured as both continuous and categorical measures. Experiencing discrimination, high levels of chronic stress and perceived constraints were each significantly associated with incident dementia compared to experiencing no stress. These associations persisted after adjusting for confounders such as sex, marital status, retirement status, BMI, comorbidity, smoking status, and alcohol consumption. These findings corroborate earlier work in a cross-sectional study where we found that higher levels of toxic stressors and lower levels of resilience resources were associated with an increased risk for neurocognitive impairment.[36 37]

We also found that sustained toxic stress across several domains is associated with faster advancement of dementia. This is consistent with prior literature that suggests that stressful conditions and circumstances such as low education, limited income, living in a disadvantaged neighborhood and exposure to racial discrimination have been linked to accelerated aging,[38] and increased risk for early onset of illness and death.[39]

Data from this study farther suggests that while overall risk in dementia onset by race/ethnicity was limited, racial differences persisted within levels of mastery for African Americans. Our finding on of no overall risk of dementia by race/ethnicity is consistent with some, but not all previous literature on differences in cognitive decline by race.[40] [41,42] However, the finding on racial differences within mastery highlights the disparities in social experiences such as racism in all its forms that exacerbate cognitive function in Older African Americans vs Caucasians, as African American vs White race -associated disadvantage in dementia incidence was evident amongst Older Americans with High mastery. This wipes out the would-be beneficial effects of high mastery for African Americans and is similar to what we reported in our earlier study.[36] Furthermore, our finding relating to earlier advancement to dementia in African Americans compared to Caucasians has been shown in some, but not all studies that evaluated racial/ ethnic differences in cognitive function.[43-45]

Findings from our study also showed that psychosocial adversity-associated risk for dementia onset in these older adults varied according to levels of mastery. This shows that mastery is protective in the face of adversity, and that mastery is associated with cognitive reserve. This is consistent with another study where individuals that had high levels of resilience traits showed less distress despite reported childhood adversities relative to those that had low resilient coping abilities.[46]

Data from this study further study suggests the deleterious effects of everyday discrimination on education. Whereas education has been associated with several beneficial effects that include: building cognitive reserve -enhanced reasoning skills, test-taking abilities, verbal and working memory- all of which translate to personal mastery, [47,48] better health behaviors, income and social opportunities, [49] the systemic structures that perpetuate racism and

discrimination overwhelm these benefits for African Americans thus adversely affecting health outcomes.[50,51] This finding confirms prior research where we found that individuals who experienced discrimination regardless of mastery, had elevated risk of neurocognitive impairment.[36] Additionally, in another study reported higher levels of allostasis for Black and Mexican Americans relative to White Americans with a college degree or higher, whereas allostasis was similar across race groups among adults with low educational achievement in same study.[52] Prior data shows that Black Americans of higher educational status report high frequency of experienced micro-aggression and work-place discrimination and more frequently report being in jobs below their qualification level.[53] Both the nature and frequency of everyday discrimination varies according to race, with African Americans more frequently on the receiving end of the most insidious forms of discrimination in occupational and social interactions – whether in healthcare, educational, financial, law enforcement by police and judicial systems.[53,54]

This study raises awareness of the influence that social determinants of health have on the development of cognitive impairment especially in African American communities. The World Health Organization's Commission on Social Determinants of Health states that the high burden of illness leading to premature death is a result of the conditions in which people are born, grow, age, work, and live. [55] It is important to address the conditions that shape a person's well-being during all stages of life. A person's well-being is multidimensional and involves dimensions such as health, education, environment, work, and physical insecurity. The domains of stressful events evaluated in this study involve these areas of a person's well-being and therefore play a role in how a person responds to the development of conditions like dementia.

Some of the strengths in this study include the implementation of a large nationally

representative prospective, study design using rigorous analytic approaches adjusted for multiple confounders. Additionally, we evaluated multiple indicators of TS and RPF as proxies for social experiences that may affect cognitive aging. However, there are limitations to consider when interpreting our results. HRS data is collected biennially and the assessment of dementia was by definition within the previous two years. Potential misclassification could have occurred with the time of dementia diagnosis, but it should not affect the association between baseline psychosocial factors and dementia over ten years. Self-reported assessments of psychosocial factors and dementia diagnosis were used, allowing for potential information bias and recall bias despite meticulous efforts made to collect data in a standardized method. Lastly, dementia outcome was based on a general definition that changed in 2010 to include dementia and Alzheimer's disease and did not allow for assessing risk for specific memory-related conditions.

Conclusion

This study provided further empirical evidence that high psychosocial adversity and low levels of RPF are important social determinants of cognitive impairment in a diverse sample of older US adults. African American race was associated with cognitive disadvantage, but only in the status inconsistent context of high mastery. Regardless of race, the benefit of high mastery for cognitive reserve among older Americans was muted among those that reported experience of discrimination. Furthermore, regardless of race, the benefit of education for cognitive reserve is lost among older Americans experiencing discrimination. These findings suggest that culturally appropriate interventions to reduce stress and public policies that value African American social perspectives and coping mechanisms should be enhanced to promote healthy wellbeing in this community.

Declarations

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Informed consent Statement: Not applicable.

Conflict of Interest: The authors declare no conflicts of interests.

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List of Tables and Figures

Table 7.1: Distribution of Toxic stress and resilience promoting factors among Older Americans enrolled in the HRS 2006-2014 sample at baseline by Race/ ethnicity.

Characteristic	All (N=6719)	White/ Caucasian (N=5607)	Black / African American (N=857)	Other (N=255)	
Dimensions of Toxic Stress	**N (%)**	**N (%)**	**N (%)**	**N (%)**	**p-value**
Cumulative Stress [a]					
Median (IQR)	2.00 (1.00, 3.00)	2.00 (1.00, 3.00)	1.00 (1.00, 3.00)	1.00 (1.00, 3.00)	
0 events	1375 (21.9)	1158 (21.8)	166 (22.2)	51 (23.0)	0.8715
1+ events	4915 (78.1)	4162 (78.2)	582 (77.8)	171 (77.0)	
Life course stress					
Median (IQR)	1.00 (0.00, 2.00)	1.00 (1.00, 2.00)	1.00 (0.00, 2.00)	1.00 (0.00, 2.00)	
0 events	1577 (25.0)	1324 (24.8)	193 (25.7)	60 (27.0)	0.9823
1-2 events	4727 (75.0)	4008 (75.2)	557 (74.3)	162 (73.0)	
Recent Stress					
Median (IQR)	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	
0 events	5155 (81.4)	4385 (81.9)	595 (78.8)	175 (77.8)	0.0415
1+ events	1176 (18.6)	966 (18.0)	160 (21.2)	50 (22.2)	
Everyday Discrimination					
Median (IQR)	1.00 (0.00, 1.00)	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	
0 events	5874 (90.8)	5021 (92.2)	653 (82.2)	200 (86.2)	< 0.0001
1+ events	595 (9.2)	422 (7.8)	141 (17.8)	32 (13.8)	
Lifetime Discrimination					
Median (IQR)	0.00 (0.00, 1.00)	0.00 (0.00, 1.00)	0.00 (0.00, 1.00)	0.00 (0.00, 1.00)	
0 events	4475 (70.8)	3868 (72.4)	447 (59.2)	160 (71.1)	< 0.0001
1+ events	1849 (29.2)	1476 (27.6)	308 (40.8)	65 (28.9)	
Chronic work Discrimination [b]					
Median (IQR)	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	
0 events	2900 (91.3)	2433 (92.3)	356 (87.2)	111 (84.1)	< 0.0001
1+ events	277 (8.7)	204 (7.7)	52 (12.8)	21 (15.9)	
Chronic stress					
Median (IQR)	3.00 (3.00, 4.00)	3.00 (3.00, 4.00)	3.00 (3.00, 4.00)	3.00 (2.00, 4.00)	
Low	4240 (70.6)	3619 (71.4)	479 (66.4)	142 (65.4)	0.0057
High	1767 (29.4)	1450 (28.6)	242 (31.5)	75(34.6)	
Perceived constraints					

Median (IQR)	2.00 (1.00, 3.00)	2.00 (1.00, 3.00)	2.00 (1.00, 3.00)	2.00 (1.00, 4.00)	
Low	4324 (67.0)	3661 (67.4)	535 (67.4)	128 (55.9)	0.0013
High	2127 (33.0)	1767 (32.6)	259 (32.6)	101 (44.1)	
Measures of resilience					
Personal mastery					
Median (IQR)	5.00 (4.00, 6.00)	5.00 (4.00, 6.00)	5.00 (4.00, 6.00)	5.00 (4.00, 6.00)	
Low	2234 (34.6)	1889 (34.8)	275 (34.7)	70 (30.4)	0.4017
High	4224 (65.4)	3546 (65.2)	518 (65.3)	160 (69.6)	
Control over health					
Median (IQR)	8.00 (6.00, 9.00)	8.00 (6.00, 9.00)	8.00 (6.00, 9.00)	8.00 (7.00, 9.00)	
Low	2875 (45.0)	2450 (45.5)	341 (43.6)	84 (37.0)	0.0294
High	3517 (55.0)	2933 (54.5)	441 (56.4)	143 (63.0)	
Control over finances					
Median (IQR)	8.00 (6.00, 10.00)	8.00 (6.00, 10.00)	8.00 (6.00, 10.00)	9.00 (7.00, 10.00)	
Low	2286 (35.6)	1948 (36.0)	265 (33.5)	73 (32.0)	0.2085
High	4141 (64.4)	3461 (64. 0)	525 (66.5)	155 (68.0)	
Control over social life					
Median (IQR)	8.00 (7.00, 10.00)	8.00 (7.00, 10.00)	9.00 (7.00, 10.00)	9.00 (7.00, 10.00)	
Low	1946 (30.4)	1669 (30.9)	210 (27.1)	67 (29.5)	0.0922
High	4454 (69.6)	3729 (69.1)	565 (72.9)	160 (70.5)	
Social support domains					
Positive Social Support (PSS)					
PSS from Spouses/ Partner					
Median (IQR)	4.00 (3.00, 4.00)	4.00 (3.00, 4.00)	3.00 (3.00, 4.00)	3.00 (3.00, 4.00)	
Low social support	1929 (42.0)	1607 (40.5)	234 (52.0)	88 (50.9)	< 0.0001
High social support	2659 (58.0)	2358 (59.5)	216 (48.0)	85 (49.1)	
PSS from Children					
Median (IQR)	3.00 (3.00, 4.00)	3.00 (3.00, 4.00)	4.00 (3.00, 4.00)	3.50 (3.00, 4.00)	
Low social support	3064 (50.9)	2637 (52.1)	321 (43.0)	106 (50.0)	< 0.0001
High social support	2959 (49.1)	2428 (47.9)	425 (57.0)	106 (50.0)	
PSS from Other Family members					
Median (IQR)	3.00 (2.00, 4.00)	3.00 (2.00, 4.00)	3.00 (3.00, 4.00)	3.00 (2.00, 4.00)	
Low social support	4380 (70.1)	3766 (71.8)	455 (58.1)	159 (70.7)	< 0.0001
High social support	1870 (29.9)	1476 (28.2)	328 (41.9)	66 (29.3)	
PSS from Friends					

Median (IQR)	3.00 (3.00, 4.00)	3.00 (3.00, 4.00)	3.00 (3.00, 4.00)	3.00 (2.00, 4.00)	
Low social support	4278 (68.9)	3634 (69.4)	489 (64.9)	155 (70.4)	0.0391
High social support	1928 (31.1)	1599 (30.6)	264 (35.1)	65 (29.6)	
PSS from all Relationship groups combined					
Median (IQR)	8.00 (7.00, 10.00)	8.00 (7.00, 10.00)	8.00 (7.00, 9.00)	8.00 (7.00, 9.00)	
Low social support	3579 (55.1)	2966 (54.3)	473 (59.1)	140 (60.1)	0.011
High social support	2917 (44.9)	2497 (45.7)	327 (40.9)	93 (39.9)	
Negative Social Support (NSS)					
NSS from Spouses/ Partner					
Median (IQR)	2.00 (2.00, 2.00)	2.00 (2.00, 2.00)	2.00 (2.00, 3.00)	2.00 (1.00, 3.00)	
Low social support	3465 (75.6)	3026 (76.3)	321 (72.0)	118 (69.0)	0.0151
High social support	1116 (24.4)	938 (23.7)	125 (28.0)	53 (31.0)	
NSS from Children					
Median (IQR)	2.00 (1.00, 2.00)	2.00 (1.00, 2.00)	2.00 (1.00, 2.00)	2.00 (1.00, 2.00)	
Low social support	2556 (42.2)	2203 (43.3)	264 (35.2)	89 (41.4)	0.0002
High social support	3499 (57.8)	2888 (56.7)	485 (64.8)	126 (58.6)	
NSS from Other Family members					
Median (IQR)	1.00 (1.00, 2.00)	1.00 (1.00, 2.00)	1.00 (1.00, 2.00)	2.00 (1.00, 2.00)	
Low social support	3542 (56.7)	3089 (59.0)	349 (44.6)	104 (46.4)	<0.0001
High social support	2703 (43.3)	2149 (41.0)	434 (55.4)	120 (53.6)	
NSS from Friends					
Median (IQR)	1.00 (1.00, 2.00)	1.00 (1.00, 2.00)	1.00 (1.00, 2.00)	1.00 (1.00, 2.00)	
Low social support	3986 (64.3)	3449 (66.0)	409 (54.2)	128 (58.2)	< 0.0001
High social support	2217 (35.7)	1780 (34.0)	345 (45.8)	92 (41.8)	
NSS from all Relationship groups combined					
Median (IQR)	5.00 (4.00, 7.00)	5.00 (4.00, 6.00)	5.00 (4.00, 7.00)	5.00 (4.00, 7.00)	
Low social support	3681 (56.6)	3124 (57.2)	438 (54.7)	119 (51.1)	0.0947
High social support	2817 (43.4)	2341 (42.8)	362 (45.3)	114 (49.9)	
Onset of Dementia					0.4987
No	6425 (95.6)	5369 (95.8)	814 (95.0)	242 (94.9)	
Yes	294 (4.4)	238 (4.2)	43 (5.0)	13 (5.1)	
Note: [a] Cumulative stress is the sum of recent and life course events, sum can be 0-17. [b] Questions on chronic work discrimination were administered to working participants only.					

Table 7.2: Race, Toxic Stress and Resilience promoting factors in relation to risk for incident dementia among older adults enrolled in the HRS 2006-2016.

Characteristic	n/N	Unadjusted HR (95%CI)	p-value	Adjusted HR[c] (95%CI)	p-value
Race					
Black(AA) vs Caucasian	43/857	**1.63 (1.12, 2.23)**	**0.0023**	**1.43 (1.03, 1.99)**	**0.0235**
Other vs Caucasian	13/255	1.50 (0.81, 2.75)	0.1911	1.28 (0.67, 2.43)	0.4420
Toxic Stress Measures					
Cumulative stress [d]					
Continuous measure	255/6290	**1.18 (1.09, 1.30)**	**0.0003**	**1.15 (1.05, 1.27)**	**0.0044**
Baseline cumulative stress					
0 events	49/1375	1.00		1.00	
1+ events	206/4915	**1.38 (1.01, 1.90)**	**0.0468**	1.29 (0.91, 1.83)	0.145
Change in stress (increase vs no change)	41/1282	1.15 (0.81, 1.64)	0.4164	1.19 (0.79, 1.80)	0.3987
Life course stress					
Continuous measure	256/6304	**1.20 (1.09, 1.31)**	**0.0002**	**1.15 (1.05, 1.27)**	**0.0038**
Baseline life course stress					
0 events	52/1577	1.00		1.00	
1+ events	204/4727	**1.41 (1.06, 1.87)**	**0.0177**	1.33 (0.99, 1.79)	0.0586
Change in stress (increase vs no change)	41/1133	1. 29 (0.89, 1.88)	0.1733	1.33 (0.87, 2.03)	0.1761
Recent stress					
Continuous measure	256/6331	1.28 (0.98, 1.66)	0.0709	1.26 (0.94, 1.68)	0.1168
Baseline recent stress					
0 events	215/5155	1.00		1.00	
1+ events	41/1176	**1.55 (1.02, 2.33)**	**0.0389**	1.45 (0.95, 2.22)	0.0838
Change in stress (increase vs no change)	15/610	1.00 (0.59, 1.68)	0.9899	1.00 (0.55, 1.81)	0.9984
Everyday discrimination					
Continuous measure	266/6469	**1.64 (1.40, 1.91)**	**< 0.0001**	**1.62 (1.36, 1.94)**	**< 0.0001**
Baseline everyday discrimination					
0 events	210/5874	1.00		1.00	
1+ events	56/595	**2.91 (2.01, 4.23)**	**< 0.0001**	**2.95 (1.95, 4.47)**	**< 0.0001**
Change in stress (increase vs no change)	9/148	**1.96 (0.99, 3.89)**	**0.0539**	**2.40 (1.22, 4.70)**	**0.0117**
Lifetime discrimination					
Continuous measure	257/6324	**1.23 (1.03, 1.46)**	**0.0017**	1.21 (0.99, 1.48)	0.0577
Baseline lifetime discrimination					
0 events	177/4475	1.00		1.00	
1+ events	80/1849	**1.40 (1.07, 1.83)**	**0.0161**	1.40 (0.99, 1.97)	0.0532
Change in stress (increase vs no change)	14/474	1.36 (0.74, 2.51)	0.3136	1.43 (0.73, 2.82)	0.2915
Chronic work discrimination					
Continuous measure	81/3177	1.02 (0.62, 1.68)	0.8236	0.75 (0.34, 1.66)	0.4718
Baseline work discrimination					
0 events	73/2900	1.00		1.00	
1+ events	8/277	1.27 (0.58, 2.77)	0.8458	0.85 (0.27, 2.69)	0.7813

Change in stress (increase vs no change)	3/064	2.06 (0.61, 6.96)	0.2383	1.52 (0.61, 3.77)	0.3624
Perceived constraints					
Continuous measure	266/6451	**1.28 (1.15, 1.42)**	**< 0.0001**	**1.26 (1.13, 1.41)**	**0.0001**
Baseline perceived constraints					
Low constraints	126/4324	1.00		1.00	
High constraints	140/2127	**1.71 (1.25, 2.35)**	**0.0012**	**1.77 (1.28, 2.46)**	**0.0009**
Change in stress (increase vs no change)	43/1083	**1.50 (0.98, 2.28)**	**0.0586**	**1.86 (1.18, 2.92)**	**0.0081**
Ongoing chronic stressors					
Continuous measure	201/5871	**1.38 (1.17, 1.62)**	**0.0002**	**1.32 (1.12, 1.56)**	**0.0016**
Baseline chronic stress					
Low chronic stress	125/4240	1.00		1.00	
High chronic stress	77/1767	**1.96 (1.42, 2.70)**	**0.0001**	**1.88 (1.30, 2.72)**	**0.0012**
Change in stress (increase vs no change)	27/855	1.41 (0.86, 2.30)	0.1637	**1.70 (1.05, 2.75)**	**0.0318**
Resilience Promoting Factors					
Personal Mastery					
Continuous measure	266/6458	**0.84 (0.75, 0.94)**	**0.003**	**0.83 (0.74, 0.94)**	**0.0031**
Baseline personal mastery					
Low mastery	135/2234	1.00		1.00	
High mastery	131/4224	**0.74 (0.58, 0.97)**	**0.03**	**0.72 (0.53, 0.98)**	**0.0356**
Change in measure (increase vs no change)	58/1208	1.43 (0.97, 2.10)	0.0705	1.31 (0.87, 1.960	0.1902
Decreased mastery	38/1058	1.12 (0.80, 1.57)	0.5091	1.16 (0.81, 1.66)	0.4014
Positive Social Support (PSS) Domains					
PSS from Spouses/ partners					
Continuous measure	179/4466	0.93 (0.75, 1.14)	0.4646	0.97 (0.78, 1.20)	0.7752
Baseline PSS (spouse/ partner)					
Low PSS	80/1929	1.00		1.00	
High PSS	100/2659	0.93 (0.67.1.28)	0.6424	1.04 (0.75, 1,44)	0.8034
Change in measure (decrease vs no change)	23/391	1.02 (0.50, 2.05)	0.9635	1.05 (0.51, 2.16)	0.8966
PSS from Children					
Continuous measure	248/5897	**0.72 (0.57, 0.90)**	**0.0054**	**0.74 (0.59, 0.94)**	**0.0139**
Baseline PSS (Children)					
Low PSS	127/3064	1.00		1.00	
High PSS	122/2959	**0.65 (0.50, 0.84)**	**0.0014**	**0.66 (0.51, 0.85)**	**0.0021**
Change in measure (decrease vs no change)	28/798	1.11 (0.69, 1.79)	0.6684	1.26 (0.79, 2.02)	0.3229
Change in measure (increase vs no change)	30/688	**1.70 (1.15, 2.52)**	**0.0092**	1.29 (0.84, 1.97)	0.2437
PSS from Other Family members					
Continuous measure	254/6250	1.05 (0.91, 1.21)	0.4894	1.04 (0.90, 1.20)	0.6092
Baseline PSS (Family)					
Low PSS	176/4380	1.00		1.00	
High PSS	78/1870	0.85 (0.63, 1.15)	0.2994	0.80 (0.58, 1.11)	0.1761
Change in measure (decrease vs no change)	34/943	1.21 (0.76, 1.93)	0.418	1.32 (0.90, 2.17)	0.2739
PSS from Friends					
Continuous measure	252/6206	0.93 (0.78, 1.12)	0.4408	0.99 (0.82, 1.21)	0.9486

Baseline PSS (Friends)					
Low PSS	186/4278	1.00		1.00	
High PSS	66/1928	0.85 (0.64, 1.13)	0.2521	0.92 (0.67, 1.27)	0.6036
Change in measure (decrease vs no change)	23/820	0.91 (0.49, 1.68)	0.7531	0.97 (0.51, 1.85)	0.9371
Change in measure (increase vs no change)	43/960	**1.49 (1.02, 2.19)**	**0.0405**	0.98 (0.73, 1.32)	0.8997
PSS from All relationship groups					
Continuous measure	269/6946	1.03 (0.97, 1.09)	0.2929	1.01 (0.96, 1.07)	0.6733
Baseline PSS (All groups)					
Low PSS	150/3579	1.00		1.00	
High PSS	119/2917	1.15 (0.89, 1.49)	0.2915	0.98 (0.72, 1.32)	0.872
Change in measure (decrease vs no change)	49/1303	1.38 (0.89, 2.14)	0.1511	1.40 (0.87, 2.27)	0.1645
Negative Social Support (NSS) Domains					
NSS from Spouses/ partners					
Continuous measure	180/4581	1.13 (0.88, 1.46)	0.3258	1.06 (0.79, 1.41)	0.6918
Baseline NSS (spouse/ partner)					
Low NSS	131/3465	1.00		1.00	
High NSS	49/1116	1.30 (0.88, 1.94)	0.184	1.18 (0.74, 1.90)	0.4782
Change in measure (increase vs no change)	18/524	1.53 (0.75, 3.09)	0.2339	1.63 (0.74, 5.58)	0.2207
NSS from Children					
Continuous measure	251/6055	**1.35 (1.10, 1.66)**	**0.0054**	**1.30 (1.03, 1.63)**	**0.0269**
Baseline NSS (Children)					
Low NSS	90/2556	1.00		1.00	
High NSS	161/3499	**1.66 (1.18, 2.35)**	**0.0048**	**1.60 (1.10, 2.33)**	**0.0144**
Change in measure (increase vs no change)	24/771	1.18 (0.71, 1.95)	0.5159	1.21 (0.70, 2.09)	0.4917
NSS from Other Family members					
Continuous measure	252/6245	**1.46 (1.19, 1.80)**	**0.0006**	**1.40 (1.10, 1.77)**	**0.0068**
Baseline NSS (Family)					
Low NSS	135/3542	1.00		1.00	
High NSS	117/2703	**1.77 (1.33, 2.35)**	**0.0002**	**1.77 (1.28, 2.46)**	**0.001**
Change in measure (increase vs no change)	39/875	**1.54 (1.01, 2.36)**	**0.0473**	**1.65 (1.06, 2.58)**	**0.0277**
NSS from Friends					
Continuous measure	252/6203	**1.42 (1.09, 1.86)**	**0.01**	**1.33 (1.02, 1.75)**	**0.0371**
Baseline NSS (Friends)					
Low NSS	145/3986	1.00		1.00	
High NSS	107/2217	**1.58 (1.13, 2.21)**	**0.0089**	**1.64 (1.16, 2.33)**	**0.0062**
Change in measure (increase vs no change)	32/693	**1.74 (1.04, 2.92)**	**0.0343**	**1.96 (1.20, 3.23)**	**0.0086**
NSS from All relationship groups					
Continuous measure	269/6498	**1.17 (1.09, 1.24)**	**< 0.0001**	**1.13 (1.04, 1.22)**	**0.0027**
Baseline NSS (All groups)					
Low NSS	145/3681	1.00		1.00	
High NSS	124/2817	**1.72 (1.32, 2.22)**	**0.0001**	**1.67 (1.25, 2.23)**	**0.0008**
Change in measure (increase vs no change)	66/1688	1.34 (0.97, 1.86)	0.0746	**1.55 (1.10, 2.18)**	**0.0129**
Control of Social life					

Continuous measure	265/6400	**0.84 (0.81, 0.87)**	**< 0.0001**	**0.84 (0.81, 0.87)**	**< 0.0001**
Baseline control of social life					
Low control	145/1946	1.00		1.00	
High control	120/4454	**0.40 (0.32, 0.51)**	**< 0.0001**	**0.43 (0.32, 0.51)**	**< 0.0001**
Change in measure (decrease vs no change)	38/1302	0.95 (0.66, 1.35)	0.7636	1.28 (0.85, 1.92)	0.2351
Control of health					
Continuous measure	262/6392	**0.88 (0.83, 0.93)**	**< 0.0001**	0.89 (0.83, 0.95)	0.0012
Baseline control of health					
Low control	155/2875	1.00		1.00	
High control	107/3517	**0.64 (0.47, 0.86)**	**0.0043**	**0.67 (0.47, 0.96)**	**0.0284**
Change in measure (decrease vs no change)	40/1360	0.91 (0.63, 1.33)	0.6231	1.00 (0.67, 1.50)	0.9953
Control of finances					
Continuous measure	265/6427	**0.87 (0.83, 0.90)**	**< 0.0001**	0.88 (0.84, 0.92)	< 0.0001
Baseline control of finances					
Low control	134/2286	1.00		1.00	
High control	131/4141	**0.44 (0.33, 0.59)**	**< 0.0001**	**0.46 (0.34, 0.63)**	**< 0.0001**
Change in measure (increase vs no change)	48/1714	0.83 (0.60, 1.15)	0.2651	**1.07 (0.74, 1.65)**	**0.723**

Note: OR (95%CI): Odds Ratios (95% Confidence Intervals); Bold indicates p-value<0.05; All models adjust for the complex sampling design of the HRS; [c] Adjusted models control for race, toxic stress and demographic factors; sex, education, alcohol consumption, smoking, BMI, moderate physical activity, retirement status and comorbidity due to Diabetes, Heart diseases and Stroke; [d] Cumulative stress is the sum of recent and life course events, sum can be 0-17. Measures of Toxic Stress and indicators of resilience were not mutually adjusted for one another in multivariable models.

Supplementary Tables

Supplementary Table 7.1: Demographic characteristics of older Americans enrolled in the HRS 2006-2016 sample at baseline by Race/ ethnicity.

Characteristic	**All (N=6719)**	**White/ Caucasian (N=5607)**	**Black / African American (N=857)**	**Other (N=255)**	
Dimensions of Toxic Stress	**N (%)**	**N (%)**	**N (%)**	**N (%)**	**p-value**
Age: mean (SD)	67.2 (7.5)	67.4 (7.6)	66.3 (7.0)	65.3 (7.4)	
Age categories (years)					< 0.0001
<=60	1254 (18.7)	1021 (18.2)	160 (18.7)	73 (28.6)	
61-70	3366 (50.1)	2762 (49.3)	481 (56.1)	123 (48.2)	
71-79	1785 (26.6)	1539 (27.4)	193 (22.5)	53 (20.8)	
>80	314 (4.6)	285 (5.1)	23 (2.7)	6 (2.3)	
Sex					< 0.0001
Male	2468 (36.7)	2119 (37.8)	251 (29.3)	98 (38.4)	
Female	4251 (63.3)	3488 (62.2)	606 (70.7)	157 (61.6)	
Marital Status					< 0.0001
Never married	167 (2.5)	112 (2.0)	47 (5.5)	8 (3.1)	
Married/ partnered	4760 (70.8)	4150 (74.0)	431 (50.3)	179 (70.2)	

Separated/Divorced	675 (10.0)	488 (8.7)	156 (18.2)	31 (12.2)	
Widowed	1117 (16.6)	857 (15.3)	223 (26.0)	37 (14.5)	
Education					< 0.0001
Less than High School/GED	1497 (22.3)	1069 (19.1)	319 (37.3)	109 (42.8)	
High-school graduate	2199 (32.7)	1879 (33.5)	261 (30.5)	59 (23.1)	
Some college and above	3022 (45.0)	2659 (47.4)	276 (32.2)	87 (34.1)	
Ever smoked					0.8833
Yes	3649 (54.9)	3054 (55.0)	461 (54.3)	134 (53.8)	
No	3004 (45.1)	2501 (45.0)	388 (45.7)	115 (46.2)	
Current alcohol use					< 0.0001
Yes	3642 (54.2)	3248 (57.9)	305 (35.6)	89 (34.9)	
No	3077 (45.8)	2359 (42.1)	552 (64.4)	166 (65.1)	
BMI					< 0.0001
BMI < 18.5 kg/m^2 (Underweight)	53 (0.8)	47 (0.8)	5 (0.6)	1 (0.4)	
BMI 18.5-24 kg/m^2 (Normal weight)	1777 (26.8)	1572 (28.4)	130 (15.3)	75 (30.0)	
BMI 25-29 kg/m^2 (Overweight)	2654 (40.0)	2259 (40.8)	303 (35.7)	92 (36.8)	
BMI ≥30 kg/m^2 (Obese)	2151 (32.4)	1658 (30.0)	411 (48.4)	82 (32.8)	
No. of comorbidities ever had					< 0.0001
None	1037 (15.4)	891 (15.9)	96 (11.2)	50 (19.6)	
One	1872 (27.9)	1599 (28.5)	191 (22.3)	82 (32.2)	
Two	1995 (29.7)	1663 (29.7)	272 (31.7)	60 (23.5)	
Three or more	1815 (27.0)	1454 (26.0)	298 (34.8)	63 (24.7)	
Retirement Status					< 0.0001
Not retired	2893 (43.1)	2470 (44.1)	314 (41.3)	77 (30.2)	
Retired plus another status	508 (7.6)	430 (7.7)	59 (7.7)	16 (6.3)	
Completely retired	3317 (49.4)	2706 (48.3)	388 (51.0)	162 (63.5)	
Moderate physical activity					< 0.0001
Never	755 (11.2)	650 (11.6)	68 (7.9)	37 (14.5)	
1-4 times per month	3328 (49.5)	2854 (50.9)	361 (42.1)	113 (44.3)	
> 1 time a week	1605 (23.9)	1302 (23.2)	244 (28.5)	59 (23.1)	
Every Day	1030 (15.3)	800 (14.3)	184 (21.5)	46 (18.0)	
Suffer from HD, T2DM or Stroke					< 0.0001
No	4529 (67.4)	3850 (68.7)	529 (61.7)	150 (58.8)	
Yes	2190 (32.6)	1757 (31.3)	328 (38.3)	105 (41.2)	
Ever had High blood pressure					< 0.0001
No	3148 (46.9)	2770 (49.4)	242 (28.3)	136 (53.3)	
Yes	3567 (53.1)	2834 (50.6)	614 (71.7)	119 (46.7)	
Ever had Stroke					0.3483
No	6404 (95.4)	5351 (95.5)	809 (94.4)	244 (95.7)	
Yes	311 (4.6)	252 (4.5)	48 (5.6)	11 (4.3)	
Ever had Diabetes					< 0.0001

No	5621 (83.7)	4792 (85.5)	646 (75.4)	184 (71.8)	
Yes	1093 (16.3)	810 (14.5)	211 (24.6)	72 (28.2)	
Ever had Heart problems					0.4102
No	5507 (82.0)	4581 (81.8)	713 (83.3)	213 (83.9)	
Yes	1206 (18.0)	1022 (18.2)	143 (16.7)	35 (15.4)	
Onset of Dementia					0.4987
No	6425 (95.6)	5369 (95.8)	814 (95.0)	242 (94.9)	
Yes	294 (4.4)	238 (4.2)	43 (5.0)	13 (5.1)	

Supplementary Table 7.2: Other factors in relation to risk for incident dementia among older adults enrolled in the HRS 2006-2016.

Characteristic	**n/N**	**Unadjusted HR (95%CI)**	**p-value**	**Adjusted HR[c] (95%CI)**	**p-value**
Demographic Characteristics					
Sex					
Male vs Female	104/2830	1.28 (0.92, 1.78)	0.1387	1.21 (0.80, 1.84)	0.3549
Education					
Less than High School vs College and above	82/1695	**1.55 (1.06, 2.27)**	**0.0236**	1.14 (0.74, 1.76)	0.5364
High School vs College and above	85/2545	1.08 (0.78, 1.50)	0.6302	1.08 (0.79, 1.47)	0.6148
Marital Status					
Never married vs Married	5/191	0.82 (0.31, 2.17)	0.6781	0.49 (0.14, 1.71)	0.2573
Separated/divorced vs Married	25/741	1.11 (0.73, 1.69)	0.6067	0.94 (0.60, 1.48)	0.7873
Widowed vs Married	66/1352	**0.63 (0.44, 0.89)**	**0.0102**	**0.61 (0.41, 0.91)**	**0.0172**
Body Mass Index					
Underweight vs normal	0/58	0	<0.0001	0	< 0.0001
Overweight vs normal	90/2967	0.88(0.63, 1.22)	0.4407	0.82 (0.58, 1.16)	0.2654
Obese vs normal	71/2418	1.16 (0.88, 1.52)	0.2907	0.94 (0.70, 1.26)	0.6853
Alcohol consumption					
No vs Yes	159/3650	**1.71 (1.20, 2.42)**	**0.0034**	**1.83 (1.27, 2.63)**	**0.0015**
Cigarette smoking					
Yes vs No	142/4148	**1.48 (1.07, 2.05)**	**0.0182**	**1.57 (1.09, 2.25)**	**0.0158**
Moderate physical activity					
1-4 times per month vs Never	98/3698	0.96 (0.57, 1.61)	0.8667	1.03 (0.62, 1.73)	0.9832
> 1 time a week vs Never	58/1804	1.15 (0.64, 2.06)	0.6282	1.12 (0.62, 2.02)	0.7017
Everyday vs Never	74/1225	1.63 (0.91, 2.92)	0.0964	1.53 (0.82, 2.86)	0.1746
Retirement Status					
Semi-retired vs Not retired		2.42 (1.59, 3.90)	0.0002	2.51 (1.56, 4.07)	0.0003
Completely retired vs Not retired		**1.44 (1.04, 2.00)**	**0.0052**	**1.49 (1.15, 1.93)**	**0.0033**
Health conditions					
Comorbid HD, Diabetes, or Stroke					
Yes vs No	126/2579	**1.43 (1.10, 1.86)**	**0.0089**	1.25 (0.90, 1.73)	0.1755

Ever had High blood pressure					
Yes vs No	157/4105	1.12 (0.82, 1.53)	0.4975	1.12 (0.81, 1.54)	0.4978
Ever had Heart disease					
Yes vs No	74/1458	1.21 (0.88, 1.65)	0.2408	1.06 (0.76, 1.47)	0.7337
Ever had Diabetes					
Yes vs No	58/1275	**1.43 (1.06, 1.91)**	**0.0182**	1.30 (0.86, 1.96)	0.2128
Ever had Stroke					
Yes vs No	47/402	**2.52 (1.71, 3.70)**	**< 0.0001**	**2.32 (1.66, 3.24)**	**< 0.0001**

Note: OR (95%CI): Odds Ratios (95% Confidence Intervals); Bold indicates p-value<0.05; All models adjust for the complex sampling design of the HRS; [c] Adjusted models control for race, toxic stress and demographic factors; sex, education, alcohol consumption, smoking, BMI, moderate physical activity, retirement status and comorbidity due to Diabetes, Heart diseases and Stroke; [d] Cumulative stress is the sum of recent and life course events, sum can be 0-17. Measures of Toxic Stress and indicators of resilience were not mutually adjusted for one another in multivariable models.

Figures

Figure 7.1: Sample selection to assess the association between Dementia and Psychosocial (stress) measures in the Health and Retirement Study, 2006-2016

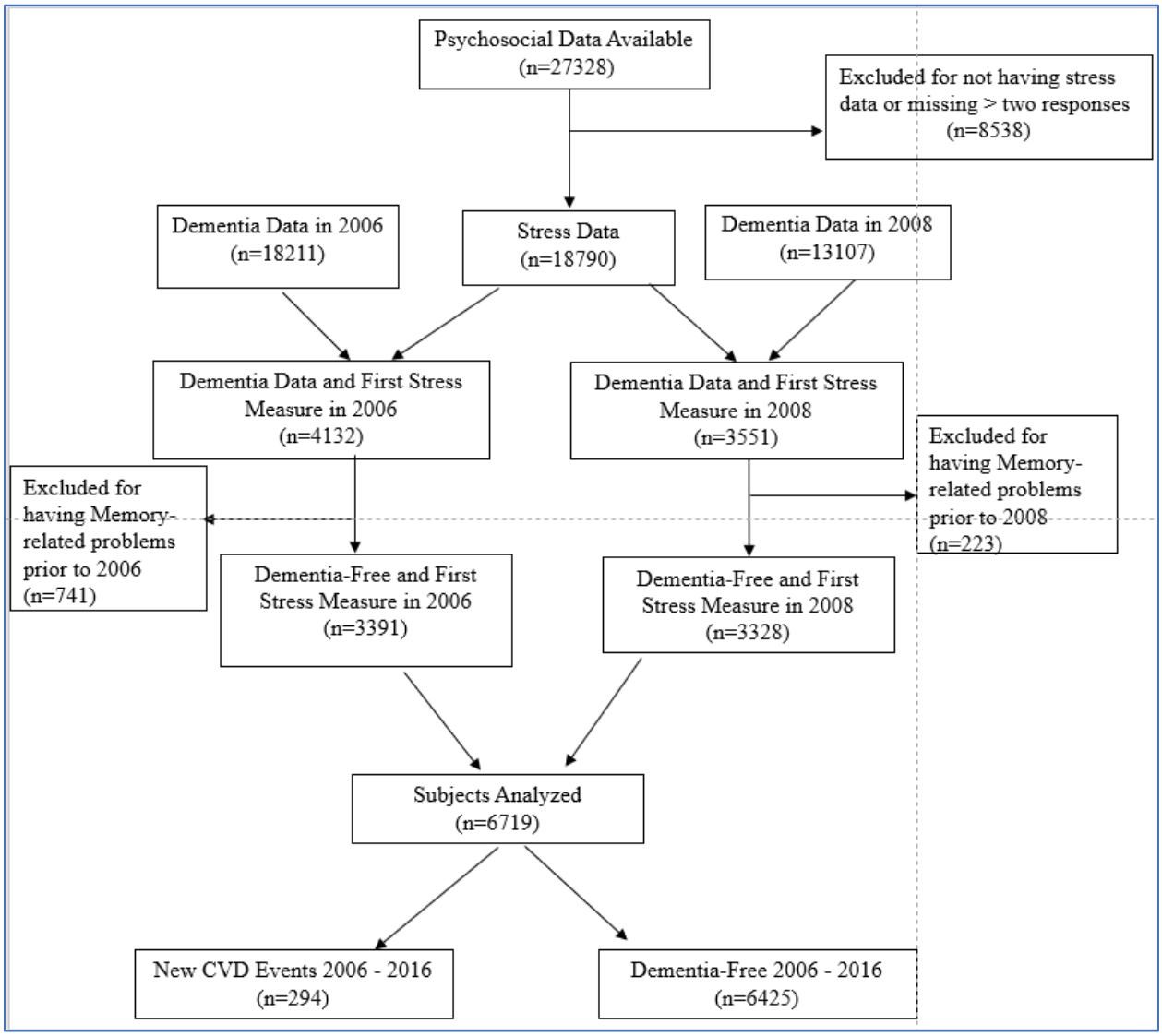


Figure 7.2: Dementia-free survival time by experiences of every day and lifetime discrimination among participants in the Health and Retirement study, 2006-2016

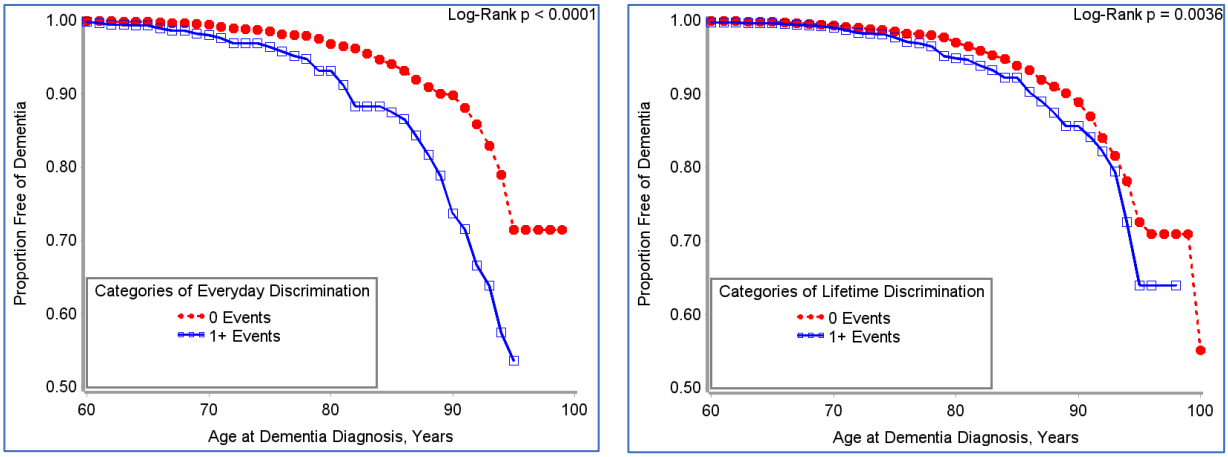


Figure 7.3: Race-related differences in risk of incident dementia vary within strata of mastery

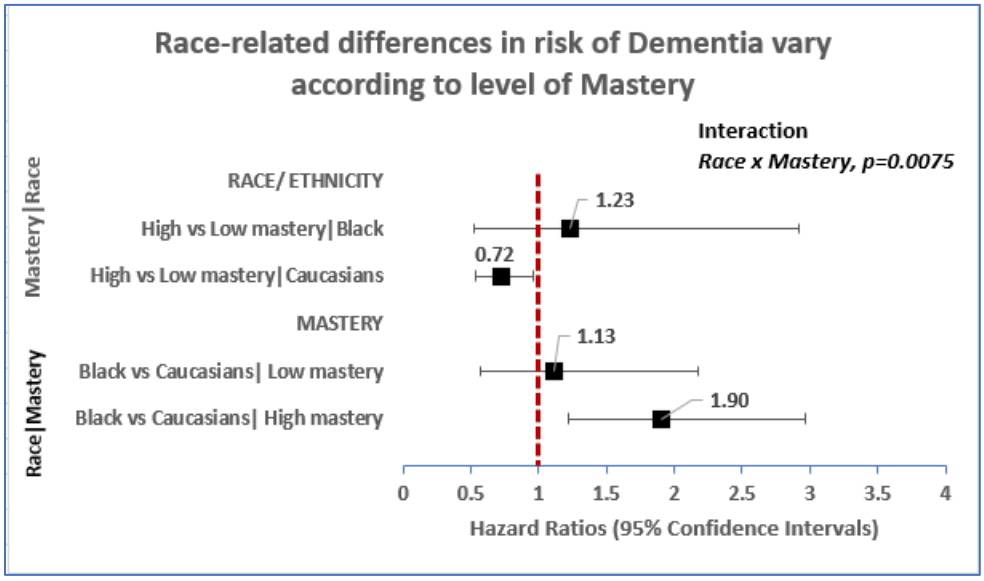


Figure 7.4: Cumulative stress-related differences in risk of incident dementia vary within strata of mastery

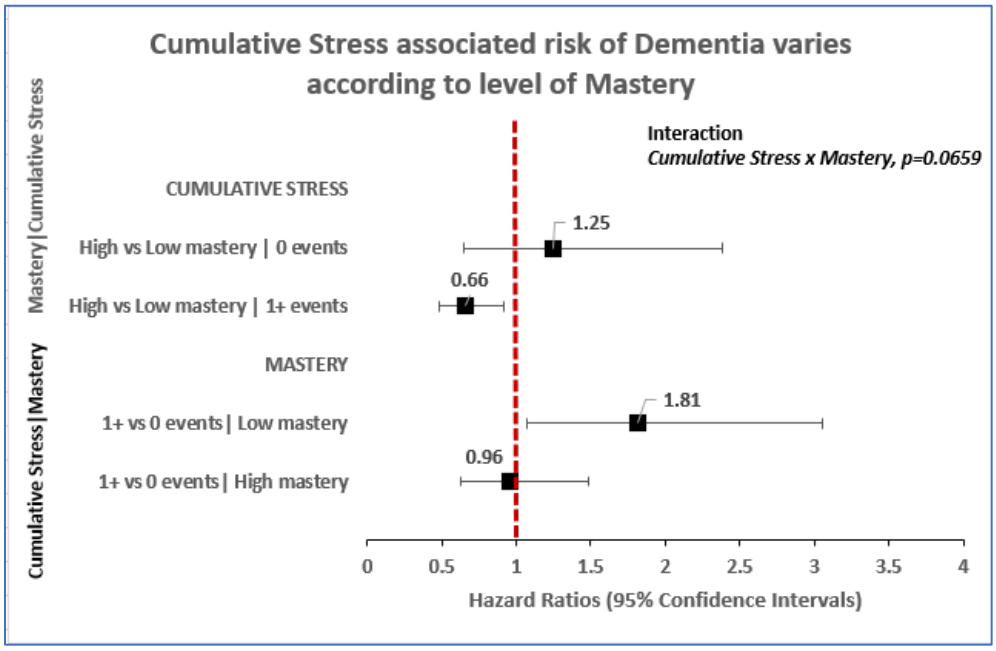
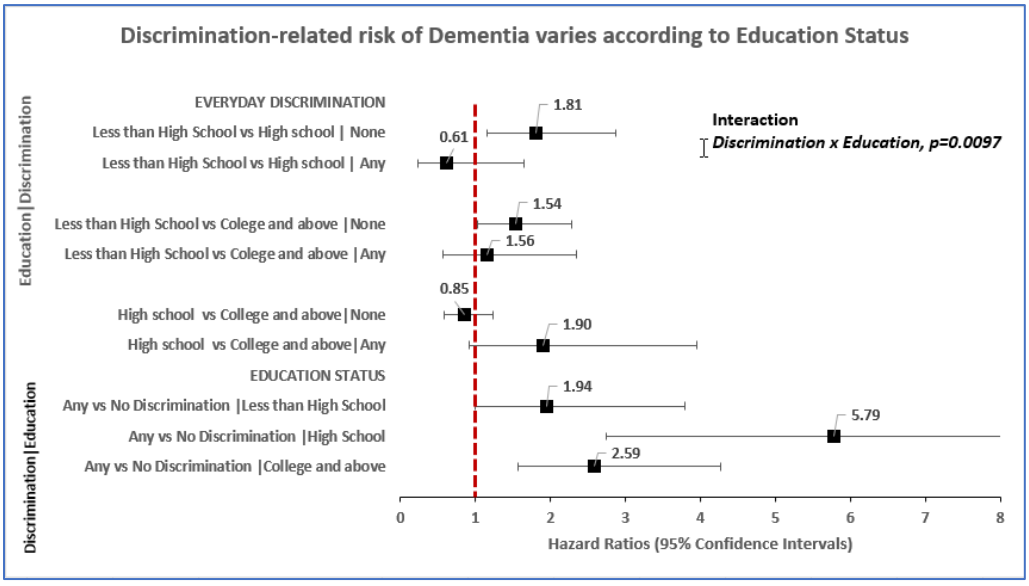


Figure 7.5: Discrimination-related differences in risk of incident dementia within strata of education



CHAPTER 8

CONCLUSIONS

Motivation

Race/ethnicity, Socio-economic status (SES), heath relevant behaviors and toxic stress combine in complex ways to affect health outcomes.[1,2] Existing literature suggests that SES not only confounds the relationship between race and health, but part of the causal pathway that links race to health.[3] Studies have documented significant relationship between race/ ethnicity and SES in health outcomes across the life-course.[4] However, it is important to note that race/ethnicity related differences in health is not entirely explained by between-race differences in SES.[5] Among the implicated determinants include: variations in health relevant behaviors and disease prevention resources,[6] environmental conditions,[7,8] access to[9] and quality of healthcare interventions. [10] Specifically designed studies in nationally representative diverse cohort of Americans are needed to explicate the roles of these multiple, complex, and sometimes subtle relationships.

Within the US population, racial disparities in the onset, severity and progression of several diseases have been noted. For example, African Americans have a higher prevalence of chronic kidney disease than White Americans, require dialysis or kidney transplantation at younger ages, and have a higher incidence of end-stage renal disease at each decade of life.[11] Further, the level of CKD risk factors in African American populations do not adequately account for their faster progression of CKD to end-stage renal disease.[11] With respect to cancers,

African American women are less likely than White women to receive initial breast cancer diagnosis. However, once diagnosed, African American women are more likely to have tumors that grow quickly, recur more often, are resistant to treatment, and to die faster from the disease.[12] Of note, a later stage at breast cancer diagnosis,[13] partly explains these disparities.[14] Of importance and not robustly investigated is the role of toxic psychosocial stressors such as discrimination, lifetime adversity and variations in resiliency enhancing factors in chronic disease progression among older Americans. Furthermore, the National Institute of Aging (NIA) has in recent years identified the need for health-disparities research related to aging that considers the role that stress, stress response, and resilience play in differential health outcomes in priority health disparity populations in the US.[15]

This dissertation has gone above and beyond the demonstration of racial/ethnic disparities in chronic disease endpoints and specifically investigated toxic stressors and deficits in resiliency promoting factors as key mediators of race-related differences in quality of life and neuro-cognitive declines in an aging population of retired and semi-retired adults with heart disease and/or diabetes.

Main Findings

Aim 1a) evaluated TS and minority race as determinants of quality of life (QOL) decline in a nationally representative sample of American adults ≥50 years old with heart disease (HD) and/or type-2 diabetes (T2DM). This study showed that among older Americans with HD and T2DM, minority race and higher TS levels are social determinants of decline in wellbeing.

Aim 1b) evaluated measures of resilience and minority race as determinants of quality of life (QOL) decline in a nationally representative sample of American adults ≥50 years old with heart disease (HD) and/or type-2 diabetes (T2DM). This study demonstrated, using various measures, that having lower levels of resilience promoting factors predicted sustained QOL declines in this population, whereas higher levels of resilience promoting factors were associated with decreased odds of QOL declines.

Aim 2a) examined whether TS and RPF are associated with neurocognitive impairment (NI) in a nationally representative sample of semi-retired and retired older American adults. The study found that higher levels of Toxic stress (TS) – i.e. chronic stress and experiences of everyday discrimination, and lower levels of resilience indicators e.g., mastery, were associated with an increased risk for neurocognitive impairment (NI). Furthermore, African American race was associated with cognitive disadvantage, but only in the status inconsistent context of high mastery.

Aim 2b) investigated whether toxic stress and resilience promoting factors were associated with onset of cognitive impairment in nationally representative sample of dementia-free adults followed longitudinally over 10 years. Findings revealed that high levels of toxic stressors including, everyday discrimination, ongoing chronic stressors and perceived constraints at baseline were associated with an increased risk of incident dementia. Furthermore sustained toxic stress was associated with faster advancement of dementia, and that experiencing discrimination wiped out the benefit of education for cognitive reserve amongst older Americans.

Implications

The implications of these research findings touch on several key aspects critical to improving the health of minority populations in the US. First, we live in a race-conscious society that has been dealing with a reckoning on race issues that have simmered for centuries, and largely left unaddressed. The recent killings of black people, the Black Lives Matter protests that ensued, and more especially the COVID-19 pandemic have exposed the pervasive impacts of long-standing systemic health and social inequities on many racial and ethnic minority populations, as minorities have been disproportionately ravaged by the pandemic .[16]

Aim 1 proposes that identifying predictors of QOL unique to different races/ ethnicities will help to better understand modifiable determinants and guide targeted interventions and policies tailored to racial/ ethnic minorities at high risk for lower QOL. Culturally grounded social, economic and health policies that address structural inequities in social experiences that shape exposure to a broad range of environmental stressors are likely to translate to improved wellbeing in a broad section of older US adults.[17] These may be targeted accordingly to reduce community level TS known to vary along racial lines in the US such as: addressing systemic racism in employment, experiences with law enforcement with expected onward benefit for reducing race-related disparities in wellbeing observed in this representative sample of US adults.

Similarly, aim 2 proposes that policy interventions that decrease psychosocial stress especially discrimination and opportunities that enhance social equity are needed to promote healthy cognitive aging regardless of race. However, specific social policies/interventions to

mitigate psychosocial adversity associated cognitive impairment must be tailored by race to maximize its effectiveness.

Suggestions For Future Research

There is great potential for future research. First this research highlights the need to increase minority participation in future research on health disparities. Additionally, future research should focus on understanding the social contexts of toxic stressors and coping resources in minority populations, encouraging data collection that is localized to the contexts that people live in. This is because people of different races tend to live in different social environments. Additionally more studies are needed to explore health disparities in integrated communities, where people of different racial groups/ ethnicities are living alongside each other. While large nationally representative studies are resourceful, they run the risk of failing to account for the localized social contexts that people live in.

There's also a need for more longitudinal studies to specifically evaluate the long-term effects of toxic stressors on age-associated diseases such as Alzheimer's' disease and other forms of dementias.[18] Depending on the nature, duration and severity of stress, physiological maladaptation may occur particularly with higher frequency and severity of occurrence exceeding the ability of individuals to cope.[19,20]

Conclusions

In general, the results of this dissertation support the hypothesis that similar rates of white vs. black disparities reported in prior research will be observed in this sample and that experiences of higher levels of toxic stress and lower levels of resilience -promoting factors will

partly mediate these race/ethnicity associations by inducing faster quality of life and neurocognitive decline in this vulnerable sub-group of older Americans.

In addition to filling a critically important knowledge gap directly relevant for informing or strengthening health policy and/or future interventions, the proposed study in a large nationally representative sample of older US adults was innovative on the following grounds. First, we conducted a specific prospective evaluation of toxic psychosocial stress as an independent risk factor or mediator of race/ethnicity- related differences, in neurocognitive and quality of life decline. Toxic stress is a highly prevalent exposure in the United States population for which its role in the onset and progression of a range of chronic diseases is unknown.

Second, the nesting of this project within the HRS allowed us to prospectively track within individual change in both toxic stress and chronic disease endpoints for as long as 10 years. The availability of prospective data with individual level change enhances causal inference with clear temporal sequence between timing of non-communicable disease diagnoses, the experiences of toxic stress and the changes in neurocognitive function and QOL that occurs over 10 years.

Third, further innovation lay in the use of rigorous analytic strategy, the ability to define and track a large vulnerable (i.e. recently diagnosed with diabetes or heart disease) cohort of aging Americans at high risk of both neurocognitive and quality of life decline.

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