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INTERSECTIONALITY BETWEEN SEX/GENDER AND RACE/ ETHNICITY ON COGNITIVE TRAJECTORIES AND DEVELOPMENT OF ALZHEIMER'S DISEASE

Justina Frances Avila-Rieger
University of New Mexico

Justina F. Avila-Rieger
Candidate

Psychology
Department

This dissertation is approved, and it is acceptable in quality and form for publication:

Approved by the Dissertation Committee:

Dr. Steven P. Verney, PhD, Chairperson

Dr. Jennifer Manly, PhD

Dr. Katie Witkiewitz, PhD

Dr. Jennifer Monzones, PhD

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by

JUSTINA F. AVILA-RIEGER

B.A., Psychology, California State University, Northridge, 2011
M.A., Clinical Psychology, California State University, Northridge, 2013

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ABSTRACT

Background: Older Blacks and Hispanics are approximately 2 to 3 times more likely than Non-Hispanic Whites (NHWs) to have AD (Gurland et al., 1998; Potter et al., 2009; Tang, Cross, Andrews, Jacobs, Small, Bell, Merchant, et al., 2001; Yaffe et al., 2013). Women are two-thirds of the population over age 65 and represent nearly two-thirds of the 5.3 million individuals aged 65 years and older with AD (Hebert, Weuve, Scherr, & Evans, 2013). Little is known about the interactive effects of race/ethnicity and sex/gender on cognitive trajectories of older adults. **Study Aims:** The specific aims of the current study were to: 1) establish measurement invariance of a comprehensive neuropsychological test

battery across sex/gender, racial/ethnic, and sex/gender by racial/ethnic subgroups; 2) examine differences in cognitive trajectories between subgroups; 3) identify specific socio-cultural/health mechanisms that account for differences in cognitive trajectories; and 4) investigate whether the relationships between socio-cultural and health indicators, cognitive trajectories, and conversion to dementia varied across subgroups. **Methods:** Participants were a total of 5258 non-Hispanic White (NHW), Black, and Hispanic men and women in the Washington/Hamilton Heights/Inwood Columbia Aging Project, age 65 years and older and not demented at baseline. Neuropsychological tests were administered at baseline and every 18–24 months. Multiple-group latent growth curve modeling was used to examine trajectories across sex/gender by racial/ethnic groups and to determine the relationship between specific socio-cultural/health indicators and cognitive decline, including childhood socioeconomic position, years of education, adult income and occupation, cardiovascular risk factors, and marital status. Cox regressions were used to estimate the effect of socio-cultural/health indicators on dementia conversion. Joint models that combine a latent growth model with a time-to-death model were used to determine whether our results were influenced by differential study attrition. **Results:** Full measurement invariance of the neuropsychological test battery was demonstrated across sex/gender groups and over repeated measurements, but only partial scalar invariance was demonstrated across racial/ethnic groups with intercept differences that varied by racial/ethnic and by racial/ethnic by sex/gender subgroups. Sex/gender differences in baseline cognitive test performance varied as a function of race/ethnicity and racial/ethnic differences in rate of cognitive decline varied as a function of sex/gender. Although differences in socio-cultural/health indicators explained a substantial proportion of the

racial/ethnic differences in cognitive trajectories, the extent to which each socio-cultural/health indicator accounted for racial/ethnic differences varied across men and women. The relationship between socio-cultural/health indicators and dementia conversion across racial/ethnic groups varied as a function of sex/gender. Finally, sex/gender by racial/ethnic-related variability in survival impacted estimates of cognitive trajectories and dementia conversion. **Conclusions:** This study takes an important first step in understanding interactions between race/ethnicity and sex/gender on cognitive trajectories by demonstrating variability in sex/gender differences across race/ethnicity. Examining interactions between sex/gender and race/ethnicity provides a more nuanced understanding of mechanisms of AD disparities and may lead to the development of new strategies to prevent or slow AD-related cognitive decline.

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INTRODUCTION

Alzheimer's disease (AD) is the most common type of dementia, representing approximately 60-80% of all dementia cases (Alzheimer's Association, 2017). AD is the 6th leading cause of death in the U.S. (Kochanek, Murphy, Xu, & Tejada-Vera, 2016) and the third most costly disease after cancer and heart disease, with the US spending over $200 billion each year to treat AD patients (Alzheimer's Association, 2017). Moreover, the number of older adults with AD is projected to increase to more than 11 million by 2050 (Sloane et al., 2002). Research has demonstrated that racial/ethnic and sex/gender minorities are disproportionately affected by AD, with older Blacks and Hispanics being 1.5 to 2 times more likely than Non-Hispanic Whites (NHWs) to have AD and women representing nearly two-thirds of those diagnosed with AD in the United States (Alzheimer's Association, 2017). The U.S. population aged 65 years and older is expected to increase exponentially over the next several decades and a significant proportion of these individuals will be racial/ethnic minorities (Lines, Sherif, & Wiener, 2014).

While there are multiple pathways to AD, factors related to genetics, vascular health, and socio-cultural experiences (e.g., residential history/immigration, early educational experiences and literacy, English language fluency, childhood and adult socioeconomic status, and social support) represent the underlying mechanisms most associated with disparities and differences across racial/ethnic and sex/gender groups. Very little attention has been paid to potential sex/gender-related variability in AD-risk factors across and within racial/ethnic groups. Testing the intersectionality between race/ethnicity and sex/gender on cognitive trajectories and development of dementia has the potential to

provide a more precise understanding of the mechanisms underlying AD disparities and lead to the development of new strategies to prevent or slow AD-related cognitive decline.

ALZHEIMER'S DISEASE

AD is characterized by unalterably progressive nerve cell degeneration within the cerebral hemispheres, resulting in progressive global cognitive deterioration (Lezak, Howieson, Bigler, & Tranel, 2012). Neurodegenerative changes associated with AD originate in medial temporal lobe limbic structures, such as the entorhinal cortex and hippocampus (Dickerson, Sperling, Hyman, Albert, & Blacker, 2007; Salmon & Bondi, 2009). Given that the medial temporal lobe structures are essential for learning and recall of new material, damage to these areas produce the first and most salient cognitive manifestation of AD- episodic memory impairment (Dickerson et al., 2007). As the disease progresses additional damage accrues in the parietal and frontal lobes, affecting language and semantic knowledge, executive functions, attention, and visuospatial abilities (Salmon & Bondi, 2009). These cognitive deficits are associated with gradual loss of the ability to carry out everyday activities independently (Dickerson et al., 2007).

Diagnostic criteria. The Diagnostic and Statistical Manual of Mental Disorders-Fifth Edition (American Psychiatric Association, 2013) characterizes two symptomatic phases of AD- mild cognitive impairment (MCI) and dementia- which are subsumed under the entities mild and major neurocognitive disorder, respectively. The DSM-V diagnostic criteria for dementia requires objective evidence, based on history and neuropsychological examination, of significant cognitive decline in one or more of the following cognitive domains: complex attention, executive functions, learning and memory, language, perceptual motor abilities, or social cognition. Additionally, there must be evidence that

cognitive deficits are sufficient to significantly impair the ability to carry out everyday activities independently. A diagnosis of MCI in the DSM-V requires modest decline in one or more cognitive domains that is not severe enough to significantly interfere with the ability to carry out daily activities. In order to arrive at a diagnosis of either MCI or dementia due to AD, the above criteria must be met for either MCI or dementia in addition to clear evidence of a gradual decline in learning and memory, steadily declining cognition without extended plateaus, and no evidence of other neurodegenerative diseases contributing to the clinical presentation. Further, the DSM-V distinguishes between probable AD and possible AD, with the latter diagnosed if there is evidence of a causative AD genetic mutation.

In 2011, the National Institute on Aging and Alzheimer's Association (NIA-AA) updated their original 1984 clinical criteria for Alzheimer's disease to include separate diagnostic guidelines for MCI (Albert et al., 2011) and AD (G. M. McKhann et al., 2011), as well as recommendations for "preclinical AD" (Sperling et al., 2011). Preclinical AD was defined as a stage of AD in which an individual is not cognitively impaired, yet they evidence abnormal AD biomarkers, such as increased amyloid tracer retention on positron emission tomography (PET) and/or low cerebrospinal fluid (CSF) β-amyloid ($A\beta_{42}$) (Jack, Albert, McKhann, Sperling, & Carillo, 2011; Sperling et al., 2011). Recommendations for the use of biomarkers and preclinical AD are intended for research rather than clinical care. However, findings from studies published since 2011, further demonstrating the relationship between imaging, CSF biomarkers- including fibrillar tau- and pathological changes in AD (Clark et al., 2011; Murray et al., 2015), have influenced recent proposals to redefine AD as a biological entity rather than a clinical-pathologic entity. Jack et al.

(2018) recently proposed a new research framework aimed at defining and staging AD across the entire disease spectrum (cognitively unimpaired, MCI, dementia). Under this framework, a research diagnosis of Alzheimer's disease would only be reserved for individuals who evidenced both abnormal CSF $A\beta_{42}$ and CSF tau, with cognitive impairment consistent with dementia. Individuals with abnormal CSF $A\beta_{42}$ and CSF tau who exhibit mild cognitive impairment or who are cognitively unimpaired are considered to be on the Alzheimer's continuum and characterized as Alzheimer's disease with MCI and preclinical Alzheimer's disease, respectively. Those who exhibit the typical AD neuropsychological symptom profile, but who have normal CSF $A\beta_{42}$ and CSF tau, are characterized as normal AD biomarkers with dementia and a diagnosis of non-Alzheimer's pathologic change with dementia is reserved for those with normal CSF $A\beta_{42}$ and abnormal CSF tau. In contrast to the NIA-AA 2011 clinical criteria, this approach treats cognitive impairment as a symptom of the disease rather than the definition. This is problematic because approximately 10% to 30% of individuals with clinically diagnosed AD do not demonstrate "AD pathology" (Nelson et al., 2011) or abnormal amyloid PET or CSF $A\beta_{42}$ (Rowe et al., 2010; Rowe et al., 2007; Jack et al., 2008; Salloway et al., 2014; Doody et al., 2014; Zwan et al., 2017; Jansen et al., 2015). Moreover, approximately 30% to 40% of older cognitively unimpaired individuals demonstrate AD pathology and abnormal amyloid PET or CSF $A\beta_{42}$ (Bennett et al., 2006; Knopman et al., 2003; Price, Davis, Morris, & White, 1991).

Neuropsychological assessment. Despite recent advances in the identification of biomarkers, neuropsychological measures continue to play an essential role in the diagnosis of AD (Smith & Bondi, 2013). In clinical settings, the number and type of

cognitive domains assessed is important for accurate identification of AD, differential diagnosis, and capturing countervailing influences on disease trajectory. Accordingly, clinical neuropsychological test batteries typically measure the broad cognitive domains of attention, executive functioning, processing speed, language, perceptual organization, and memory.

Neuropsychological profile of AD. The typical neuropsychological presentation in AD includes prominent deficits in episodic memory with additional impairments in the domains of language and semantic knowledge, executive functions, attention, and visuospatial abilities (Salmon & Bondi, 2009). Using measures of immediate and delayed recall of verbal and non-verbal material to identify episodic memory impairments, prior literature has demonstrated specific performance profiles in AD. For example, individuals with AD tend to demonstrate impaired scores on measures of both delayed recall and recognition of previously learned information, a combination that suggests significant difficulty in the acquisition and retention of information (i.e., abnormally rapid forgetting of previously learned information) (Lezak et al., 2012; Salmon & Bondi, 2009; Smith & Bondi, 2013). Additionally, on measures of free recall, AD patients tend to exhibit greatest losses on the earliest stimuli presented in a series (Lezak et al., 2012; Smith & Bondi, 2013). Moreover, memory does not benefit from semantic encoding of information due to degraded gist memory (Gallo, Shahid et al., 2006; Hudon et al., 2006).

As the neuropathology of AD spreads to the association cortices of the temporal, frontal, and parietal lobes, individuals with AD develop a semantic memory deficit characterized as a loss of general knowledge and language deficits (Salmon & Bondi, 2009). These deficits are exhibited by impaired performance on tests of confrontation

naming, verbal fluency, semantic categorization, and recall of overlearned facts (Chan, Salmon, & Butters, 1998; Hodges & Patterson, 1995; Nebes, 1989). Executive functioning deficits are typically observed on measures that require set-shifting, self-monitoring, or sequencing (Perry & Hodges, 1999). Deficits in attention and visuospatial abilities are less salient in the early stages of the disease. Attention deficits are typically evident on tasks requiring shifting of attention and working memory tasks that are dependent on attentional control (Butters, Salmon, Cullum, Cairns, & Troster, 1988; Storandt, Botwinick, Danziger, Berg, & Hughes, 1984). Visuo-spatial deficits associated with AD usually affect abilities associated with complex visuo-perceptual discriminations, mental rotation of spatial images, and simple constructional tasks (Cronin-Golomb & Amick, 2001).

Differential diagnoses. Given that AD-related pathological changes primarily occur in, but are not restricted to, cortical brain structures, AD is often characterized as a *cortical* dementia (Arango-Lasprilla et al., 2006; Smith & Bondi, 2013). Subcortical or frontal-subcortical dementias, for which pathological changes primarily occur in subcortical brain regions, include degenerative neurological diseases such as Huntington's disease, vascular dementia, and frontotemporal dementia. The cognitive deficit profile associated with a cortical dementia, like AD, can be distinguished from that of a subcortical dementia through neuropsychological assessment (Smith & Bondi, 2013). Subcortical dementias typically demonstrate slow processing speed, early prominent deficits in executive abilities and visuo-spatial and constructional abilities, as well as mild to moderate impairments in memory and language that are quantitatively and qualitatively distinct from those of AD. For example, on measures of episodic memory, individuals with AD tend to exhibit rapid forgetting deficits on both free recall and recognition tasks, while

subcortical dementias tend to demonstrate retrieval deficits with impaired recall but improved recognition (Smith & Bondi, 2013). Additionally, the language deficits characteristic of AD (i.e., loss of semantic knowledge) can be distinguished from the search-retrieval language deficits characteristic of subcortical dementia with measures of semantic and phonemic fluency (Henry, Crawford, & Phillips, 2004). Pattern analysis (recall vs recognition, letter vs. category fluency) is useful in differential diagnosis (Salmon & Bondi, 2009; Smith & Bondi, 2013).

Prevalence/incidence. An estimated 5.5 million Americans are currently living with AD (Alzheimer's Association, 2017). These estimates include nearly one third of the U.S. population who are 85 years and older. As mentioned previously, the literature has consistently demonstrated disparities in the prevalence and incidence of AD between sex/gender and racial/ethnic groups.

DISPARITIES IN ALZHEIMER'S DISEASE

The following review will focus on the three major racial/ethnic groups in the U.S., Blacks, Hispanics, and non-Hispanic Whites (NHW). Sex refers to biological differences between males and females (i.e., chromosomal, gonadal, or hormonal differences), while gender refers to socio-culturally constructed characteristics of women and men (Mielke, Vemuri, & Rocca, 2014). These terms are often used interchangeably yet most studies only ask participants whether they are male or female and sex or gender is inferred based on their response. To avoid further inconsistent/inaccurate use of sex or gender, we use the term "sex/gender" in this article.

Racial/ethnic disparities. Per capita, older Blacks and Hispanics are more likely than older NHW to have AD or other dementias (Demirovic et al., 2003; Dilworth-

Anderson, Hendrie, Manly, Khachaturian, & Fazio, 2008; Harwood & Ownby, 2000; J. J. Manly & Mayeux, 2004; Perkins et al., 1997; Steenland, Goldstein, Levey, & Wharton, 2015). Frequently cited estimates from the Alzheimer Association (2010) suggest that Hispanics are approximately one- and one-half times more likely than NHWs to have AD, while Blacks are about twice as likely than NHWs to have the disease.

Estimates from the Alzheimer Association were derived from the Aging, Demographics, and Memory Study (ADAMS; Plassman et al., 2007) and the Washington Heights-Inwood Columbia Aging Project (WHICAP; Gurland et al., 1999). ADAMS is the only study completed to date that conducted standardized diagnostic evaluations on a nationally representative sample large enough to derive valid prevalence estimates across race/ethnic groups. Additionally, WHICAP is the only such study that has reported prevalence estimates for the three largest racial/ethnic groups in the United States (Alzheimer Association, 2010). Participants in ADAMS constituted a representative sample of the U.S. population aged 71 and older (Plassman et al., 2007). Study findings demonstrated prevalence rates to be 21.3% for Blacks and 11.2% for NHW participants (Potter et al., 2009), suggesting that the Black participants in this study were almost two times more likely than their similarly aged NHW counterparts to have AD or other dementias. While the ADAMS sample included Hispanics, the number of participants was too small to provide valid prevalence rate estimates.

Prevalence estimates from WHICAP were based on a sample Caribbean-Hispanic, Black, and NHW participants aged 65 and older (Gurland et al., 1999). Reported prevalence estimates of AD and other dementias were 20.8% in Hispanics, 18.8% in Blacks and 7.8% in NHWs. Prevalence rates tended to vary by age across racial/ethnic groups.

Specifically, while rates for Blacks aged 75 and older were twice that of similarly aged NHWs, Blacks between the ages 65 and 74 were approximately three times more likely than NHWs to have AD and other dementias. Additionally, Hispanics between the ages 65 and 84 were two and a half times more likely than NHWs to have AD and other dementias. Lower prevalence rates in different Hispanic subpopulations have been reported. For example, a population-based study of Mexican-Americans in Sacramento, California, reported a 1.2% prevalence of AD or other dementias in participants, aged 65 to 74 years of age, with rates increasing to 26.1% of those aged 85 and older (Haan et al., 2003). Disparate findings between the two studies may reflect true differences among Hispanic subgroups and/or differences in study methodology (Alzheimer's Association, 2010).

Not all epidemiological data have been consistent or conclusive. A population-based study of NHWs and Blacks in Maryland, North Carolina, Pennsylvania, and California, reported prevalence rates for NHW with AD and other dementias to be 8.9% for those aged 70 and younger and 46.9% for those aged 85 and older; however, prevalence for Blacks in the study was approximately 1.6 times higher compared to the NHW's across age groups (Lopez et al., 2003). In a cohort of Black participants in Indianapolis, Indiana, Hendrie and colleagues (1995) reported prevalence rates for AD or other dementias to range from 2.6% to 32.4% of those aged 65-74 and those aged 85 and older, respectively. Fillenbaum and colleagues (1998), found no significant difference in AD prevalence among Black (7.0%) and NHW (7.2%) participants aged 68 and older in Piedmont, North Carolina.

More recently, Mayeda and colleagues (2016) examined racial/ethnic disparities in dementia incidence among Black, American Indian/Alaska Native (AI/AN), Latino,

Pacific Islander, NHW, and Asian American older adults covered by Kaiser Permanente Northern California (KPNC) health insurance. The authors estimated the 25-year cumulative incidence of dementia for each group and found that dementia incidence was highest among Blacks, followed by AI/ANs, with the lowest incidence rates among Asian Americans. While they found these racial/ethnic differences across both men and women, the differences were wider for men. This was most notable for differences between Blacks and Asian Americans, where dementia rates were 60% higher for Black women compared to Asian American women but 93% higher for Black men compared to Asian American men. Within each racial/ethnic group, the authors found similar incident dementia rates between men and women until ages 90+ years, when rates were higher for NHW women compared to NHW men.

Findings regarding racial/ethnic differences in rate of cognitive decline have also been mixed. For example, while several studies have reported faster rates of decline in Hispanics (Alley, Suthers, & Crimmins, 2007) and Blacks (Castora-Binkley, Peronto, Edwards, & Small, 2013; Masel & Peek, 2009; S. K. Park et al., 2006; Yaffe et al., 2009) compared to NHWs, others have found slower rates of decline (Barnes et al., 2005) and longer survival rates in Blacks (Mehta et al., 2008) or similar rates of decline in Hispanics compared to NHWs (Castora-Binkley et al., 2013; Masel & Peek, 2009). Variability in results across studies may be due to, at least in part, variation in sample composition, participation rates, and methods used to identify AD and other dementias; however, it is possible that much of the variability may be explained by the vast heterogeneity within racial/ethnic groups, particularly in regard to various socio-cultural experiences.

Sex/gender differences. Recent AD prevalence estimates suggest that women make up approximately two-thirds of the individuals diagnosed with AD (Hebert et al., 2013). Of course, estimates of disparities in prevalence rates vary. Of the individuals in ADAMS diagnosed with AD or other dementias, 16% were women and 11% were men (Alzheimer's Association, 2010). While some studies have reported no sex or sex/gender differences in AD (Rocca et al., 1998; Bachman et al., 1993; Ganguli et al., 2000; Kawas et al., 2000; Hebert et al., 2001; Kukull et al., 2002; Edland et al., 2002), other research has suggested that disparities may only be present at older ages. Both the Cache County Study (Miech et al., 2002) and the Mayo Clinic Study of Aging (Roberts et al., 2013) found that AD prevalence rates were similar for women and men under the age of 79, but, for those aged 80 and older, rates for women tended to be higher than men. Further, a meta-analysis that included studies from US, Europe, and Asia demonstrated that women were at greater risk of developing AD, but not other dementias, compared to men (Gao, Hendrie, Hall, & Hui, 1998).

Some studies demonstrating stronger associations between AD pathology and clinical AD in women compared to men. Barnes and colleagues (2005) found that the odds of clinical AD increased by 20 with each unit of AD pathology in women, while only a 3 times increase was demonstrated in men. However, no clear sex/gender differences in amyloid burden or tau have been found in the literature (Ferretti et al., 2018).

Regarding differences in rates of cognitive decline, some studies have demonstrated that women demonstrate a faster rate of cognitive and functional decline after receiving a diagnosis of AD (Aguero-Torres, Fratiglioni, GUo, Viitanen, & Winbald, 1998; Tschanz, Corcoran, & Schwartz, 2011). Chapman et al. (2011) found that decline in

memory performance was approximately 1.6 times greater in women compared to men. On the other hand, some studies have found no difference in rate of decline (Mielke et al., 2014).

Inconsistent findings in sex/gender research may be due to a variety of factors. The higher frequency and lifetime risk of dementia in women is likely due to the fact that women live longer than men and men who survive as long as women tend to have above average cardiovascular health (Chene et al., 2015). Issues related to selective survival may hurt our ability to make conclusions about differences between men and women. Additionally, some research has indicated that sex/gender differences are more pronounced at higher socioeconomic status (SES) levels and in cultures with wider sex/gender stratification (i.e., roles of men and women are controlled into distinct spheres and duties) (Reilly, 2012). Moreover, most sex/gender research is predominantly based on NHW samples and it is unclear whether these differences are present in racial/ethnic minority populations.

POTENTIAL REASONS FOR DISPARITIES

Genetic and biological mechanisms. There are several genetic and biological risk factors associated with the development of AD. The following genetic and biological mechanisms are the most relevant to racial/ethnic and sex/gender differences in AD.

Genetics. A multitude of genetic variations associated with increased risk of AD have been identified by large-scale genome-wide association studies (see Reitz & Mayeux, 2014 for review). Nonetheless, for more than a decade, the apolipoprotein E (APOE) gene has demonstrated the strongest association with AD (Reitz & Mayeaux, 2014; Smith & Bondi, 2013). The APOE gene provides the building blocks for a protein that transports

cholesterol in the bloodstream. Individuals inherit one of three forms of the gene (i.e., e2, e3, or e4) from each parent (Mahley & Rall, 2000). Individuals with a single APOE-e4 allele have a 2- to 3-fold increased risk of developing AD, while those with two copies have a five-fold increased risk (Kuusisto et al., 1994). In addition, each inherited APOE-e4 allele lowers the age-at-onset 6 to 7 years (see Reitz & Mayeux, 2014 for review). Moreover, the APOE-e4 allele has been associated with lower performance on memory tasks, MCI, and progression from MCI to dementia (Barabash et al., 2007; Petersen et al., 1995; Tyas et al., 2007).

Most of the AD genetic research has demonstrated that the effects of APOE-e4 are more prominent in women than in men (see Farrer et al., 1997 for review). Some studies have reported that, in women, the APOE-e4 allele had more harmful effects on hippocampal pathology, functional connectivity changes, and memory performance compared to men (Laws, Irvine, & Gale, 2016). Greater amyloid plaque and neurofibrillary tangle pathology has also been reported among women who were APOE-e4 carriers in autopsy studies (Corder et al., 1993). On the other hand, the APOE gene is a weak or inconsistent predictor of AD in Blacks and Latinos (Crean et al., 2011). These findings are likely due to racial/ethnic minority groups being largely neglected by genomic research (Reitz & Mayeaux, 2014).

Hormones. Animal models have consistently demonstrated the neuroprotective effects of estrogen on neuropathic processes affecting AD (Murphy & Segal, 1996; Han et al., 2013; Aenlle et al., 2009). Both women and men experience estrogen loss in late-life; however, compared to men, women experience a much more severe and rapid loss of ovarian sex hormones after menopause (Mielke et al., 2014). The impact of estrogen loss

or the benefit of hormone replacement therapy (HRT) on the risk of AD in women is unclear. Several observational studies have reported reduced AD risk associated with initiating HRT shortly after menopause (Morrison, Brinton, Schmidt, & Gore, 2006). In contrast, findings from a large clinical trial of HRT reported a two-fold increase risk of dementia in women receiving HRT (Shumaker, Legault, & Kuller, 2004). A potential explanation for the different findings between observational studies and clinical trials is that women who use HRT typically come from higher SES backgrounds, have higher education attainment, and/or are in better health (Rocca, Gossardt, & Shuster, 2010), suggesting that socio-cultural factors may mediate the relationship between hormones and risk of AD.

Cerebrovascular disease and cardiovascular risk factors. Cerebrovascular disease (CVD) is presumed to increase the risk of dementia via cerebrovascular changes, including hemorrhagic infarcts, ischemic cortical infarcts, and white matter changes. Infarcts and white matter hyperintensities can damage brain regions, such as the thalamus and thalamo-cortico projections involved in memory. Increase in AB deposition may also result from these cerebrovascular changes, leading to cognitive decline or inducing an inflammatory response that impairs cognitive function (Reitz & Mayeaux, 2014).

Specific cardiovascular risk factors such as hypertension, high cholesterol, body weight, and diabetes have been associated with increased risk for later-life cognitive impairment, dementia, and AD (see Reitz & Mayeux, 2014 for review). Compared to men, women generally suffer more atherosclerosis due to smaller and stiffer hearts and cardiac vessels (Li & Singh, 2014). Women account for nearly 55% of the approximately 16 million Americans with diabetes, with type 2 diabetes being more pronounced in females

(Li & Singh, 2014). Sex differences in cardiovascular risk of AD has been demonstrated in some studies, suggesting that men with high TG and low HDL-cholesterol levels have an increased incidence of dementia but not AD, whereas low TG levels in were associated with a decreased risk of AD in women (Ancelin et al., 2013).

Cardiovascular risk factors are more prevalent in Blacks and Hispanics compared to NHWs (Glymour & Manly, 2008). Blacks in the U.S. have some of the highest rates of hypertension in the world (Lloyd-Jones, Adams, & Brown, 2010). Nearly half (44%) of the Black women in the U.S. have hypertension (Center for Disease Control, 2015). Moreover, older blacks have a higher burden of diabetes, characterized by higher prevalence of risk factors related to diabetes and more diabetes-related conditions compared to older NHWs (Barnes & Bennett, 2014). While Hispanics have been shown to have lower rates of congenital heart disease and total CVD, they tend to demonstrate higher rates of CVD risk factors compared to other racial/ethnic groups (Graham, 2014).

Risk factors tend to differ depending on Hispanic subgroup. For example, Mexican-Americans tend to have a higher prevalence of hypertension and pre-hypertension compared to NHW (Allison et al., 2008). However, Puerto Ricans have the highest rates of hypertension-related deaths compared to other Hispanic subgroups (Morales, Leng, & Escarce, 2011). Diabetes prevalence in Mexican-Americans and Puerto Ricans is over twice the prevalence of NHWs (Reaven et al., 2003). Studies have also demonstrated an increase in CVD related risk factors between first- and second-generation Mexican-Americans (Parikh, Enriquez, & Selzer, 2008). Moreover, racial/ethnic minorities are less likely to receive effective CVD-related treatment and have less frequent access to invasive procedures such as cardiac catheterization, percutaneous coronary intervention, coronary

artery bypass graft, and implantation of defibrillators (Cram et al., 2009; Farmer et al., 2009; Mukamel et al., 2007).

Socio-cultural mechanisms. Racial/ethnic and sex/gender categories are socially constructed and serve as proxies for a myriad of socio-cultural experiences and significant with-in group variation exists with respect to socio-cultural characteristics.

Residential histories and immigration. Most elderly Blacks in the U.S. were born and raised in the South (Ruggles, Sobek, & Alexander, 2004), during a time when Jim Crow laws enforced segregation and limited opportunities such as education, health care, housing, and the labor market (Barnes & Bennett, 2014). The geographic distribution of the U.S. Black population dramatically altered between 1910 and 1970, when approximately three million Blacks migrated from the South during the Great Migration. The atrocities of the Jim Crow South combined with employment opportunities afforded by labor shortages in the industrial North during World War I (Lemann, 1991; Tolnay, 2003) prompted the flight from poverty and oppression toward the promise of opportunity and freedom. In 1900, approximately 90% of Blacks lived in the South and, at the conclusion of the migration, this number dropped to 53% (McHugh, 1987). Nonetheless, the effects of early life experiences of elderly U.S. Blacks are likely profound and may play a role in explaining disparities in AD (Glymour & Manly, 2008).

Geographic variation in the prevalence of CVD and CVD risk factors has been widely demonstrated. Higher rates of hypertension, diabetes, heart disease, cigarette smoking, obesity, as well as higher stroke mortality has been found among residents of rural southern regions of the U.S. (Stroke Belt region) (Liao et al., 2009). Such geographical disparities are presumed to be associated with differences in regional dietary

patterns such as differences in sodium, fiber, fatty acid, and cholesterol consumption (Hajjar & Kotchen, 2003). Using data from the Reasons for Geographic and Racial Differences in Stroke (REGARDS) cohort study of over 30,000 Black and NHW Americans aged 45 years or older, Judd and colleagues (2013) found that adherence to a southern style diet (e.g., fried food, organ meat, and sweetened drinks) was more common among individuals residing in the South, as well as among Black participants in the study. The authors also reported that adherence to this dietary pattern was a stronger mediator in the racial disparity in stroke than hypertension and atrial fibrillation.

Interestingly, higher stroke rates tend to persist despite migrating out of the South (Glymour & Avendano, 2007). Some studies have indicated that Southern born individuals have a greater risk of stroke compared to their non-Southern born counterparts. For example, Fang and colleagues (1996) found that Southern-born Black New York City residents had higher rates of CVD-related mortality compared to their Northeastern and Caribbean born counterparts.

In 2013, foreign-born Blacks accounted for 8.7% of the U.S. black population and approximately half of these black U.S. immigrants are from the Caribbean (Pew Research Center, 2013). Indeed, research has demonstrated better health outcomes in recent black Caribbean immigrants compared to U.S. born blacks (Waters, 2000); however, this advantage tends to diminish overtime (Portes & Zhou, 1993; Portes, 1995; Perlmann & Waldinger, 1997). Similar findings have been reported in Hispanic immigrants from Mexico, Central, and South America (Cho et al., 2004; Lara et al., 2005). Potential explanations for the diminishing immigrant advantage include acculturative stress, changes in health behavior, and environmental exposures (Glymour & Manly, 2008). Taken

together, differences in geographic exposures and residential histories between racial/ethnic minorities and NHWs in the U.S. are associated with disparate health outcomes that disproportionately put racial/ethnic minorities at increased risk for AD compared to NHWs. Moreover, residential histories also have downstream effects on other AD risk factors such educational experiences, literacy, and English language fluency.

Educational experiences. The influence of education on cognitive test performance has been repeatedly demonstrated throughout the literature, suggesting that individuals who are more educated perform better on neuropsychological tests (Rosselli & Ardila, 2003). Moreover, educational attainment has been associated with the development of dementia, with more years of schooling serving as a protective factor (Stern, 2009). It is possible that early education fosters aspects of cognitive and neural development during childhood or provides basic skill sets that provide protection against late-life cognitive decline (Glymour & Manly, 2008; Zahodne, Stern, & Manly, 2015). Educational attainment is often used as a proxy variable to index cognitive reserve. According to the theory of cognitive reserve, certain life experiences that promote the adaptive use of neural networks, such as more years of education, mitigate the impact of brain pathology on cognitive functioning (Stern, 2002, 2009). Thus, despite similar levels of brain pathology, an individual with high cognitive reserve will demonstrate different cognitive test performance and different time-to-dementia than an individual with low cognitive reserve.

In the literature, educational experiences tend to be characterized in terms of educational attainment, such as years of schooling completed or degrees attained. However, educational quality has also varied widely across the US throughout history (Berkman & Glymour, 2006). Quality of education is characterized by differences in

school and peer characteristics, such as pupil expenditure, teacher quality, pupil/teacher ratios, presence of special facilities such as science labs, or length of school years/days attended (J. J. Manly, Byrd, Touradji, Sanchez, & Stern, 2004). Elderly Blacks who attended primary school in the South during the influence of Jim Crow laws, received a significantly lower quality of education compared to their NHW counterparts (Glymour & Manly, 2008). Thus, educational attainment does not always imply an equivalent type or level of education, especially when comparing across racial/ethnic groups. Moreover, prior research has demonstrated that, in racial/ethnic minorities, quality of early educational experiences tends to be a better predictor of the cognitive benefit from education than traditional measures of educational attainment (Dotson, Kitner-Triolo, Evans, & Zonderman, 2009; J. J. Manly et al., 1999; J. J. Manly, D.M. Jacobs, P. Touradji, S. A. Small, & Y. Stern, 2002; J. J. Manly, Touradji, Tang, & Stern, 2003; Touradji, Manly, Jacobs, & Stern, 2001).

Hispanics residing in the U.S. have some of the lowest reported levels of educational attainment (Ryan & Siebens, 2009). The benefit of education on cognition and neuropsychological test performance tends to be more pronounced in U.S. born Hispanics compared to their Hispanic counterparts who permanently reside outside of the U.S. (Zeki Al-Hazzouri, Haan, Galea, & Aiello, 2011). Education systems in many small towns/cities in Central and South America are unable to implement standards and regulations regarding educational practices and teacher qualifications due to poverty, extremely low SES, limited academic resources, and few or no qualified instructors (Torres, Hoelzle, & Vallejo, 2016). Nonetheless, the benefit of obtaining more education in the U.S. on cognitive test performance is likely dependent of the quality of U.S. education received.

Socioeconomic position. Less schooling or poor quality of education tends to sustain lower social rank through lower paying jobs (Torres et al., 2016). In a group of racial/ethnically diverse older adults residing in New York City, Zahodne and colleagues (2015) found that income fully mediated that relationship between cognitive decline and education level, suggesting that late-life cognitive decline may also be influenced by lifetime dis/advantage. Considering that minorities earn less than their NHW counterparts at every education level (Williams, Mohammed, Leavell, & Collins, 2010), lower SES can have a differential impact on the neuropsychological test performance of racial/ethnic minority groups.

SES is the product of income, education, and occupation (Adler & Stewart, 2010). The implications of SES on cognitive outcomes include various home environment (e.g., parental education, housing conditions, and nutrition) and geographic factors (e.g., rural communities, access to health care, and environmental exposures) (Suzuki, Naqvi, & Hill, 2013). Social chains of risk associated with SES extend from childhood to old age. The influence of SES on test performance has been demonstrated across the literature on measures of IQ and cognitive ability, with children from lower SES family backgrounds obtaining, on average, lower scores on IQ tests compared to their high SES peers, and this difference tends to widen through development (von Stumm & Plomin, 2015).

Having comfortable childhood circumstances, including high paternal education and occupational prestige, have been found to serve as protective factors against cognitive decline among aging adults (Faul, 2008). Lee and colleagues (2003) found increased odds of cognitive decline among women whose fathers were farmers compared to those whose fathers were white-collar workers, above and beyond the effects of childhood household

income. Individual occupational prestige and income has also been found to predict the development of AD (Evans et al., 1997). Considering that men have had more opportunities than women in the past century for higher education and higher occupational attainment, women aged 65 and older are more at risk for developing AD due to the absence of a lifetime of cognitively advantageous experiences (Mielke et al., 2014).

Cultural factors and English-language fluency. Elderly Hispanics in the US are more likely to be foreign-born and predominantly Spanish speakers (Torres et al., 2016). While low English-Language fluency has been associated with an increased risk of dementia (Miranda, Gonzalez, & Tarraf, 2011), this relationship is likely dependent on socio-cultural factors such as education and acculturation. Language fluency/preference is often used as an indicator of integration into the US culture, as language use has been found to explain most of the variance in acculturation (Padilla & Perez, 2003). Moreover, Miranda and colleagues (2011) reported that the relationship between cognitive function and indicators of acculturation (i.e., place of residence during formative years, length of residence in the U.S.) was mediated by English proficiency among elderly Mexican-Americans. Other studies have demonstrated a higher probability of cognitive impairment was associated with English proficiency and social affiliation (Simpao, Espino, Palmer, Lichtenstein, & Hazuda, 2005).

Social Situation. Having important social relationships, such as being married and/or living with someone, has been associated with a lower risk of developing dementia (Crooks, Lubben, Petitti, Little, & Chiu, 2008; Fratiglioni, Wang, Ericsson, Maytan, & Winbald, 2000; Zunzunegui, Alvarado, & Del Ser, 2003) and slower rates of cognitive decline (Ertel, Glymour, & Berkman, 2008; Hakansson, Rovio, & Helkala, 2009). A recent

meta-analysis (Kuiper et al., 2015) demonstrated that less social participation, infrequent social contact, and feelings of loneliness may be associated with an increased risk of developing dementia. Social interaction may protect against dementia through engagement in intellectual, social and physical activities. For example, stimulating and socially engaging environments and lifestyles have been associated with neurogenesis and an increase of synaptic density (Fratiglioni, Paillard-Borg, & Winbald, 2004). Lack of social interaction and support may also lead to increased stress and subsequent structural changes in the hippocampus, which may be associated with an increased risk of developing AD (Fratiglioni et al., 2004; Wilson et al., 2007). Nonetheless, there is lack of agreement concerning which components of social interaction affect which specific cognitive domains (Berkman, 2000).

Few studies have examined differences in the effect of social interactions to cognitive outcomes between racial/ethnic minorities and NHWs and results have been mixed. Barnes and colleagues (2004) found that the relationship between social interaction and cognitive functioning was stronger for NHWs compared to blacks, yet Ertel and colleagues (2008) found similar effect sizes across racial/ethnic groups. While black and Hispanic social networks are often assumed to be larger and more supportive than those of NHWs, lack of consistent findings may be due to varying social interaction patterns across geographical and social contexts (Peek & O'Neill, 2001; Small, 2007).

INTERSECTIONALITY BETWEEN SEX/GENDER AND RACE/ETHNICITY

Race/ethnicity and sex/gender constrain or bolster resources, opportunities, and life chances, thereby structuring lived experiences. Viewing health as a life chance, it can be assumed that race/ethnicity and sex/gender also structure susceptibility and resistance to

illness (Richardson & Brown, 2016). While it has been increasingly recognized that racial/ethnic and sex/gender disparities in health are both consequences and contributors to social stratification across the life course, little has been done to understand how race/ethnicity and sex/gender intersect to define the health of older Americans (Warner & Brown, 2011). When race/ethnicity and sex/gender have been included in previous AD disparities research, the effects of race/ethnicity are typically examined while stratifying by sex/gender or vice versa. Race/ethnicity and sex/gender are fundamental determinants of opportunity structure and, thus, their affects cannot be understood separately. An intersectionality approach posits that race/ethnicity and sex/gender vary as a function of each other and are mutually reinforcing. These interlocking systems of oppression simultaneously structure the lived experience and life chances of the individuals occupying them through the creation of unique social locations (Collins, 2000).

Examining race/ethnicity and sex/gender as separate entities fails to recognize the differences between the socio-cultural contexts in which minority women and NHW women experience sex/gender-related disadvantage (Spelman, 1988). For example, since the 1940's, Black women have had consistently higher levels of educational attainment compared to Black men (McDaniel, DiPrete, Buchmann, & Shwed, 2011), while rates for NHW and Hispanic women have only recently surpassed their male counterparts (Logan, 2014). Racism in the labor market has served to counteract the benefits of schooling for Black Americans, albeit more for Black men than Black women. Black men have had lower employment rates than NHW men across education levels; however, until the 1980's, Black women were more likely to be employed than NHW women across education levels (McDaniel et al., 2011). Recent research has demonstrated that, conditional on parental

income, the black-white income gap is entirely driven by substantial wage and employment rate differences between Black and NHW men- no such difference was found between Black and NHW women (Chetty, Hendren, Jones, & Porter, 2018). Despite similar incomes, the authors found that Black women still had much lower levels of household income compared to NHW women, as Black women were less likely to be married and Black men earn less than NHW men. Moreover, other research has demonstrated that the wage gap between NHW women and men is much larger than that between Black men and women and Hispanic men and women (Hegewisch & Williams-Baron, 2018).

To date, no known studies have examined the intersectionality between race/ethnicity and sex/gender on cognitive trajectories to AD; however, available literature on intersectionality and physical health outcomes in older adults can be used to draw parallels to AD. Warner and Brown (2011) used an intersectionality approach to examines trajectories of disability in the nationally representative US Health and Retirement Study, in NHW, Black, and Mexican American Men and Women. Results demonstrated that all demographic groups exhibited worse functional limitation trajectories compared to NHW Men. While the NHW men in the study had the lowest disability levels at baseline, Black and Hispanic women had the highest disability levels, with NHW women and racial/ethnic minority men exhibiting intermediate disability levels. Further, Black women demonstrated a more rapid accumulation of functional limitation compared to all other groups. Similar studies have demonstrated the simultaneous impacts of race/ethnicity, sex/gender, SES, and education on health outcomes among Black and NHW older adults, with less educated, low income Black women having the lowest health outcomes (Ailshire & House, 2011; Hinze, Lin, & Andersson, 2012).

A central tenant of the intersectionality approach is that the simultaneous relationship between race/ethnicity and sex/gender is multiplicative, rather than additive (Richardson & Brown, 2016). An additive relationship would suggest that the disparities experienced by racial/ethnic minority women are the sum of disparities associated with being a racial/ethnic minority and those associated with being female (Richardson & Brown, 2016). Spelman (1988) argues that the additive approach fails to recognize the differences between the socio-cultural contexts in which minority women and NHW women experience sex/gender-related disadvantage and assumes that racial/ethnic identity can be deducted from a woman's combined sex/gender and racial/ethnic identity.

A recent study by Richardson and Brown (2016) provides further evidence that the race/ethnicity and sex/gender relationship is multiplicative rather than additive when examining hypertension risk trajectories of Black, Hispanic, and NHW men and women in the U.S. Health and Retirement Study. The authors found that being a Black or Hispanic female increased the odds of hypertension above and beyond the risk imposed by race/ethnicity and sex/gender separately. Testing the additive effect of race/ethnicity and sex/gender or hypertension risk trajectories, the authors found that race/ethnicity, but not sex/gender, shaped hypertension risk; thus, the additive approach obscured the important finding that among Blacks and Hispanics, being female was associated with greater odds of hypertension, while it served as a protective factor among NHWs. The above study demonstrates that explicitly testing the simultaneous impacts of race/ethnicity and sex/gender on health yields a more nuanced understanding of disparities. Intersectionality research in AD disparities is lacking and failure to examine this relationship raises the

potential of obscuring important differences in the onset and maintenance of AD, undermining efforts to eliminate disparities.

STATISTICAL TECHNIQUES TO EXAMINE AD DISPARITIES OVER TIME

Measurement invariance. Neuropsychological assessment provides critical information about the onset and progression of AD and other dementias and is an essential component of longitudinal research aimed at understanding disparities in dementia. However, it is imperative that neuropsychological measures have comparable measurement across racial/ethnic and sex/gender groups in order to make valid interpretations of demographic differences in cognitive aging.

Neuropsychological measures used to diagnose dementia have been developed and validated with primarily US-born, highly educated, monolingual English speaking NHWs. As previously discussed, an overwhelming amount of literature suggests that cognitive test performance is influenced by a myriad of socio-cultural factors including acculturation level, quality of education, socio-economic status, and English language proficiency. When criterion measures are vulnerable to socio-cultural factors, the potential for measurement validity issues increases. Failure to account for potential measurement issues can lead to inaccurate classification of cognitive impairment and, ultimately, hinder efforts to eliminate age-related cognitive health disparities.

Measurement invariance (i.e., equivalence) is an essential component of neuropsychological research examining group differences. Measurement invariance is observed when measures of interest represent the same theoretical constructs under different conditions (Horn & McArdle, 1992). Different conditions may include groups and/or time of measurement. In the context of measurement invariance, researchers can

examine whether neuropsychological tests measure the same cognitive constructs (equal factor structure), demonstrate equivalent relationships to hypothesized constructs across different subpopulations or contexts (equal factor loadings), and whether observed scores differ between subpopulations or contexts at equivalent levels of true score (equal intercepts) (T. A. Brown, 2015).

Previous studies have examined measurement invariance of cognitive abilities across age groups (Bowden, Weiss, Holdnack, & Lloyd, 2006; Hertzog & Schaie, 1986; Schaie, Willis, Jay, & Chipuer, 1989; Taub, McGrew, & Witta, 2004), clinical presentations (Hayden et al., 2011; L. Q. Park et al., 2012; Siedlecki, Honig, & Stern, 2008), language groups (Mungas, Widaman, Reed, & Farias, 2011; Siedlecki et al., 2010; Tuokko et al., 2009), sex/gender (Blankson & McArdle, 2013; Maitland, Intrieri, Schaie, & Willis, 2000), race/ethnicity (Barnes et al., 2016; Dolan, 2008; Edwards & Oakland, 2006; Mungas et al., 2011), and time (Barnes et al., 2016; Blankson & McArdle, 2013; Hayden et al., 2011). However, most of the previous research has been conducted on population-based samples that lack the racial/ethnic, linguistic, and socio-cultural diversity that is characteristic of community-based samples. Additionally, the few studies that have examined measurement invariance across race/ethnicity and/or sex/gender and time have done so by examining race/ethnicity and sex/gender separately.

Potential racial/ethnic-related variability in sex/gender groups has not been recognized in prior research examining measurement invariance across men and women. While these studies suggest that the same attributes are being measured across men and women, it is unclear whether the same attributes are being measured between NHW and Black men or NHW women and Hispanic men. To the best of our knowledge, no prior

studies have examined measurement invariance of neuropsychological measures across race/ethnicity and sex/gender subgroups (e.g., Black women vs. NHW women). Establishing measurement invariance across race/ethnicity and sex/gender subgroups would enable researchers to look at interactions between sex/gender and race/ethnicity in cognitive trajectories.

One method to examine measurement invariance is multiple-group confirmatory factor analysis (CFA). Multiple-group CFA allows all aspects of measurement invariance to be examined, including differences in factor structure, factor loadings, intercepts, residual variances, factor variances, factor covariances, and latent means (T. A. Brown, 2015). It is important to note there is variability in terminology for various tests of invariance (Vandenberg & Lance, 2000), which will be reviewed briefly here. Evaluation of equal factor structure, or equal number of factors and pattern of indicator-factor loadings, is often referred to as a test of *configural invariance* (Horn, McArdle, & Mason, 1983). Configural invariance is the most basic form of invariance and is tested by constraining the measurement model to be equal across groups while allowing all parameters (factor loadings, intercepts) to be freely estimated within groups (Kline, 2011). *Metric invariance* (Horn & McArdle, 1992) refers to equality of factor loadings across groups. An additional restriction is added to the previous configural model to test metric invariance by constraining the unstandardized factor loadings of each indicator (i.e., items) to be equal across groups. If the metric model does not fit worse than the configural model, then it is assumed that item indicators are related to latent factors in the same way across groups. *Scalar invariance* (i.e., strong invariance) adds another restriction to this model by constraining intercepts of the observed variables (items) to be the same across groups

(Widaman & Reise, 1997). This model assumes that at the same level of the latent construct, individuals will be at the same level (i.e., intercept) of each item response. Again, if the scalar model does not fit worse than the metric model, then it is assumed that item responses are the same, at the same level of the latent factor, across groups. In practice, scalar invariance is often hard to achieve, particularly when racial/ethnic groups vary on several socio-cultural factors that may impact item responding (Hambleton, Merenda, & Spielberger, 2005; van de Vijver, 2015).

It is often simply assumed that neuropsychological tests are similarly invariant across different demographic groups, as well as across assessment time points. However, if this assumption of invariance is incorrect and not explicitly tested, then interpretation of results based on neuropsychological test performance is likely to be inaccurate (Blankson & McArdle, 2013). Yet, very few longitudinal studies in cognitive aging with diverse populations have tested measurement invariance. In order to move AD disparities research forward, it is imperative to determine the comparability of neuropsychological test scores among those most at risk for AD.

Modeling cognitive decline. Cross-sectional approaches to examining differences in cognitive test performance and cognitive outcomes across racial/ethnic and sex/gender groups have been widely used throughout the literature. However, cross-sectional approaches tell us little about change processes and the potential mechanisms influencing change. Previous studies have demonstrated that the trajectory, or slope of decline, in cognitive performance can differentiate individuals who develop AD from those who do not (Mungas et al., 2010; Zahodne, Wall, et al., 2015). Heterogeneity in late life cognitive change trajectories has been well documented in the literature, in that, older individuals

demonstrate different rates of cognitive decline, as well as stable cognitive function, and, in some cases, improvement (See Mungas et al., 2010, for review). Many methods used to examine change over time, such as repeated measures analysis of variance (ANOVA), are unable to account for such individual differences in cognitive change.

Latent Growth Modeling (LGM) is a valuable method for examining trajectories of change and cognitive decline that allows for examination of within-person change and between-person variability, as well as examination of mechanisms of change (Preacher, Wichman, MacCallum, & Briggs, 2008). LGM stems from structural equation modeling (SEM), which is a modeling framework for testing patterns of relationships among measured (observed) and latent (unobserved) variables. In LGM, the observed variables are repeated measures of the same outcome (i.e., memory performance) and the latent variables describe trends over time in the outcome. Generally, two to three latent factors are specified. One represents the initial level of the outcome, or the intercept (i.e., baseline memory performance), and the other two represent the linear and/or quadratic rates at which the outcome changes, or the linear and quadratic slopes. Moreover, LGM can be extended to accommodate individually varying times of observation, which is common in longitudinal aging research. Failure to account for individual variation in time scores can bias estimates of intercept and slope (Coulombe, Selig, & Delaney, 2015). Individually varying time scores can be easily accommodated in LGM by replacing fixed time scores with individual-specific time scores, or random effects (Sterba, 2014). Thus, loadings are no longer fixed to universal values but rather loadings for each individual are constrained to the observed values of that individual's own time scores.

Selective attrition. Selection issues related to differential enrollment, attrition and/or survival are a major concern in cognitive aging research. When selection processes are systematically related to cognitive outcomes and determinants of these outcomes, estimates of the relationship between cognition and risk factors of interest may be biased (Banks, Muriel, & Smith, 2011). Individuals with impaired cognition and dementia are at heightened risk of poor health (Chodosh et al., 2004; Welmerink et al., 2010; Dodge, Du, Saxton, & Ganguli, 2006), death (Yaffe et al., 2010; Bassuk, Wypij, & Berkman, 2010), and study attrition (Euser et al., 2008; Chatfield, Brayne, & Matthews, 2005; Matthews et al., 2006). Additionally, risk factors associated with cognitive trajectories and outcomes, including education and socioeconomic status, are also associated with increased mortality (Weuve et al., 2015). Individuals who end up surviving longer in a study may be healthier, have higher levels of cognitive functioning, and at a lower risk for developing dementia compared to those who were lost at follow-up due to death. Not only will the surviving sample be less representative of the original population of interest, but differential survival across different groups (i.e., men and women) hinders the ability to make valid conclusions about group differences. For example, since men are more likely than women to die, men who end up surviving in the study as long as women may be healthier and have higher levels of cognitive functioning compared to surviving women. As a result, it will be unclear whether this difference in cognitive test performance is an actual difference between men and women or reflects higher attrition due to death among cognitively impaired men (Rouanet, 2016).

Selective attrition may also lead to spurious associations between risk factors and cognitive outcomes, such that harmful exposures may appear protective or protective

exposures may appear harmful (Weuve et al., 2015). Since death and dementia share common risk factors, failure to account for the relationship between the two may lead to biased estimates of the effect of a risk factor on dementia. Truncation due to death introduces interval censoring because dementia diagnoses can only be made at follow-up visits (Rouanet, 2016; Weuve et al., 2015). It is possible that individuals who are free of dementia at their last session before death progressed to a dementia status before dying; however, since this progression went unmeasured because they died before a diagnosis could be made at the follow-up visit, their dementia status at death is unknown. This type of interval censoring in the context of competing risks of death and dementia can lead to underestimated rates of incident dementia and biased estimates of the relationship between a risk factor and dementia (Joly, Commenges, Helmer, & Letenneur, 2002; Leffondre, Touraine, Helmer, & Joly, 2013).

Several approaches have been used to address study attrition due to drop-out (Enders, 2011); however, it has been argued that such approaches are limited in the context of survival (Weuve et al., 2015). When data is missing from an individual at a particular time-point due to non-death drop-out, the data is defined but missing. But, if data is missing due to death, then data is considered undefined because no such values exist (Wen, Terrera, & Seaman, 2018). One approach to account for the relationship between longitudinal data and selection processes is joint modeling that combines LGM with a time-to-event model into a single model. Joint models allow for the assumption of both dependence and association between longitudinal data and time-to-event to better assess the relationship between trajectories and risk factors of interest (Ibrahim, Chu, & Chen, 2010). Joint models characterize the status of the entire sample with respect to longitudinal response and death

(Kurland, Johnson, Egleston, & Diehr, 2009). In other words, the entire sample is described at each time point, not just those who survived. The joint response of being alive and cognitive test performance are defined at each time point making the longitudinal data balanced. As a result, cognitive trajectories are less likely to be affected by differential survival.

OVERALL SIGNIFICANCE OF THE CURRENT STUDY

As the elderly and ethnically diverse population in the U.S. continues to grow, more racial/ethnic minorities will be at risk for AD. While clear differences exist in prevalence and incidence rates of AD between racial/ethnic groups, the higher frequency of AD for women compared to men is likely due to selective survival. Additionally, previous research on sex/gender differences in cognitive test performance is limited by the lack of racially/ethnically diverse study samples. Not only is it possible that sex/gender differences in cognitive trajectories vary as a function of race/ethnicity, but racial/ethnic differences may also vary across sex/gender groups. Factors related to genetics, vascular health, and socio-cultural experiences (e.g., childhood socioeconomic status, educational experiences, adult socioeconomic resources), represent underlying mechanisms, mediators, and pathways most associated with racial/ethnic disparities in AD (Glymour & Manly, 2008; Lines et al., 2014). Although the role of socio-cultural factors in explaining differences in cognitive outcomes between men and women has been largely ignored in the sex/gender literature, sex/gender are fundamental determinants of opportunity structure. It is likely that socio-cultural experiences underlie sex/gender differences and differentially contribute to cognitive outcomes in men and women across and within racial/ethnic groups. Little has been done to understand how race/ethnicity and sex/gender intersect to define the cognitive

health of older Americans. Thus, the overall goal of the current study was to highlight the intersectionality of race/ethnicity and sex/gender as determinants of specific socio-cultural experiences that shape cognitive trajectories leading to AD.

The Washington Heights-Inwood Columbia Aging Project (WHICAP) is a community-based, longitudinal study of aging and dementia that has collected data from over 6,500, Medicare-eligible Black, Hispanic, and NHW women and men residing in northern Manhattan, NY. Data regarding cognitive trajectories and age of onset of AD has been collected via direct testing over time. The WHICAP participants have a diverse range of socio-cultural experiences, including those associated with residential history/immigration, early educational experiences and literacy, childhood and adult socioeconomic status, and social support. The observed heterogeneity in socio-cultural experiences is well-suited for rigorous evaluation of the intersectionality between sex/gender and race/ethnicity to understand the multiple layers of contributory factors to the risk of AD in an ethnically diverse group of older adults.

Establishing measurement invariance, or comparability of cognitive constructs, is an essential first step in research examining group differences in cognitive test performance. Research examining measurement invariance across sex/gender by racial/ethnic groups is lacking. It is possible that measures that are invariant across sex/gender groups may not demonstrate full measurement invariance across men and women of different racial/ethnic backgrounds. The current study aimed to establish measurement invariance of the WHICAP neuropsychological test battery across sex/gender by racial/ethnic subgroups over repeated assessments.

Research has consistently demonstrated sex/gender differences in cognitive test performance, with an advantage for women on episodic memory tests and an advantage for men on visuo-spatial functioning (De Frias, Nilsson, & Herlitz, 2006; Proust-Lima et al., 2008; Wetherell, Reynolds, Gatz, & Pedersen, 2002). Given that each of the aforementioned studies on sex/gender differences are based on samples that are primarily NHW, it is unclear whether these differences are present in racial/ethnic minority populations. However, racial/ethnic differences in educational opportunities, norms/expectations about women's work, and economic gains (Boustan & Collins, 2014) suggests that sex/gender may have a different effect on cognition in Blacks and Hispanics. The current study aimed to highlight the importance of examining the multiplicative influence of race/ethnicity and sex/gender on cognitive trajectories by examining whether initial cognitive test performance and rates of change differed across sex/gender, racial/ethnic, and sex/gender by racial/ethnic groups.

Race/ethnicity and sex/gender are fundamental determinants of opportunity structure that constrains or bolsters resources, opportunities, and life chances (Warner & Brown, 2011). As a result, these categories serve as proxies for unique socio-cultural experiences that underlie racial/ethnic and sex/gender disparities in health outcomes. Research has demonstrated that accounting for differences in life-course socio-cultural and health indicators attenuates racial/ethnic differences in cognitive outcomes (Mehta et al., 2008; Zhang, Hayward, & Yu, 2016). The current study aims to extend previous research by demonstrating that socio-cultural experiences and health indicators also explain sex/gender differences across and within racial/ethnic groups, as well as demonstrate variability in the relationship between socio-cultural experiences and cognitive outcomes

across sex/gender by racial/ethnic subgroups. Moreover, given that failure to account for differential attrition due to drop-out or death may lead to biased trajectory estimates, we sought to determine the extent to which differential attrition influenced estimates of cognitive trajectories and determinants of cognitive trajectories and dementia.

SPECIFIC AIMS

Specific Aim 1. Evaluate the measurement invariance of the WHICAP neuropsychological battery across sex/gender, racial/ethnic, and racial/ethnic by sex/gender subgroups over repeated measurements.

Hypothesis 1.1. The battery will demonstrate configural and metric invariance across repeated measurements, as well as across sex/gender, racial/ethnic, and sex/gender by racial/ethnic subgroups.

Hypothesis 1.2. We also expect that the battery will demonstrate scalar invariance over repeated administrations and across men and women.

Hypothesis 1.3. Due to socio-cultural heterogeneity between racial/ethnic groups, we hypothesize that scalar invariance will not be fully demonstrated across racial/ethnic and sex/gender by racial/ethnic subgroups.

Specific Aim 2. Examine sex/gender, racial/ethnic, and sex/gender by racial/ethnic differences in cognitive trajectories and examine the influence of selective attrition on trajectory estimates.

Hypothesis 2.1. We hypothesize that patterns of racial/ethnic and sex/gender differences in test performance will reflect previous findings. Namely, NHWs will obtain higher scores than Blacks and Hispanics, women obtain higher scores on memory, men

obtain higher scores on visuo-spatial abilities, and no sex/gender differences on language measures.

Hypothesis 2.2. When performance is examined across sex/gender by racial/ethnic groups, we expect sex/gender differences to vary as a function of racial/ethnic identity, with sex/gender differences between NHW men and women and not Black and Hispanic men and women.

Hypothesis 2.3. We expect cognitive decline to be associated with an increased risk of death across all groups and that joint models will provide trajectory estimates that demonstrate steeper cognitive decline compared to the models that do not account for death.

Specific Aim 3. Identify specific socio-cultural & health mechanisms, including childhood socioeconomic status, early educational experiences, occupational status, adult income, marital status, and cardiovascular disease burden, that account for sex/gender by racial/ethnic differences in cognitive trajectories.

Hypothesis 3.1. We expect childhood SES, educational attainment, occupation, and income to account for most of the differences in initial cognitive test performance and rates of change across sex/gender by racial/ethnic subgroups.

Hypothesis 3.2. We expect the remaining differences to be accounted for by marital status and cardiovascular disease burden.

Specific Aim 4. Investigate the relationship between socio-cultural and health indicators, cognitive trajectories, conversion to dementia, and differential attrition due to death across sex/gender by racial/ethnic subgroups.

Hypothesis 4.1. We expect socio-cultural experiences will be differentially related to cognitive trajectories across sex/gender by racial/ethnic subgroups. Previous research has suggested differential educational and economic returns on cognitive functioning in later life between NHWs and racial/ethnic minorities (Barnes et al., 2011; Boen, 2016). Thus, we hypothesize that the relationship between socio-cultural experiences and cognitive trajectories will be stronger for NHWs compared to Blacks and Hispanics, but the magnitude of this relationship will vary across sex/gender groups. Given the higher prevalence of cardiovascular/cerebrovascular disease in racial/ethnic minorities compared to NHWs, we also expect that cardiovascular disease burden will be more strongly associated with cognitive trajectories for Blacks and Hispanics. Further, we hypothesize that being married will have a positive impact on cognitive trajectories similarly across groups.

Hypothesis 4.2. We expect socio-cultural and health indicators will be differentially related to dementia conversion across sex/gender by racial/ethnic subgroups. We also hypothesize that lower childhood SES, educational attainment, occupation, and income, as well as higher CVD burden, will be related to greater risk of dementia conversion and this relationship will be stronger for Blacks and Hispanics compared to NHWs. We also expect that the magnitude of this relationship will vary across sex/gender groups.

Hypothesis 4.3. We hypothesize that many of the socio-cultural and health indicators associated with cognitive trajectories and dementia conversion will also be associated with differential attrition due to death across sex/gender by racial/ethnic subgroups. We also expect that models simultaneously estimating dementia conversion and death will demonstrate lower probabilities of incident dementia and slightly attenuated

estimates of the relationship between socio-cultural and health indicators and dementia conversion.

METHODS

PARTICIPANTS

Participants were community-living Medicare recipients 65 years and older recruited from northern Manhattan to participate in the Washington Heights-Inwood Columbia Aging Project (WHICAP) (Tang, Cross, Andrews, Jacobs, Small, Bell, & Mayeux, 2001). Potential participants were identified based on residence in U.S. census tracts within the study catchment area. Recruitment occurred in three waves: 1992 (N = 2,126), 1999 (N = 2,174) and 2009 (N = 2,128). Participants completed a baseline assessment and were followed up at 18 to 24-month intervals for up to 25 years. During each session, participants were administered a neuropsychological battery and asked about their general health, functional ability and medical history. Evaluations were conducted in English or Spanish, based on language preference. This study was approved by Institutional Review Boards at Columbia Presbyterian Medical Center, Columbia University Health Sciences, and the New York State Psychiatric Institute.

Figure 1 summarizes sample selection procedures. The current sample included only participants who self-reported their primary race/ethnicity to be Non-Hispanic White (NHW), Black, or Hispanic. Of the 6,639 participating individuals, 6,163 completed neuropsychological testing. Participants who self-reported a primary race/ethnicity other than NHW, Black, or Hispanic (N=86) and those missing data on years of education (N=20) were excluded from the current analyses. The remaining sample included a total of 6,057 NHW male (n=554), NHW female (n=876), Black male (n=549), Black female

(n=1,332), Hispanic male (n=834), and Hispanic female (n=1,912) participants. Information on sample demographics are presented in Table 1.

Diagnosis of all-cause dementia and mild cognitive impairment (MCI) was determined via consensus case conference based on neurological, neuropsychological, functional, medical, and psychiatric data collected from participants and/or informants, and followed standard research criteria for all-cause dementia (J.J. Manly et al., 2008; Guy M. McKhann et al., 2011). Follow-up diagnoses were made blind to prior diagnoses. Estimated MCI prevalence at baseline was 15.0% in Black women, 16.6% in Black men, 16.9% in NHW men, 17.0% in NHW women, 17.9% in Hispanic men, and 18.8% in Hispanic women. Dementia prevalence at baseline was 4.0% in NHW men, 6.8% in NHW women, 11.7% in Black men, 13.9% in Hispanic men, 14.6% in Black women, and 15.6% in Hispanic women.

In order to maximize the generalizability of our measurement invariance analyses, all 6,057 participants were included in the analyses for Specific Aim 1. For Specific Aims 2 through 4, we excluded the 621 participants who met criteria for dementia at their baseline visit. The remaining sample (N = 5,258) included 530 NHW men, 812 NHW women, 483 Black men, 1,127 Black women, 714 Hispanic men, and 1,592 Hispanic women. Approximately 60% of the participants were administered study protocols in English. Spanish was the preferred language of administration for 94% of the Hispanic participants.

MEASURES

Demographic measures. Self-reported race/ethnicity was classified based on the 1990 US Census guidelines. Participants were first asked whether they were Hispanic or

Latino and then asked to classify themselves racially as White, Black, Asian, American Indian, Pacific Islander, or other. Participants were asked whether they are male or female; however, this method does not allow us to know whether participants reported their sex or gender (Tannenbaum, Greaves, & Graham, 2016). Thus, we use the term "sex/gender".

Socio-cultural and health measures. Several variables were selected to represent each of the previously discussed socio-cultural and health domains that are presumed to influence late-life cognitive functioning and the subsequent development of AD.

Childhood socioeconomic status (CSES). Confirmatory factor analysis was used to create a CSES factor score from several measures of family socioeconomic status: maternal education, paternal education, highest parental occupation, and number of siblings. Maternal and paternal education was measured using 7 categories: no formal education, grades 1-8, grades 9-11, high school, some college, college graduate, graduate degree. Parental occupation was categorized as "low" for unskilled/semi-skilled jobs, "medium" for skilled/clerical jobs, and "high" for managerial/professional jobs. Number of siblings was specified as a binary variable (0 = 5 or more siblings, 1 = 0 to 4 siblings). Factor scores were saved for each participant and ranged from -1.465 to 2.073, with higher/lower scores representing higher/lower CSES. Individuals with values in the lowest tertile of CSES scores were more likely to have parents with no formal education, low occupational status, and more than 5 siblings. Those with values in the middle tertile had parents with education ranging from 1 to 12 years, medium occupation, and 0 to 4 siblings. Those with values in the highest tertile had parents with at least a high school education, high occupation, and 0 to 4 siblings. CSES was included in all analyses as a continuous variable and centered at the sample mean (-0.012).

Educational attainment. Highest completed grade of school was used for educational attainment. Education was included in all analyses as a continuous variable and centered at the sample mean of 10 years.

Occupational status. Self-reported highest occupational status during the lifetime was measured using three categories: unskilled/semi-skilled, skilled/clerical, and managerial/professional.

Monthly income. Self-reported monthly household income at baseline was measured using 9 categories: $750 or less, $751-1000, $1001-1250, $1251-1500, $1501-1750, $1751-2000, $2001-3000, $3001-4000, and greater than $4000.

Marital status. Self-reported marital status at baseline was specified as a binary variable (0 = not married [widowed, never married, divorced, separated], 1 = married).

Cardiovascular disease burden (CVD burden). Self-reported history of hypertension, diabetes, heart disease, and stroke was used to create a cardiovascular disease risk score by adding the number of conditions endorsed (0-4) (Luchsinger et al., 2005).

Recruitment cohort. Recruitment cohort was categorized as a binary variable (0 = 1992 cohort, 1 = 1999 and 2009 cohorts).

Neuropsychological assessments. Cognitive functioning was assessed via a comprehensive neuropsychological battery (see Stern et al., 1992, for details on battery development). Confirmatory factor analysis (CFA) has been conducted previously on this battery (Siedlecki et al., 2010), summarizing it into four cognitive domains that are invariant across Spanish and English speakers: Memory, language, visuo-Spatial functioning, and processing speed. However, participants from the 1992 recruitment cohort were not administered measures of processing speed at their baseline assessment. To retain

samples sizes across groups and cohorts, processing speed measures were not analyzed in the current study. Presented below is a summary of the neuropsychological measures and corresponding cognitive domains that were included in the current study.

Cognitive Domain	Neuropsychological Measure	Variable Name
Memory	Selective Reminding Test (SRT)	SRT Total Recall
		SRT Delayed Recall
		SRT Recognition
Language	Boston Naming Test, Modified 15-item	Naming Total
	Verbal Fluency	Letter Fluency
		Category Fluency
	Wechsler Adult Intelligence Scale-Revised	Similarities
	Boston Diagnostic Aphasia Evaluation	Repetition
		Comprehension
Visuo-Spatial	Benton Visual Retention Test (BVRT)	BVRT Recognition
		BVRT Matching
	Rosen Drawing Test	Rosen
	Mattis Dementia Rating Scale	Identities & Oddities

Selective Reminding Test (SRT; Buschke & Fuld, 1974). In this word recall measure, participants were read a list of 12 words over six trials and asked to recall as many words as possible after each trial. The *SRT Total* score was calculated as the total number of words correctly recalled after all six trials. The *SRT Delayed Recall* score refers to the number of words correctly recalled after a 15-minute delay. Participants were also administered a delayed recognition test in which they were asked to recognize each of the 12 words among three distracter words. The *SRT Delayed Recognition* score was calculated by the difference between number of words correctly recalled and number of words correctly recognized divided by number of recognition items administered.

Boston Naming Test, Modified 15-Item (BNT; Kaplan, Goodglass, & Weintraub, 1983). Participants were presented with 15 line drawings of objects and asked to identify each. Participants were provided with a semantic cue if they are unable to name the object 20 seconds after it is presented to them. Phonemic cues were provided if the participant was unable to name the object 15 seconds after a semantic cue was presented. The *Naming Total* score refers to the total number of objects spontaneously named (i.e., without cueing).

Verbal Fluency. For the letter fluency portion of this test, participants were given one of three letters at a time (i.e., C, F, L) and asked to generate as many words as possible that begin with each letter in one minute. The *Letter Fluency* score refers to the total number of words generated across the three letters. For the category fluency portion, participants were presented with a category (e.g., animals) and asked to spontaneously generate as many semantically related words as possible within one minute. The *Category Fluency* score refers to the total number of words generated across categories (Siedlecki et al., 2010).

Wechsler Adult Intelligence Scale-Revised, Similarities subtest (WAIS-R; Wechsler, 1987). Participants were presented with two words at a time and asked to describe how the two sets of words were similar. The *Similarities* variable refers to the total number of points obtained on this task.

Benton Visual Retention Test (BVRT; Benton, 1955). This test was comprised of two parts. In the first part, participants were presented with a design for 10 seconds and then asked to select the design among three distracters. The *BVRT Recognition* score refers to the total number of designs correctly recognized. The second part of the test asks participants to match each of the previously learned designs to identical designs among

four smaller designs. The total number of designs correctly matched is quantified as the *BVRT Matching* score.

Boston Diagnostic Aphasia Evaluation, Repetition subtest (BDAE; Goodglass, 1983). Participants were asked to read phrases that were read to them by an examiner. The *Repetition* variable refers to the total number of phrases correctly repeated.

Boston Diagnostic Aphasia Evaluation, Comprehension subtest (BDAE; Goodglass, 1983). Participants were asked basic comprehension questions and the number of questions correctly answered was recorded.

Rosen Drawing Test (Rosen, 1981). Participants were presented with five different designs and asked to copy each on a piece of paper. The total number of correctly copied designs was quantified as the *Rosen* variable.

Dementia conversion. Dementia conversion status was based on diagnosis by consensus conference, based on NIA-AA criteria for all-cause dementia and Alzheimer's disease, at any visit subsequent to the baseline visit. Dementia conversion was specified as a binary variable (0 = no conversion, 1 = conversion).

Selective attrition. Selective attrition due to death was based on informant report and/or social security death index search and was specified as a binary variable (0 = survived, 1 = loss to follow-up due to death). Information collected on date of death was used to create a time-to-death variable representing number of years from baseline until death. Selective attrition due to death or non-death drop-out was characterized as a binary variable (0 = survived, 1 = loss to follow-up due to death or non-death drop-out). Individuals with intermittent drop-out (e.g., missing at visit 2, participated at visit 3,

missing at visit 4) were not included in analyses using this variable. A time-to-dropout variable was created that represented the number of years in the study.

STATISTICAL ANALYSES

Specific Aim 1. A series of confirmatory factor analyses and measurement invariance analyses were conducted to evaluate the measurement invariance of the WHICAP neuropsychological battery across sex/gender, racial/ethnic, and racial/ethnic by sex/gender subgroups over repeated measurements.

Basic dimensional structure. Confirmatory Factor Analysis (CFA) was used to evaluate the dimensional structure of the WHICAP neuropsychological battery. The original WHICAP factor structure described in Siedlecki et al. (2010) summarized 15 WHICAP measures into four cognitive domains: Memory, Language, Visuo-spatial Functioning, and Processing Speed.

Memory was represented by total recall, delayed recall, and delayed recognition from the SRT. Language abilities were measured by naming total, category and letter fluency, and WAIS-R similarities subtest. The BDAE repetition and comprehension subtests were initially included in the model as part of the language factor; however, both measures demonstrated poor psychometric properties and standardized factor loadings below 0.40. A residual correlation between category and letter fluency improved model fit. Residual correlations among items relax the conditional independence assumption by accounting for any shared variance among the items that may not represent meaningful variance explained by the underlying latent variable (in this case language) construct (Mungas et al., 2011). The visuospatial factor was comprised of the BVRT recognition and

matching subtests, the Rosen Drawing Test, and the Identities and Oddities subtest. A model diagram for the hypothesized factor structure is provided in Figure 2.

Invariance of model across groups. Multiple-group CFA was used to test whether the model measured the same constructs across race/ethnicity, sex/gender, and race/ethnicity by sex/gender groups. Configural invariance was assessed by examining the overall fit of the model when model structure is constrained to be equal across groups, but indicator factor loadings, intercepts, and residual variances are freely estimated for each group. Metric invariance was assessed by adding an additional model constraint of equivalent loadings across groups for all indicators. The metric model fit was compared to the configural model fit to determine whether there was a significant decrement in model fit with the additional model constraint. Scalar invariance was then evaluated by adding an additional model constraint of equivalent item intercepts across groups for all indicators. Invariance across structural parameters was examined by constraining factor variances and covariances. Measurement invariance was first assessed across racial/ethnic groups, followed by sex/gender groups, then racial/ethnic by sex/gender groups.

To examine measurement invariance across time, we used a single-group longitudinal CFA framework that allowed residual correlations for the same indicators that were measured at different occasions, taking into account the longitudinal nature of the data (Fokkema, Smits, Kelderman, & Cuijpers, 2013). Attempts were made to fit the three-factor model across five time points simultaneously, however, results were inadmissible with non-positive definite estimated matrices due to estimated factor correlations across time being greater than 1.0. As a result, several longitudinal analyses were conducted

comparing baseline to the subsequent timepoints (e.g., baseline vs. time 2, baseline vs. time 3, etc.,) in each racial/ethnic group by sex/gender group individually.

Model estimation was performed with Mplus version 7.4 (L. K. Muthen & Muthen, 1998-2011) using a maximum likelihood estimator for continuous variables applied to a mean and covariance data structure. Goodness of fit indices were used to assess model fit and to compare the fit of each constrained model to the previous model. Overall chi-square was evaluated; however, given the large difference in group size, the root mean square error of approximation (RMSEA; Browne & Cudeck; Steiger & Lind, 1980) and Comparative Fit Index (CFI; Bentler, 1990) were primarily used for assessment of acceptable model fit. Model fit was determined as having acceptable fit if RMSEA values were less than 0.10 and CFI values greater than 0.90 (Hu & Bentler, 1999; MacCallum, Browne, & Sugawara, 1996). Change in CFI and RMSEA were used to interpret whether the fit of the models was significantly different, with change in CFI equal to or less than -.01 and change in RMSEA less than 0.015 indicating that the invariance hypothesis should not be rejected (Chen, 2007).

Specific Aim 2. A series of unconditional single-group, multiple-group, and joint multiple-group latent growth models were estimated to examine sex/gender, racial/ethnic, and sex/gender by racial/ethnic differences in cognitive trajectories.

Estimation of latent growth models. Based on the factor structure estimated in Specific Aim 1, each of the cognitive variables were converted to z-scores using means and standard deviations from the entire sample at baseline. Composite scores were computed by averaging the z-scores within each of the three domains at each occasion. Scores were then corrected for age by regressing baseline composite scores on baseline age

separately for each cognitive domain. The constant and slope from each regression were used to adjust baseline and follow-up composites. Age-corrected scores of zero indicate performance equal to what would be expected for the given baseline age.

Longitudinal changes within each cognitive domain over five study waves (approximately 15 years in the study) were estimated. Missing data were handled using full information maximum likelihood (FIML). Model fit was assessed using the Bayesian Information Criterion (BIC) (Schwarz, 1978). Relative model fit, as assed by the BIC, is based on a log-likelihood value that rewards better model fit while penalizing the presence of more model parameters. Models with a higher log-likelihood value and few parameters will have smaller BIC values (B. O. Muthen, 2004).

Unconditional analyses. Unconditional random-effects latent growth models, specified to include no covariates, were estimated across the entire sample for each cognitive domain, followed by unconditional multiple-group random-effects latent growth models and unconditional multiple-group joint models.

Unconditional growth models across the entire sample. Cognitive trajectories for each domain were characterized by estimating three separate unconditional latent growth curve models, with random effects, specified to include no covariates, across the entire sample. To accommodate individually varying times of observation, time scores were created indicating the time (in years from baseline) each participant participated in each follow-up session. Unconditional latent growth models that allowed only linear change were compared to models allowing both linear and quadratic change. A spline modeling retest was included if evidence of practice effects was noted (McArdle, Ferrer-Caja,

Hamagami, & Woodcock, 2002). The best fitting models based on BIC were used for subsequent analyses.

Unconditional multiple-group growth models. Three sets of analyses were conducted for each cognitive domain to examine intercept and slope differences between sex/gender, racial/ethnic, and sex/gender by racial/ethnic subgroups. For each model, mixture estimation procedures were employed with a single latent class comprised of multiple known classes, or manifest groups (Kim, Mun, & Smith, 2014). This known grouping variable is incorporated into the model as a moderator variable, allowing model parameters to vary as a function of membership to the identified groups. The multiple-group approach is preferable to treating race/ethnicity or sex/gender as covariates in the model, which would impose equalities between groups that may not be valid, such as associations between socio-cultural variables and trajectory estimates (Bradshaw, Schaeffer, Petras, & Lalongo, 2010). This approach is analogous to the traditional multiple-group LGM approach because latent classes are known. However, rather than estimating group-specific covariance structures with individually varying time scores, as is required for the traditional multiple-group growth model, the mixture estimation approach estimates the covariance structure of entire data as a whole (Kim et al., 2014). This will allow for increased model flexibility when estimating subsequent models that are more complex. Sex/gender was specified as the known grouping variable for the first set of analyses (Model 1), race/ethnicity for the second set (Model 2), and sex/gender by race/ethnicity for the third set (Model 3). For each model, intercept, slope, and residual variance parameters were allowed to vary across groups. Differences in intercept and slope were examined using the "Model Constraint" option in Mplus.

Unconditional multiple-group joint models. Given the potential relationship between cognitive impairment/decline and attrition due to death, three separate multiple-group joint models were estimated for each cognitive domain. Joint models explicitly account for the dependency between longitudinal change and attrition by combining a growth model with a continuous-time survival model. We estimated a multiple-group Cox proportional hazards regression model as the continuous-time survival model. Observed continuous survival time data represent the time to an event (i.e., time-to-death). Death was used as a censoring variable that identified those who died before the end of the study and those who survived. For those who remained alive throughout the study, survival times are right-censored. Building from Model 1, Model 4 included the Cox proportional hazards regression model by regressing the hazard function on growth trajectories. Baseline hazards were allowed to vary across men and women, as was the relationship between hazards and growth parameters. Similarly, Model 5 added the cox regression to Model 2 and allowed all parameters to vary across racial/ethnic groups and Model 6 added the cox regression to Model 3 and allowed all parameters to vary across sex/gender by racial/ethnic groups.

Additional sensitivity analyses were conducted to examine the relationship between cognitive trajectories and attrition due to either death or non-death drop-out. In these models, the time-to-event variable was time-in-study and the censoring variable identified those who either dropped-out or died before the end of the study and those who remained alive. Cox regressions were then regressed on growth trajectories and model parameters were allowed to vary across sex/gender groups (Model 7), racial/ethnic groups (Model 8), and sex/gender by racial/ethnic group (Model 9). Given that the precise date of and reason

for non-death drop-out is unknown, the model estimating only attrition due-to-death (Model 6) was used for the subsequent analyses detailed below.

Specific Aim 3. A series of conditional multiple-group joint models were estimated to identify specific socio-cultural & biological mechanisms, including Childhood socioeconomic status, early educational experiences, occupational status, adult income, marital status, and cardiovascular disease burden, that account for sex/gender by racial/ethnic differences in cognitive trajectories.

Conditional Analyses. A series of conditional analyses, that include covariates, were estimated for each cognitive domain across sex/gender by racial/ethnic groups. Socio-cultural and health indicator variables were included in a series of nested models to examine whether socio-cultural and health differences across groups contributed to differences in baseline performance and rates of decline. The unconditional multiple-group joint model across sex/gender by racial/ethnic groups was used as our base model (Model 6). In Model 6A we included CSES, followed by education (Model 6B), occupation (Model 6C), income (Model 6D), CVD burden (Model 6E), and marital status (Model 6F). The final model (Model 6G), further controlled for recruitment cohort. Parameter estimates for intercept, slope, and the relationship between covariates and growth factors were allowed to vary across groups for each model. Differences in parameter estimates were compared across the nested models to assess the contribution of each variable in accounting for differences in trajectories.

To further examine the impact of attrition due-to-death on parameter estimates, all covariates were added to Model 3 (Model 3G) and noted differences in parameter estimates between Model 3G and the joint model (Model 6G) were described.

Multiple imputation. Approximately 12% of CSES, 4% of Occupation, 9% of monthly income, 20% of CVD burden, and 1% of marital status data were missing. We determined that data was missing at random based on missing variable analyses conducted in SPSS. Multiple imputation was used for each analysis that included covariates. Multiple imputation procedures generate multiple copies of the dataset, with unique estimates of missing values drawn at random, and then pools parameter estimates across each data set and adjusts for within and between imputation variance (Rubin, 1987).

Specific Aim 4. Conditional multiple-group joint models, multiple-group cox proportional hazards models, and competing risk models were employed to investigate the relationship between socio-cultural experiences, cognitive trajectories, conversion to dementia, and differential attrition across sex/gender by racial/ethnic subgroups.

Socio-cultural/health indicators and cognitive trajectories. Group differences in parameter estimates for the relationship between socio-cultural and health variables and growth trajectories were examined using the "Model Constraint" command in Mplus for Model 6G.

Socio-cultural/health indicators and dementia conversion. To examine differences in risk factors of incident dementia across sex/gender by racial/ethnic groups, we estimated a multiple-group Cox regression model (Model 10) with the time variable defined as years from baseline to first visit a diagnosis of dementia was assigned. Time-to-dementia diagnosis was regressed on CSES, education, occupation, income, CVD burden, marital status, and age at baseline (centered at 75 years). Manifest groups were defined as sex/gender by racial/ethnic groups and baseline hazards and log hazard ratios were allowed to vary across each group.

Competing risk model. The relationship between mortality and the socio-cultural/health variables was estimated using a multiple-group cox regression model (Model 11) with the time variable defined as years from baseline to death (time-to-death). Time-to-death was regressed on the socio-cultural/health variables and baseline hazards and log hazard ratios were allowed to vary across each sex/gender by racial/ethnic group.

As discussed previously, if the relationship between dementia and death is not accounted for, parameter estimates of the relationship between socio-cultural/health risk factors and dementia may be biased. Further, since individuals can only be diagnosed during each follow-up visit the exact time of dementia onset may be unknown for individuals who die before the visit following dementia onset (Rouanet, 2016). Thus, we consider death as a competing risk. To account for the competing risk of death we estimated competing risk models for each sex/gender by racial/ethnic group separately in R using the *survival* package. In this model, death is an event that prevents the occurrence of dementia (Austin & Fine, 2017). A new time variable was created (time-to-event) to capture the time to either dementia or death (whichever came first). A new event variable was then created to specify 3 different states: 0 = censoring (those who survived throughout the study), 1 = dementia, 2 = death. Model parameters were then estimated by incorporating weights in the partial likelihood function, which allows for two different types of hazard functions to be estimated: cause-specific hazard function and subdistribution hazard function (Austin & Fine, 2017). The cause-specific hazard function for dementia represents the instantaneous rate of occurrence of dementia in individuals who are free of both dementia and death. The subdistribution hazard function is the instantaneous rate of occurrence of dementia for individuals who have not yet experienced a dementia event but may have

experienced death. In other words, individuals who die before being diagnosed with dementia are "immortalized" and retained in the risk sets for subsequent dementia events (Baker, Cook, Arrighi, & Bullock, 2011). This model will allow us to measure the possible unobserved transition to dementia for those who were free of dementia but died before their next visit to be diagnosed once they progressed to dementia, as well as differentiate the effects of socio-cultural/health indicators on dementia and death. Estimated regression coefficients for each socio-cultural/health variable were compared between the traditional cox regression model (Model 10) and the competing risk model.

RESULTS

DEMOGRAPHIC CHARACTERISTICS

Demographics for the sample without prevalent dementia are presented in Table 2. Female participants were older and completed fewer years of education compared to their male counterparts. The NHW participants had the highest level of educational attainment followed by the Black participants and then Hispanic participants. While NHW and Hispanic men had higher levels of educational attainment compared to their NHW and Hispanic female counterparts, Black women completed more years of education compared with Black men. NHW men and women had the highest CSES, followed by Black men and women, and then Hispanic women who had higher CSES than Hispanic men. Regarding occupational status, NHW men were more likely than all other groups to report high occupational status, while Hispanic women were the most likely to report low occupational status. Similarly, NHW men were the most likely to report income in the highest monthly income category and Hispanic men and women were most likely to report income in the lowest category. NHW women had the lowest CVD burden count, followed by NHW and

Black men who had lower counts compared to Black women and Hispanic men and women. Women were more likely than men to not be married at their baseline visit. Finally, rates of incident dementia were considerably lower for NHW men and women compared with Black and Hispanic men and women.

SPECIFIC AIM 1

Initial CFA. Results for the entire sample indicated good model fit (χ^2 [40] = 874.65, p <0.001; CFI=0.975, TLI=0.965, RMSEA=0.059 [90% CI 0.055, 0.062], SRMR=0.035). Standardized factor loadings were above 0.40 for all measures. Indicator variables varied in their strength of factor loadings, with the strongest factor loadings for SRT immediate recall (0.95), phonemic fluency (0.82), Benton recognition (0.82) and Similarities (0.82) and the weakest loadings for identities/oddities (0.60) and SRT delayed recognition (0.61). Residual misfit was noted based on correlation residuals exceeding 0.10 (Kline, 2011), with a correlation residual of -0.290 for Benton matching with SRT delayed recall; however, average residual correlation was acceptable based on the standardized root mean square residual (SRMR = 0.036). Factor correlations ranged from .687 to .877 with the strongest correlation between the language and visuospatial factors and lowest between the visuospatial and memory factors.

Model fit was good across each racial/ethnic group, sex/gender group, and race/ethnicity by sex/gender group, with RMSEAs of 0.042 to 0.062 and CFIs of .951 to .978. Model fit indices by groups are presented in Table 3.

Measurement Invariance Across Groups. Results from measurement invariance analyses are presented in Tables 4 through 7.

Sex/Gender. The configural model fit well across sex/gender groups (χ^2 [80] = 900.58, p<.001, RMSEA = 0.058 [90% CI = 0.055-0.062], and CFI = 0.974). Examination of goodness of fit indices indicated that the data fit full scalar invariance, with no substantial changes in model fit when models became more restricted. Additionally, full structural invariance was obtained between men and women.

Racial/Ethnic. Across racial/ethnic groups, the configural model fit well (χ^2 [120] = 865.74, p <.001, RMSEA = 0.055 [90% CI = 0.052-0.059], and CFI = 0.973) (Table 4). Change in model fit was substantial when comparing the metric and scalar models (Δ CFI = -0.020). Evaluation of fit indices for each variable intercept when constrained separately indicated that the largest reductions in fit were associated with the constraints on the Naming Total indicator for the NHW and Hispanic groups and the Similarities indicator for the NHW group. When the Naming Total and Similarities intercept was unconstrained in the respective groups change in model fit was no longer substantial (Δ CFI = -0.006, Δ RMSEA = 0.003). Regarding structural invariance, the model met factor variance invariance after the Language and Visuospatial factor variances were unconstrained for the NHW and Hispanic groups. Evaluation of factor covariances was not permitted given noninvariant factor variances.

Sex/Gender by Racial/Ethnic. The configural model fit well across the six racial/ethnic by sex/gender groups (χ^2 [240] = 989.91, p < .001, RMSEA = 0.056 [90% CI = 0.052-0.059], and CFI = 0.973) (Table 6). Similar to the results demonstrated across racial/ethnic groups, change in model fit was substantial when comparing the metric and scalar models (Δ CFI = -0.021). Partial scalar invariance was achieved after freeing the intercept for the Naming Total indicator in the female and male NHW and female Hispanic

groups and the Similarities indicator in the male NHW group. Results from the structural invariance analyses indicated that factor variance invariance was met once the Visuospatial factor variance was unconstrained for the female and male NHW and female Hispanic groups and the language factor variance for the female NHW groups, suggesting that the amount of within-group variability of this factor differed across these groups compared to the other racial/ethnic by sex/gender groups. Examination of equality of factor covariances was not conducted due to noninvariant factor variances.

Results from the invariance analyses across time indicated that the data fit full scalar invariance and full structural invariance in the entire sample, as well as in each racial/ethnic by sex/gender group except for Hispanic men (Table 7). For Hispanic men, full scalar and structural invariance was met for time 1 compared to times 2, 3, and 4; however, due to a large proportion of missing data at time 5, fit indices could not be calculated for the model assessing invariance between time 1 and time 5 due to a non-positive definite matrix.

SPECIFIC AIM 2

Unconditional models across entire sample. As reflected in Table 8, unconditional models allowing only linear change fit better than the models allowing both linear and quadratic slopes. Evidence of practice effects were noted for the language model but not the memory or visuo-spatial models, so a spline for retest was only included in the language model.

Unconditional models across subgroups. Results from the unconditional models for sex/gender, racial/ethnic, and sex/gender by racial/ethnic subgroups across each domain

are presented in Tables 9 through 11. Estimated trajectories for each model are presented in Figures 3 through 5.

Unconditional models across sex/gender subgroups. Sex/gender differences were noted for baseline performance across all three cognitive domains. Women demonstrated higher average baseline memory scores than men (B = -0.135; 95% CI = [-0.173, -0.096]) and men obtained higher scores on the language (B = 0.106; 95% CI = [0.063, 0.149]) and visuo-spatial (B = 0.076; 95% CI = [0.039, 0.113]) domains. Rates of decline were similar across sex/gender groups for all three domains.

Unconditional models across racial/ethnic subgroups. Baseline performance differed between all racial/ethnic groups. For each cognitive domain, NHWs had the highest baseline scores, followed by Black participants who had higher baseline scores compared to Hispanics. Compared to NHWs, Blacks demonstrated steeper rates of decline on the memory (B = 0.010; 95% CI = [0.003, 0.020]), language (B = 0.008; 95% CI = [0.001, 0.015]), and visuo-spatial (B = 0.007; 95% CI = [0.002, 0.013]) domains. NHW and Hispanic participants demonstrated similar rates of decline across the three cognitive domains.

Unconditional models across sex/gender by racial/ethnic subgroups. Differences in baseline performance and rate of change were noted on the sex/gender by race/ethnicity models. Sex/gender differences in baseline memory performance were found within each racial/ethnic group, with women obtaining higher baseline memory scores. While NHW women demonstrated the highest baseline memory performance, NHW men obtained higher scores than Black (B = 0.155; 95% CI = [0.087, 0.223]) and Hispanic women (B = 0.319; 95% CI = [0.382, 0.445]). Baseline scores were similar for Hispanic women and

Black men. Memory decline was steeper for Black women compared to NHW women (B = 0.016; 95% CI = [0.004, 0.028]). Sex/gender differences were found on the visuo-spatial domain for Hispanics, with higher baseline scores for men than women (B = 0.091; 95% CI = [0.032, 0.149]). Rate of language decline was similar across sex/gender by racial/ethnic groups, however, decline for Black women on visuo-spatial functioning was steeper compared with NHW women (B = 0.010; 95% CI = [0.01, 0.02]).

Selective attrition. Figure 6 summarizes selective attrition across the entire sample by study visit. Approximately half of each group was lost to follow-up before their third visit and between 77% and 86% of each group was lost to follow-up before their fifth visit. Of those lost to follow-up, 26% to 46% were lost to follow-up due to death. However, as seen in Figure 6, some participants died after the three-year follow-up window.

Controlling for baseline age, NHW (hOR = 0.738 [0.622, 0.876]), Black (hOR = 0.851 [0.726, 0.996]), and Hispanic (hOR = 0.536 [0.457, 0.628]) women were less likely than NHW men to die during the course of the study (Table 12). Table 13 presents the average number of years from baseline each group was seen at time points 2 through 5 (e.g., On average, Hispanic women were seen for their third assessment session 4.15 years after their baseline assessment). Selective attrition is summarized in Table 14, showing a maximum follow-up of 20 years in 3-year intervals. The probability of surviving past the first two years in the study was highest for Hispanic women (0.94) and lowest for Black men (0.89). As seen in Figure 7, after adjusting for baseline age, Hispanic women have the highest probability of surviving across the entire study period. While Black men have the lowest probability of surviving for their first 12 years in the study, survival rates for NHW men after 12 years are similar or lower than that of Black men.

Unconditional joint models across subgroups. To determine the extent to which selective attrition may have influenced our findings, unconditional joint models were estimated for each domain. Results from the unconditional joint models for sex/gender, racial/ethnic, and sex/gender by racial/ethnic subgroups across each domain are presented in Tables 15 through 17. Estimated trajectories for each model are presented in Figures 8 through 10.

Unconditional joint models across sex/gender subgroups. Lower risk of death was related to less decline for men on the memory (hOR = 0.342 [0.220, 0.464]), visuo-spatial (hOR = 0.119 [-0.049, 0.288]), and language (hOR = 0.174 [0.051, 0.293]) domains, as well as for women on the memory (hOR = 0.391 [0.259, 0.523]), visuo-spatial (hOR = 0.154 [-0.013, 0.322]), and language (hOR = 0.231 [0.094, 0.373]) domains. Regarding sex/gender differences, findings were identical to the unconditional model that did not include death.

Unconditional joint models across racial/ethnic subgroups. Higher baseline scores were related to a lower risk of death for NHWs on the memory (hOR = 0.672 [0.505, 0.839]) and visuo-spatial (hOR = 0.581 [0.400, 0.762]) domains, Blacks on the memory domain (hOR = 0.653 [0.516, 0.790]), and Hispanics on the language domain (hOR = 0.776 [0.774, 0.779]). Lower risk of death was related to less decline for all three groups on the memory and visuo-spatial domains and on the language domain for the Black and Hispanic groups. Regarding racial/ethnic differences, there was no longer a difference in language decline between the NHW and Black groups (B = 0.003; 95% CI = [-0.023, 0.028]). All other findings were identical to the unconditional model that did not include death.

Unconditional joint models across sex/gender by racial/ethnic subgroups. Higher baseline memory scores were related to a lower risk of death for NHW women (hOR = 0.564 [0.413, 0.715]), Black men (hOR = 0.527 [0.357, 0.697]), and Black women (hOR = 0.439 [0.261, 0.617]), lower baseline visuo-spatial scores for NHW women (hOR = 0.500 [0.311, 0.689]), and lower baseline language scores for NHW women (hOR = 0.574 [0.464, 0.684]), Black men (hOR = 0.649 [0.472, 0.827]), Black women (hOR = 0.671 [0.534, 0.808]), and Hispanic women (hOR = 0.681 [0.498, 0.864]). Lower risk of death was also associated with less decline in across domains for all groups.

Sex/gender differences in baseline memory performance remained within each racial/ethnic group, with women obtaining higher baseline memory scores. Sex/gender differences in baseline performance were noted between Hispanic men and women for the visuo-spatial (B = 0.130; 95% CI = [0.068, 0.193]) and language (B = 0.088; 95% CI = [0.031, 0.145]) domains, with higher baseline scores for men than women. The largest racial/ethnic differences were between NHW and Hispanic women for the language (B = 0.819; 95% CI = [0.757, 0.880]) and visuo-spatial (B = 0.790; 95% CI = [0.742, 0.838]) domains, as well as between NHW and Hispanic men for the language domain (B = 0.774; 95% CI = [0.696, 0.853]). Memory decline was steeper for Black (B = 0.016; 95% CI = [0.004, 0.028]) and Hispanic (B = 0.012; 95% CI = [0.001, 0.022]) women compared to NHW women. Visuo-spatial decline was also steeper for Black women compared to NHW women (B = 0.008; 95% CI = [0.001, 0.016]) and Hispanic women (B = 0.009; 95% CI = [0.002, 0.017]). Decline in language abilities was steeper for NHW men compared to NHW women (B = 0.013; 95% CI = [0.003, 0.022]) and Hispanic women (B = 0.013; 95% CI =

[0.004, 0.021]), as well as for Black women compared to Hispanic women (B = 0.009; 95% CI = [0.002, 0.016]).

Sensitivity analyses. We ran sensitivity analyses that accounted for both death and non-death dropout in a single indicator (Models 7 through 9). Results from these analyses are presented in Tables 18 through 20. Most of the models yielded similar results to the joint models only including death, except for the memory models across racial/ethnic and sex/gender by racial/ethnic subgroups. In the memory model across sex/gender by racial/ethnic groups, the difference in rate of memory decline between Black and NHW women lessened (B = 0.013; 95% CI = [0.001, 0.027]), while the difference between Hispanic and NHW women widened (B = 0.021; 95% CI = [0.009, 0.033]).

Figures 11 through 13 compare the latent growth curve model (Model 3), joint model that only included death (Model 6), and joint model including death and non-death drop-out (Model 9) across sex/gender by racial/ethnic groups. Across cognitive domains, rate of decline was steeper in Model 6 compared to Model 3, suggesting that failing to account for the relationship between growth trajectories and death underestimates cognitive decline. With the exception of Hispanic women on the memory domain, rate of decline for Model 6 was steeper than or similar to that for Model 9. For Hispanic women rate of memory decline in Model 9 was slightly steeper than Model 6.

SPECIFIC AIM 3

The multiple-group joint models only including death were used for the remaining analyses. Figures 14 through 19 summarize changes in baseline performance and average rate of decline across groups for each model and cognitive domain.

Model 6A. Including CSES in Model 6A accounted for differences in rate of memory decline; however, differences in baseline performance were only slightly reduced across domains. The largest reductions in differences was in baseline language performance between NHW men and Hispanic men (from a 0.774-point difference in Model 6 to a 0.612-point difference in Model 6A) and NHW men and Hispanic women (from a 0.862-point difference in Model 6 to a 0.700-point difference in Model 6A). Higher CSES was related to higher baseline visuo-spatial and language performance across all groups, with the strongest relationship for Black men (B = 0.219; 95% CI = [0.126, 0.312]) and women (B = 0.219; 95% CI = [0.161, 0.277]) on the language domain. Higher CSES was related to less memory decline for NHW men (B = 0.010; 95% CI = [0.002, 0.020]) and women (B = 0.010; 95% CI = [0.001, 0.019]), as well as higher baseline memory performance for all groups except NHW women and Hispanic men and.

Model 6B. Including education in Model 6B accounted for baseline differences between NHW men and Black and Hispanic women for the memory domain and differences between Black and Hispanic men and women for the visuo-spatial and language domains. The largest reduction from Model 6A was on the language domain between NHW men and Hispanic women (from a 0.700-point difference in Model 6A to a 0.414 point differences in Model 6B). Higher education was related to higher baseline performance across groups and cognitive domains with parameter estimates ranging from 0.098 (Black men on the language domain) to 0.031 (NHW women on the visuo-spatial domain). Higher education was related to memory slope for NHW women and Black women, as well as visuo-spatial slope for NHW women and Black men. CSES remained associated with memory slope for NHW men, baseline language performance for Black

women and Hispanic men and women, and baseline visuo-spatial performance for Hispanic men.

Model 6C. Introducing occupational status in Model 6C accounted for baseline memory differences between NHW and Hispanic men, reducing the difference from 0.174 points in Model 6B to 0.099 points in Model 6C. Higher occupational status was related to higher baseline memory and visuo-spatial performance for NHW women and Black women. Higher occupational status was related to less memory decline for Hispanic men (B = 0.020; 95% CI = [0.003, 0.036]) and higher baseline language performance for all groups except Hispanic women. The relationship between baseline performance and education slightly decreased across groups. CSES remained associated with baseline language performance for Hispanic women and baseline visuo-spatial and language performance for Hispanic men.

Model 6D. Model 6D added monthly income, which accounted for baseline memory differences between NHW and Hispanic women, as well as differences between NHW and Black men. Differences in monthly income also accounted for differences in baseline visuo-spatial and language performance between Black men and NHW men and women and rate of visuo-spatial and language decline. The largest reduction in difference was between NHW men and Hispanic women on baseline language performance (difference reduced by 0.389 points from previous model). Higher income was related to higher baseline memory for all but Black men. Occupation remained associated with baseline memory for Black women and memory decline for Hispanic men.

Model 6E. When cardiovascular disease risk was added in Model 6E, baseline differences in memory performance dissipated between NHW men and women (from a

0.262-point difference in Model 6D to a 0.176-point difference in Model 6E) and between Black and NHW women (from a 0.166-point difference in Model 6D to a 0.096 difference in Model 6E). Higher CVD burden was related to lower baseline memory performance for NHW men (B = -0.093; 95% CI = [-0.154, -0.032]), Black women (B = -0.062; 95% CI = [-0.106, -0.018]), Hispanic women (B = -0.046; 95% CI = [-0.080, -0.011]), lower baseline language performance for NHW men (B = -0.067; 95% CI = [-0.128, -0.005]), Black women (B = -0.039; 95% CI = [-0.078, -0.001]), Hispanic men (B = -0.061; 95% CI = [-0.106, -0.015]), Hispanic women (B = -0.045; 95% CI = [-0.074, -0.017]), and lower baseline visuo-spatial performance for Hispanic men (B = -0.060; 95% CI = [-0.104, -0.016]), Hispanic women (B = -0.066; 95% CI = [-0.104, -0.028]). Additionally, higher CVD burden was related to less memory decline for Black men (B = 0.019; 95% CI = [0.005, 0.034]).

Model 6F. The addition of marital status in Model 6F did not account for additional differences between groups. Marital status was related to less memory decline for NHW women (B = 0.020; 95% CI = [0.002, 0.037]) and less visuo-spatial decline for Black women (B = 0.018; 95% CI = [0.004, 0.033]).

Model 6G. In model 6G we further controlled for recruitment year. In this final model, differences in baseline memory performance between all women and Hispanic men and between NHW women and Black men persisted. While baseline visuo-spatial differences between NHWs compared to Black women and Hispanic men and women were reduced, these differences were not completely accounted for in the final model. As for the language domain, baseline differences persisted, with Hispanic men and women demonstrating higher baseline scores compared to NHW and Black women. As seen in

Figure 16, despite similar baseline visuo-spatial performance between Black men and women in Model 6 through Model 6B, performance diverged in Model 6C and differences were maintained through Model 6G.

As seen in Figures 17 through 19, differences in slope fluctuated across models. In some cases, previously accounted for differences would widen when another variable was added. The most volatile changes in slope were with the memory and language domains. Most of the slope differences were accounted for in the final model; however, the wide confidence intervals likely indicate high dispersion.

SPECIFIC AIM 4

Socio-cultural/health indicators and cognitive trajectories. As seen in Tables 21 through 23, educational attainment and monthly income were positively and significantly related to baseline performance across groups and cognitive domains, with the exception of income on language performance for Hispanic men. Across cognitive domains, Black men benefitted the most from achieving more education (0.046 to 0.069 points per year of education achieved), Black women benefitted most from higher occupational status (0.083 to 0.163 points per increase in occupation category), and NHW men benefitted most from higher monthly income (0.037 to 0.078 points per increase in income category). Higher CVD burden was consistently related to lower baseline performance across domains for Black and Hispanic women (0.040 to 0.064-point decrease per one-unit increase in CVD burden count). Interestingly, higher CVD burden was related to less memory decline for Black men. Net of adult SES indicators, higher CSES was related to less memory decline for NHW men. Being married at the baseline visit was related to less memory decline for NHW women and less visuo-spatial decline for Black women.

Compared to Hispanic men, Hispanic women benefitted more from more from more years of education in terms of baseline language (B = 0.016; 95% CI = [0.001, 0.031]) and visuo-spatial performance (B = 0.016; 95% CI = [0.001, 0.031]). The relationship between education and baseline visuo-spatial performance was stronger for Black men compared to Black women (B = 0.023; 95% CI = [0.002, 0.044]) and NHW men (B = 0.024; 95% CI = [0.004, 0.045]). Compared to Hispanic women, occupation was more strongly related to baseline language performance for NHW women (B = 0.123; 95% CI = [0.028, 0.219]), Black women (B = 0.123; 95% CI = [0.028, 0.219]), and Hispanic men (B = 0.118; 95% CI = [0.027, 0.209]). NHW and Black men and women benefitted more than Hispanic men and women with higher income levels, in terms of baseline language performance.

As seen in Table 24, risk of death was associated with several of the socio-cultural/health indicators across groups and cognitive domains. Tables 25 through 27 provide estimates for the conditional multiple-group latent growth model (Model 3G). Per visual inspection, there is very little change in parameter estimates compared to the joint model.

Dementia conversion. Compared to NHW men, being a Black or Hispanic man or women was associated with increased risk of dementia (Table 28). As seen in Figure 20, after controlling for baseline age, NHW men and women have higher probabilities of being dementia free for most of the study compared to other groups. There were no sex/gender differences in risk of dementia within each racial/ethnic group.

Results from the multiple-group cox regression model (Table 29) demonstrated that each year of education past 10 was associated with a 7.3% to 7.7% lower hazard for

dementia conversion for Black and Hispanic men and women. Higher monthly income was associated with a 13.2% to 14.4 % lower hazard for NHW, Black, and Hispanic men and a 9.3% lower hazard for Black women. Having more than one CVD risk factor was associated with a 28.2% and 24.4% higher hazard for dementia conversion for Black women and Hispanic women, respectively. NHW women who reported being married at baseline had a 44.9% lower hazard for dementia conversion than non-married NHW women. Older age at baseline was associated with an 8.7% to 12.0% increase in hazard across groups. Of note, income was related to dementia conversion for NHW women (hOR = 0.908 [0.819, 0.996]) before marital status was included in the model.

Dementia and Death. As seen in Table 30, the relationship between specific socio-cultural factors and death varied across groups. Higher income was associated with lower hazards for death during the study for NHW men (6.7%), NHW women (5.3%), and Black men (6.6%). Higher occupational status was associated with a 30% increase in hazard for death for Hispanic men. Having more than one CVD risk factor was associated with higher hazards for NHW men (21.9%), NHW women (37.9%), Black women (18.6%), Hispanic men (25.7%), and Hispanic women (25.2%). Older age at baseline was associated with increased hazards for death across groups.

Unfortunately, we were unable to use multiple imputation for the competing risk models in R and, as a result, only age and education were included in the models since these were the only variables with no missing data. Competing risks models were compared to traditional cox regression models that only include age and education as covariates. As seen in Figure 21, for the most part, the traditional cox regression model for dementia (not

accounting for death) overestimated survival probabilities across groups; however, survival probabilities were underestimated in later years for some groups.

Parameter estimates for the traditional cox regression models and competing risk models are presented in Table 31. The cause-specific hazards represent the relative change in the instantaneous rate of occurrence of an event (either dementia or death) in individuals who are free of either event. As seen in Table 31, the cause-specific hazards are generally similar to the hazards in the traditional cox model. The only difference is that education is no longer associated with risk of death for Black women with the cause-specific hazards. The subdistribution hazards show some slightly different results. Regarding the subdistribution hazards for dementia, which represents the relative change in the instantaneous rate of occurrence of dementia in individuals who are dementia free or who have experienced death, baseline age is no longer associated with risk of dementia for NHW men. Regarding the subdistribution hazards for death, which represents the relative change in the instantaneous rate of occurrence of death in individuals who are death free or who have dementia, baseline age is no longer associated with risk of death for Black and Hispanic men and education is no longer associated with risk of death for Black men. These results should be interpreted with caution as other, relevant, socio-cultural/health indicators were not included in these models.

DISCUSSION

The overall goal of the current study was to highlight the intersectionality of race/ethnicity and sex/gender as determinants of specific socio-cultural experiences that shape cognitive trajectories leading to AD. We leveraged longitudinal data from a large, well-characterized, and socio-economically and racially/ethnically diverse cohort of older

adults. An intersectionality approach was applied to all of our analyses, whereby we determined whether findings across sex/gender groups varied as a function of race/ethnicity. We first determined whether our neuropsychological test battery measured the same cognitive constructs across sex/gender, racial/ethnic, and sex/gender by racial/ethnic subgroups over repeated measurements. We then examined differences in cognitive trajectories (i.e., initial cognitive test performance and rate of cognitive decline) between sex/gender, racial/ethnic, and sex/gender by racial/ethnic subgroups across memory, language, and visuo-spatial domains and examined the influence of selective attrition on cognitive trajectory estimates. Next, we identified specific socio-cultural and health mechanisms, including childhood socioeconomic status, educational attainment, occupational status, adult monthly income, marital status, and CVD burden, that account for sex/gender by racial/ethnic differences in cognitive trajectories. We also investigated whether the relationships between socio-cultural and health indicators, cognitive trajectories, and conversion to dementia varied across sex/gender by racial/ethnic subgroups. Finally, we used competing risks analyses to examine the influence of differential attrition due to death on estimates of dementia risk.

MEASUREMENT INVARIANCE

Consistent with our hypotheses, full measurement invariance was demonstrated across sex/gender groups, and only partial scalar invariance was demonstrated across racial/ethnic groups with intercept differences that varied by racial/ethnic and by racial/ethnic by sex/gender subgroups. Examination of model modification indices suggested that the source of misfit in the partially invariant models was due to group differences on indicator intercepts for the language factor. This finding was not surprising

given differences in educational attainment across racial/ethnic groups. The three-factor model was also stable over time within each racial/ethnic by sex/gender group as criteria were met for all levels of invariance across five time points.

The current study replicated findings from Siedlecki et al. (2014) by demonstrating invariant factor structure and factor loadings for this neuropsychological test battery in the racial/ethnically and linguistically diverse WHICAP sample. We add to the previous findings by expanding the current sample to include a range of cognitive functioning levels across racial/ethnic, sex/gender, and racial/ethnic by sex/gender groups, at five time-points. The previous study also demonstrated intercept noninvariance for the Naming Total and Similarities indicators. In that study, these intercepts were invariant when post-hoc invariance analyses were conducted across education-matched subsamples, suggesting that the intercept differences likely reflect the significant difference in educational attainment across groups.

When intercepts are noninvariant, observed indicator values will differ between groups at any given level of the factor. Although the Naming Total and Similarities indicators were related to the Language factor similarly across racial/ethnic by sex/gender groups, the location parameter of each intercept differed for some groups, and all predicted observed scores will differ at various levels of the factor as a result (T. A. Brown, 2015). For example, predicted scores for NHW men on the Similarities indicator will be higher than the other racial/ethnic by sex/gender groups with the same Language factor score. Similarly, predicted scores on the Naming Total indicator will differ for NHW men and women and Hispanic women compared to Black men and women and Hispanic men who will have similar Naming Total scores at the same level of the Language factor. These

findings indicate that observed group differences on the Naming Total and Similarities indicators are not completely due to group differences on the Language factor. Differences are likely due to construct-irrelevant factors causing group differences in test scores (McDonald, 1999), such as educational attainment and quality of education, acculturation level, quality of education, socio-economic status, and English language proficiency. Group comparisons on the Language factor mean should be approached with caution, especially when comparing NHW men and women with Hispanic women.

Examination of cognitive trajectories leading to AD or other dementias is essential to understand differences in onset and maintenance of cognitive disparities. In the absence of longitudinal measurement invariance, it cannot be determined if any group differences in cognitive trajectories are due to true change or to change in the structure or measurement of the cognitive constructs over time (McArdle, 2007). The current study demonstrated full measurement invariance over multiple assessment time points for each racial/ethnic by sex/gender group, thus, allowing for comparisons across groups and over time.

To the best of our knowledge, this is the first study to evaluate the interaction between race/ethnicity and sex/gender on neuropsychological test performance among older adults across time. Overall, the current study demonstrated intercept differences for indicators on the Language factor between NHW men and women and Hispanic women but not all other groups. Thus, combining racial/ethnic by sex/gender subgroups into one overall sex/gender group for analyses can obscure important sex/gender differences that vary by race/ethnicity. Researchers should not assume that measures that are invariant across sex/gender will demonstrate full measurement invariance across men and women of different racial/ethnic backgrounds.

DIFFERENCES IN COGNITIVE TRAJECTORIES

Examination of sex/gender differences in cognitive trajectories supported previous literature demonstrating a baseline advantage for women in memory and for men in visuo-spatial skills (De Frias et al., 2006; Proust-Lima et al., 2008; Wetherell et al., 2002); however, consistent with our hypothesis, these differences varied as a function of race/ethnicity. The sex/gender by race/ethnicity model also demonstrated differences in rates of decline on memory and visuo-spatial abilities that were not detected when looking at sex/gender and race/ethnicity separately.

Research has consistently demonstrated an advantage for women on episodic memory tests and an advantage for men on visuo-spatial functioning. The advantage of women over men on tests of verbal memory has been documented throughout the life-course (Ferreira, Ferreira Galduroz Santos, Perri, & Fernandes Galduroz, 2014). Studies have demonstrated that this advantage is maintained during the prodromal stage of AD (Sundermann, 2016), suggesting a greater resilience or cognitive reserve that protects from age-related cognitive decline in older women. None of the aforementioned studies examined whether these sex/gender differences varied across race/ethnicity.

In the current study, women obtained higher baseline memory scores than men and men obtained higher scores than women on the language and visuo-spatial domains. When performance was examined across sex/gender by race/ethnicity groups only Hispanic men outperformed their female counterparts on the visuo-spatial and language domains, while NHW and Black men performed similarly to their female counterparts. Black and Hispanic women had a relative advantage over Black and Hispanic men on memory performance, respectively, but NHW women obtained higher scores than all sex/gender by racial/ethnic

groups. These findings highlight the major limitations associated with not accounting for racial/ethnic variability in sex/gender differences.

Research on differences in rates of cognitive decline between race/ethnicity and sex/gender has been inconsistent, particularly across sex/gender groups (Ferreira et al., 2014). In the current study, after accounting for the relationship between death and cognitive trajectories, racial/ethnic differences in rate of memory and visuo-spatial decline were noted between the NHW and Black groups. When these differences were further teased apart in the sex/gender by race/ethnicity model, Black and Hispanic women demonstrated a steeper decline in memory compared with NHW women, Black women declined at a steeper rate than NHW and Hispanic women on the visuo-spatial domain, and rate of language decline was steeper for NHW men and Black women compared with NHW and Hispanic women. Black and Hispanic men tended to decline at similar rates across domains. Again, these findings highlight a major limitation in previous research.

Overall, we found that sex/gender differences in baseline performance varied as a function of race/ethnicity and racial/ethnic differences in rate of cognitive decline varied as a function of sex/gender. In most cognitive aging research, the effects of race/ethnicity are typically examined while stratifying by or controlling for sex/gender, or vice versa. This approach fails to recognize potential racial/ethnic-related variability in sex/gender groups in cognitive trajectories leading to AD.

SOCIO-CULTURAL/HEALTH EXPLANATIONS OF DIFFERENCES IN COGNITIVE TRAJECTORIES

Differences in socio-cultural experiences explained a substantial proportion of the racial/ethnic differences in cognitive trajectories; however, the extent to which each socio-

cultural/health indicator accounted for racial/ethnic differences varied across men and women and cognitive domain. CVD burden and marital status explained little of the remaining differences, although both variables were associated with cognitive trajectories.

Previous work has demonstrated that the wide gap between NHWs and racial/ethnic minorities on indicators of life-course experiences (i.e., childhood SES, education, occupation, income) accounts for a substantial proportion of the racial/ethnic gap in cognitive test performance (Mehta et al., 2004; Schwartz et al., 2004; Yaffe et al., 2013; Zhang et al., 2016). In the current study, NHW men were more likely to report higher CSES, educational attainment, occupational status, and monthly income compared to their Black and Hispanic counterparts. Once this wide gap in childhood and adult socio-cultural indicators was accounted for, differences in cognitive test performance between NHW men and Black and Hispanic men were substantially reduced across cognitive domains (Figures 14 through 16). The women in our study demonstrated a similar pattern of differences in childhood and adult socio-cultural indicators, although the gap between NHW women and Black and Hispanic women was not as wide as that seen with men. As a result, reductions in cognitive performance differences were not as profound for women as they were for men. The slightly different findings between men and women highlight the importance of taking an intersectionality approach to understanding racial/ethnic differences in cognitive trajectories.

Research on sex/gender differences has paid little attention to racial/ethnic variability across men and women, and even less attention to potential socio-cultural explanations of differences. In the current study, sex/gender differences in childhood and adult socio-cultural indicators accounted fully explained baseline sex/gender differences

among Hispanics on the language and visuo-spatial domains, as well as baseline differences between NHW men and Black and Hispanic women on the memory domain. Additionally, differences in socio-cultural experiences explained a large proportion of the differences between NHW men and women and Black men and women on baseline memory performance. Researchers have long believed that sex/gender differences in cognitive test performance are linked to biological differences between men and women, such as early organizational and later activational effects of sex steroid hormones (Laws et al., 2016; Li & Singh, 2014). However, if this were a valid hypothesis then we would expect sex/gender differences to be consistent across racial/ethnic groups and we would not expect socio-cultural experiences to play a role in these differences.

Regarding differences in cognitive decline, initial differences between groups were accounted for by differences in socio-cultural experiences; however, slope estimates fluctuated quite a bit for some groups each time a new variable was added to the model. Although all differences were accounted for in the final model, very few of the socio-cultural/health indicators were associated with rate of change. Research on the relationship between socio-cultural/health indicators and cognitive decline has been mixed, with some studies demonstrating no relationship between socio-cultural indicators and decline (Brewster, Melrose, & Marquine, 2014; Zahodne et al., 2011) and others finding a relationship between literacy, ApoE-e4, and current recreational activities (Brewster et al., 2014). Future research should examine the role of these other indicators on cognitive decline across sex/gender and racial/ethnic groups.

Several baseline performance differences were not accounted for in the final models, including differences between all women and Hispanic men and NHW women and

Black men on the memory domain, between Hispanic women and NHW and Black women on the language domain, and between NHW and Hispanic men, NHW women and Black and Hispanic women, and Black men and women on the visuo-spatial domain. Many of these differences were due to specific variables having a stronger effect on performance for certain groups. For example, as seen in Figure 16, setting occupation to "low" and income to "$450 or less" reduced Black women's baseline visuo-spatial performance 0.234 points from Model 6B to Model 6D. As a result, baseline scores in the final model were at -0.042 for Black men and -0.254 for Black women. However, if we were to set occupation at "medium" and income to the median category ($1001 to $1250), baseline scores in the final model would be at 0.044 for Black men and 0.019 for Black women.

On the other hand, fixing variables to higher values does not attenuate differences between all women and Hispanic men on the memory domain or Hispanic women and NHW and Black women on the language domain. It is important to note that approximately 98% of the Hispanic men and women in the current study were foreign-born and emigrated to the U.S. in their early mid-life (average age 41.24). Since most of their life experiences were outside of the U.S., it is possible that our measures of CSES, education, occupation, and income do not translate into the same resources or cognitive benefits in this group compared to their U.S. born counterparts (Vable et al., 2018). There are a host of other socio-cultural indicators related to cognitive test performance and risk of dementia that were not captured with the measures used in this study that may be contributing to these differences, including proportion of education received in the U.S., level of acculturation, bilingualism, and literacy. Moreover, we cannot ignore our measurement invariance findings of intercept differences for indicators on the language factor between the NHW

men and women and Hispanic women. Group comparisons of language factor means would only be problematic if more than half of the items on the factor were invariant (Steenkamp & Baumgartner, 1998; Vandenberg & Lance, 2000). While we only found two of the five language indicators to be invariant, interpretation of group differences in language should be approached with caution.

VARIABILITY IN RISK FACTORS FOR COGNITIVE TRAJECTORIES AND DEMENTIA CONVERSION

As expected, the relationship between socio-cultural/health indicators and cognitive trajectories and dementia conversion across racial/ethnic groups varied as a function of sex/gender. Thus, providing further support for the utility of using an intersectionality approach to understand the underlying determinants of cognitive trajectories and outcomes. However, our hypotheses regarding variability in strength of relationships between socio-cultural/health indicators and outcomes across groups were only partially supported.

Education, often viewed as a proxy for cognitive reserve, may be a source of cognitive stimulation that protects cognitive health through strengthened neuronal connections and increased brain plasticity that, in turn, enables an individual to better cope with brain damage (Stern, 2009). Higher educational attainment may also increase familiarity with cognitive test stimuli, procedures, and skills, as well as increase access to financial resources that promote better health (Glymour & Manly, 2008). In the current study educational attainment was consistently related to higher baseline performance across groups and cognitive domains. While NHWs did not benefit more than Blacks and Hispanics from more years of education, the effect of education on baseline performance

was not consistently stronger in any particular group across cognitive domains. Of course, the effect of education on cognitive trajectories in the current study may be underestimated in Blacks and Hispanics because we only considered educational quantity, rather than educational quality. On the other hand, our hypothesis that the relationship between education and dementia conversion would be stronger in Blacks and Hispanics compared to NHWs was supported. In the traditional cox model only including age and education we found that more years of education was associated with a lower risk for dementia conversion for Black and Hispanic men and women but not NHW men and women.

Our findings are consistent with previous literature demonstrating the protective effects education on dementia risk in racial/ethnic minorities (Rodriguez, Aranda, Lloyd, & Vega, 2018). However, the lack of relationship between education and dementia in NHWs was unexpected. Several studies have found that higher education is associated with an increased risk of mortality (Amieva et al., 2010; Stern, Tang, Denaro, & Mayeux, 1995), which may obscure the effect of education on dementia risk. In the current study, once death was accounted for in the competing risks model, education was associated with a lower hazard for dementia for NHW women but continued to not be associated with dementia for NHW men. While this finding may reflect a stronger protective effect of cognitive reserve against dementia for NHW women and Black and Hispanic men and women, the low number of NHW men in our sample who converted to dementia may have influenced our power to detect an effect of education in this group. Alternatively, educational attainment may not be the most appropriate proxy for cognitive reserve in NHW men, as it is a static measure that is less likely to be altered over time (Malek-Ahmadi et al., 2017). Also, it is unclear whether the relationship between education and dementia

noted for NHW women in the competing risks model will remain once other socio-cultural variables are included in the model.

Individuals with higher income are more likely to have the financial resources that ensure access to health-enhancing material conditions that may buffer the risk of cognitive impairment (Glymour & Manly, 2008). Independent of education, income was consistently associated with baseline cognitive test performance for all groups, except for Hispanic men on the language domain. Our hypothesis that NHWs would benefit more from higher income was only partially supported, as this was only seen for NHWs compared to Hispanics on the language domain. Black men and women also benefitted more than Hispanic men and women from higher income on the language domain. Regarding dementia conversion, higher income was associated with lower hazards for dementia conversion for Black men and women and Hispanic and NHW men. These findings are also consistent with literature suggesting that, while closely intertwined, education and income contribute to cognitive outcomes in unique ways (Cagney & Lauderdale, 2002; Zahodne, Manly, Smith, Seeman, & Lachman, 2017).

Our finding that income was related to dementia risk in Black women but not Hispanic or NHW women is interesting and may reflect different sex/gender role norms and ideals. Most of the women in our sample were born between 1918 and 1934 and grew up during a time when it was valued for middle-class NHW women to stop working once married in order to devote themselves to domestic roles (Abrams, 2012). However, Black women have been expected to work and take care of their families since slavery. With labor force discrimination and mass incarceration of Black men, Black women have had to rely on their own income rather than that of their spouse. Thus, for Black women, the role that

income plays in dementia risk is likely more similar to that of men. Also, in the cox models that excluded marital status, higher income was related to a lower risk of dementia for NHW women, suggesting that marital status may alter the relationship between income and dementia in this group. Interpretation of these findings should be approached with caution as higher income was also associated with an increased risk of mortality for NHW women.

Occupational status has been consistently linked to cognitive functioning, with studies showing a positive association between higher cognitive complexity/greater mental demands in the work environment and higher cognitive test performance (Andel et al., 2007; Bosma et al., 2003; Marquie et al., 2010; Ribeiro, Lopes, & Lourenco, 2013). In the current study higher occupational status was related to higher baseline performance for Black women across domains, NHW women on the language and visuo-spatial domains, and Black and Hispanic men on the language domain, as well as less memory and language decline for Hispanic men. Previous work has linked occupational cognitive requirements to declines in episodic memory (Singh-Manoux et al., 2011; Then et al., 2015) and baseline global cognitive function (Pool et al., 2016). While it is possible that specific occupational duties fostered specific skill-sets relevant to the cognitive domains measured in this study, the mechanisms underlying this relationship are difficult to interpret as we did not use measures of occupational complexity. Of note, occupation was not related to performance for NHW men and Hispanic women. This is likely due to reduced intra-group variability across occupational categories for these two groups, as approximately 60% of NHW men reported high occupational status and 81% of Hispanic women reported low occupational status.

In the final model, higher CSES was only related to less memory decline for NHW men and higher baseline visuo-spatial performance for Hispanic men. Poor childhood SES, as measured by parental education, occupation, and resources, has been consistently associated with poor cognition in later life (M. T. Brown, 2010; Everson-Rose, de Leon, Bienlas, Wilson, & Evans, 2003; Fors, Lennartsson, & Lundberg, 2009; G. A. Kaplan et al., 2001; Lyu & Burr, 2016; Zeki Al-Hazzouri et al., 2011). Low childhood SES is associated with exposure to a variety of risk factors, such as poor nutrition, environmental toxins, illness, greater overall stress, and lower quality education, that can negatively impact the developing brain (Greenfield & Moorman, 2018). Early-life disadvantages, particularly during critical periods of brain development, may result in long-term biological ramifications that may not manifest until later in life (Hamil-Luker & O'rand, 2007). Thus, for NHW men, early advantages may have provided a buffer against cognitive decline. However, for all other groups, the effect of CSES on cognitive trajectories diminished once adult socio-cultural indicators were included in the models. This is consistent with the social trajectory hypothesis (Richards & Sacker, 2003), which suggests that CSES shapes later life experiences and risk factors that directly affect later life cognition. For example, access to higher quality education promotes cognitive skills that are directly related to cognition via cognitive reserve and test taking skills. Higher educational attainment also influences labor market opportunities, which, in turn, increase financial resources that ensure access to health-enhancing material conditions that may buffer the risk of cognitive impairment (Glymour & Manly, 2008).

The current study found that the relationship between CVD burden and cognitive trajectories and dementia varied across sex/gender groups within and across race/ethnicity.

Higher CVD burden was related to lower baseline performance across cognitive domains for Hispanic and Black women, as well as lower baseline visuo-spatial and language performance for Hispanic men. Interestingly, higher CVD burden was related to less memory decline for Black men. There is some evidence suggesting that later-life hypertension may be protective against cognitive decline (Corrada et al., 2014; Kennely, Lawlor, & Kenny, 2009), as well as mixed evidence regarding the protective effect of treatments for hypertension (Chang el al., 2011; Rouch et al., 2015). It is also possible that the Black men in this study possess some unmeasured socio-cultural or biological trait that buffers the deleterious effects of CVD risk factors on cognitive decline. However, ascertainment of CVD risk factor history via self-report can be unreliable, especially since we did not consider onset or duration of CVD risk factors nor did we distinguish between risk factors that were being treated and those that were not. The current study also found that higher CVD burden was related to cognitive test performance for NHW men but not NHW women. This finding is in contrast to recent research conducted in an affluent NHW sample that found a higher association of CVD risk with cognitive test performance among women compared with men (Laughlin et al., 2011).

Nonetheless, CVD burden was only associated with an increased risk of dementia for Black and Hispanic women. Similar results have been reported in prior work in racial/ethnically diverse samples (Zeki Al-Hazzouri et al., 2013). Accumulation of CVD risk factors manifest in the brain as small vessel cerebrovascular disease, which can be measured via T2-weighted MRI by quantifying white matter hyperintensity (WMH) burden (Pantoni & Garcia, 1997). Higher WMH burden has been associated with an increased risk of dementia (Brickman et al., 2012; Prins, van Dijk, & Andrews, 2004;

Yoshita, Fletcher, & Harvey, 2006), which is likely due to the impact of CVD risk factors on the blood-brain barrier that, in turn, increases susceptibility for neuronal dysfunction and neurodegeneration (Z. Zhao, Nelson, Betsholtz, & Zlokovic, 2015). A. M. Brickman et al. (2008) found greater WMH volumes among Blacks and Hispanics compared to NHWs in the WHICAP sample, but no significant race/ethnicity X sex interaction. However, it is possible that results might differ using a multiple-group approach that allows the effect of other covariates (e.g., vascular disease history) to vary across sex/gender by racial/ethnic subgroups. Possible explanations for sex/gender differences in WMH burden may be related to differences in white matter microstructure and higher prevalence of arterial stiffness in women compared to men (Shaw, Bugiardini, & Merz, 2009). Several studies have also demonstrated the impact of life-course socioeconomic disadvantage on arterial stiffness (Puolakka et al., 2017; Trudel et al., 2016) and white matter microstructure (Ozernov-Palchik et al., 2019; Ursache & Noble, 2016), suggesting that differences in CVD burden are rooted in socio-cultural differences across the life-course. It is also possible that the traditional cox model underestimated the effect of CVD burden on dementia conversion for some groups, as CVD burden was related to death for NHW men and women and Hispanic men.

Being married at baseline did not confer to the same cognitive benefits across groups. In the current study men were more likely than women to be married at their baseline visit. Among women, NHWs and Hispanics were more likely than blacks to be married and approximately half of the black women reported that they were widowed. Several studies have demonstrated the relationship between social support, including being married, and cognitive decline (Ertel, Glymour, & Berkman, 2008; Holtzman et al., 2004;

Seeman, Lusignolo, Albert, & Berkman, 2001). Independent of childhood and adult socio-cultural and health indicators, being married was associated with less memory decline for NHW women and less visuo-spatial decline for Black women. It is unclear why marital status would buffer decline in different cognitive domains for NHW and Black women. However, our finding that being married was also associated with a decreased risk of dementia in NHW women suggests that marital status is an important protective factor for this group. Our findings are not only consistent with previous literature (Brenowitz, Kukull, Beresford, Monsell, & Williams, 2014; Sommerland, Ruegger, Singh-Manoux, Lewis, & Livingston, 2017), but we also add to this body of work by demonstrating that, for NHW women, the cognitive health benefits associated with being married may have both psychosocial and economic pathways.

Across groups, several of the socio-cultural/health indicators associated with cognitive trajectories were also associated with dementia risk, while other indicators were only associated with cognitive test performance. The socio-cultural/health indicators associated with both cognitive trajectories and dementia may represent important risk factors for the development of AD and important treatment targets. On the other hand, it is possible that the socio-cultural/health indicators only associated with cognitive trajectories are more reflective of familiarity with test-taking skills. Regardless, both types of indicators are important for neuropsychologists to consider when making diagnoses and treatment recommendations.

SELECTIVE ATTRITION

Sex/gender by racial/ethnic variability in survival had an impact on estimates of cognitive trajectories and probabilities of developing dementia during the study. It is well

known that women tend to live longer than men (Ginter & Simko, 2013). In the current study, however, while Black and NHW men were more likely than all other group to die over the course of the study, Hispanic men had similar rates of survival as NHW and Black women, and Hispanic women had the highest rates of survival compared to all other groups. These findings highlight the value of examining selective survival through an intersectionality lens, as sex/gender differences in survival vary as a function of race/ethnicity.

We found that survivors tended to have higher baseline cognitive test performance scores and less steep rates of decline compared to those who died during the study, suggesting that the probability of dying depended on their performance at a previous visit (Rouanet, 2016). As expected, results from the joint models demonstrated that rate of decline was underestimated in the models not accounting for death. The joint models also revealed differences between sex/gender by racial/ethnic groups on rate of decline that were obscured in previous models (Model 3) by differential attrition of study participants. Our findings are consistent with other studies showing steeper rates of decline when accounting for death (Rouanet, Helmer, Dartigues, & Jacqmin-Gadda, 2017). Examination of death and non-death drop-out was less informative and, with the exception of Hispanic women, cognitive trajectories were generally similar to the traditional LGM. This is likely due to combining both types of attrition (i.e., death and non-death-drop-out) in a single indicator. This approach is limiting as it may mask important differences between death and non-death drop-out processes (Dufouil, Brayne, & Clayton, 2004). The steeper rate of memory decline for Hispanic women in Model 9 suggests that non-death drop-out is affecting cognitive trajectories above and beyond the effect of death. Future research

should explore the differences between death and non-death drop-out processes by modeling competing risks of death and non-death drop-out in a joint model that combines cognitive trajectory data (Rouanet, 2016).

Results from the competing risks analyses showed that after accounting for death the probability of being dementia free was higher for NHW and Black men than what was previously estimated in the traditional cox regression model. For NHW and Black women and Hispanic men and women, the traditional cox model underestimated the probability of being dementia free but then overestimated these probabilities in later years. While our inability to use multiple imputation in R prevented us from examining estimates for most of the socio-cultural/health indicators on dementia risk, results from the analyses including age and education revealed slight differences in parameter estimates from the traditional cox model. For NHW men, age was no longer associated with dementia when examining the subdistribution hazard in the competing risks model. This finding is odd and highlights a major limitation with subdistribution hazards. If a variable, such as age, is related to two events but more strongly related to one event (i.e., death) then the other event (i.e., dementia), the subdistribution hazards would reduce the likelihood that dementia events would be observed because age increased the risk for death (Austin & Fine, 2017). Future research should examine this more closely and/or employ different types of competing risks models, such as an illness-to-death model, which examines three states (health, dementia, and death) and simultaneously estimates three transitions (health to dementia, dementia to death, and health to death) (Leffondre et al., 2013; Rouanet, 2016).

STUDY LIMITATIONS

The current study leveraged longitudinal data from a large, well-characterized, and socio-economically and racially/ethnically diverse cohort of older adults. Examining data from this cohort makes a unique contribution to the field by allowing for increased knowledge about groups most at risk for cognitive decline and dementia and the diversity of participants enables explicit examination of racial/ethnic by sex/gender differences in the mechanisms underlying AD. Despite these strengths, the socio-cultural risk factors experienced by these residents of Northern Manhattan may differ from older adults residing in other parts of the country. Of note, approximately 35% of NHW men and 39% of NHW women in the current study were European immigrants. This is unique from other NHW cohorts in the U.S. and may explain the lack of support for some of our hypotheses in Specific Aim 4. Additionally, the Hispanic participants in the current study were primarily emigrants from the Caribbean (Puerto Rico, Dominican Republic, and Cuba). Again, this is a major strength since most research on cognitive aging in Hispanic populations is conducted with Mexican-American immigrants (Torres et al., 2016); however, findings from the current study may not generalize given considerable differences in the cultural, immigration, and educational experiences of other Hispanic subgroups. Future studies should examine variability among different Hispanic subgroups and determine whether some of these findings persist in these other populations. Additionally, more research needs to be conducted in racial/ethnic groups other than NHWs, Blacks, and Hispanics. Given findings from Mayeda et al., (2016) that AI/ANs have similar dementia incidence rates to Blacks, AI/ANs are disproportionately at risk for dementia yet very few studies have examined determinants of cognitive decline and dementia risk in this population.

The socio-cultural and health indicators used in this study also present several limitations. Measures of educational attainment, occupation, and income are prone to measurement error due to differential responding, underreporting, and inconsistency over time (Elo, Preston, Rosenwaike, Hill, & Cheney, 1996). As stated previously, the current study examined racial/ethnic by sex/gender differences in educational quantity, rather than educational quality. There are well-known differences in the quality of education received by different racial/ethnic groups and, as a result, the pay-offs associated with a given level of educational attainment will not be commensurate across groups. This may explain, in part, why racial/ethnic differences in the current study persisted despite accounting for differences in educational attainment. Previous work using measures of reading ability or literacy as proxies of educational quality have found that these indicators are more powerful at reducing racial/ethnic differences in cognitive test performance than traditional measures of educational attainment (Dotson et al., 2009; J. J. Manly et al., 1999; J. J. Manly et al., 2002; J. J. Manly et al., 2003; Touradji et al., 2001). More research should be conducted to determine whether literacy would account for a larger proportion of the cognitive test performance differences between Hispanic and NHW and Black women than what was accounted for by educational attainment in the current study.

Our measure of monthly income was based on self-report and classification of each income category was arbitrarily decided at the beginning of the study in 1992. The cognitive health benefits associated with a particular income category in 1992 may not be associated with that same income category for the 1999 and 2009 cohorts. Also, it is unclear whether income translates to the same economic resources across each racial/ethnic by sex/gender group as measures of household monthly income do not take into account the

meaning and complexity of socioeconomic status across racial/ethnic groups (Landrine & Corral, 2014). For example, income does not take into account household size (Silverman & Patterson, 2012), housing discrimination (Krieger, Williams, & Moss, 1997; Yinger, 2001), credit and retail discrimination (Dunn et al., 2011; Talukdar, 2008), and yearly fluctuations (Franks, Muenning, Lubetkin, & Jia, 2006). Alternatives to monthly income that should be included in future research, include equivalence adjusted income that takes into account household size (DeNavas-Walt, Proctor, & Smith, 2013), wealth (Williams et al., 2010), and geographic area measures of SES (Landrine & Corral, 2014). Moreover, our findings are limited by our use of time-invariant socio-cultural/health indicators as the magnitude of the relationship between indicators and cognitive outcomes may vary across time and different birth cohorts (Weuve et al., 2015).

Several variables known to be related to cognitive trajectories and dementia risk were not included in the current study due to either lack of measurement or large amounts of missing data, including residential history, level of acculturation, bilingualism, perceived discrimination, locus of control, depression, and ApoE-e4 status. Data on level of acculturation, perceived discrimination, and locus of control were not collected in the WHICAP study; however, it is worth collecting data on these variables in future studies as they have been shown to mediate the relationship between race/ethnicity and cognitive test performance (Barnes & de Leon, 2004; Mirowsky & Ross, 2007; Zahodne et al., 2017). Although data was collected on bilingualism, it did not make sense to include in the current analyses as most of the Black and NHW participants were monolingual English-speakers. Data on residential history, depression symptomatology, and ApoE-e4 was only available for a subset of study participants. Since we wanted to maximize our sample size and since

it would not make sense to impute values for these specific variables, we decided not to include them in the current analyses. In the future, we hope to replicate these analyses in the subset of participants with data on these variables. Applying an intersectionality approach to examine the relationship between ApoE-e4 and cognitive trajectories and dementia will be particularly important, given that research has demonstrated that sex/gender moderates the effect of ApoE-e4 on cognitive outcomes (see review in Synder et al., 2016) in predominantly NHW samples.

As stated previously, gender identity was not measured in the current study. While sex and gender should be distinguished between in research, most studies only ask participants whether they are male or female and sex or gender is inferred based on their response. Participants may even respond with their gender despite being asked about their sex. To avoid further inconsistent/inaccurate use of sex or gender, the current study used the term sex/gender. Tannenbaum and colleagues (2016) suggested that the best approach to distinguishing between sex and gender is to ask participants: 1) their sex assigned at birth and 2) how they currently self-identify (gender). The authors also recognize the complex entanglement between these two concepts (Jahn, Bornhorst, Gunther, & Brand, 2017). Future research should examine both their independent contributions and their interactions across racial/ethnic groups.

Bias from selective study enrollment is another limitation that was not accounted for in the current study. The socio-cultural/health indicators measured associated with survival in the study period may also be associated with survival prior to study enrollment. Thus, the individuals enrolled in WHICAP may represent a select group of people who survived until the age of enrollment and demonstrate less disadvantage on socio-

cultural/health indicators than those who did not survive until the age of study enrollment. This may explain the lack of association between many of the socio-cultural/health indicators in the current study, as selective enrollment has been found to underestimate the relationship between life-course exposures and cognitive decline in simulation studies (Mayeda, Filshtein, Tripodis, Glymour, & Gross, 2018). Statistical modeling techniques, such as inverse probability weighing (weighting the inverse of the probability of selection) and joint modeling of death, non-death drop-out, and enrollment with cognitive trajectories, have been suggested as potential approaches to address bias from selective study enrollment (Weuve et al., 2015).

SUMMARY, IMPLICATIONS, AND CONCLUSIONS

The overall goal of the current study was to highlight the intersectionality of race/ethnicity and sex/gender as determinants of specific socio-cultural experiences that shape cognitive trajectories leading to AD. The current study highlighted the importance of using an intersectionality approach in cognitive aging research in several ways: 1) full measurement invariance of the WHICAP neuropsychological test battery was demonstrated across sex/gender groups and over repeated measurements, but only partial scalar invariance was demonstrated across racial/ethnic groups with intercept differences that varied by racial/ethnic and by racial/ethnic by sex/gender subgroups; 2) sex/gender differences in baseline cognitive test performance varied as a function of race/ethnicity and racial/ethnic differences in rate of cognitive decline varied as a function of sex/gender; 3) while differences in socio-cultural/health indicators explained a substantial proportion of the racial/ethnic differences in cognitive trajectories, the extent to which each socio-cultural/health indicator accounted for racial/ethnic differences varied across men and

women; 4) the relationship between socio-cultural/health indicators and cognitive trajectories and dementia conversion across racial/ethnic groups varied as a function of sex/gender; and 5) sex/gender by racial/ethnic-related variability in survival impacted estimates of cognitive trajectories and dementia conversion. Research, clinical, and policy implications are discussed.

Research on racial/ethnic disparities has increasingly focused its efforts toward identifying and understanding the socio-cultural/health determinants of racial/ethnic differences in cognitive trajectories and cognitive outcomes. This research has increased understanding of early-life conditions, geographic exposures, educational experiences, socioeconomic position, structural and individual discrimination, health behaviors, and culture and linguistic influences on cognitive test performance and incident dementia (Glymour & Manly, 2008). Although there is more work to be done to understand how these environmental and socio-cultural experiences become biologically embedded, research demonstrating racial/ethnic differences in CVD and genetic risk factors has increased knowledge of differential pathways to AD. For example, vascular disease and socio-cultural disadvantage across the life-course has been found to have a stronger impact on cognitive function and incident AD among racial/ethnic minorities (Brickman et al., 2012; Adam M. Brickman et al., 2008; Liu, Glymour, Zahodne, Weiss, & Manly, 2015; J. J. Manly, Byrd, Touradji, & Stern, 2004; Jennifer J. Manly, Diane M. Jacobs, Pegah Touradji, Scott A. Small, & Yaakov Stern, 2002), while APOE-ε4 and smaller hippocampal volume may be more predictive of AD in older NHWs (Brickman et al., 2015; Tang et al., 1998).

Findings from the current study contribute to this growing body of research by further demonstrating the contribution of life-course socio-cultural/health experiences on racial/ethnic differences in cognitive trajectories and risk of dementia. Our findings also highlight the limitations of simply controlling for sex/gender when examining racial/ethnic differences, as this obscures important variability between men and women across and within racial/ethnic groups. Unfortunately, research on sex/gender differences has done little to further knowledge about the socio-cultural determinants underlying differences between men and women on cognitive test performance and dementia risk.

In 2014, the Alzheimer's Association Facts and Figures reported, for the first time, that women were at increased risk to develop AD compared with men (Alzheimer's Association, 2014). Since then, research in the U.S. has failed to re-demonstrate the sex/gender differences in incident dementia found in European studies (Snyder et al., 2016) and findings from animal studies linking estrogen depletion to increased risk of dementia have not held up in human studies (Mielke et al., 2014). Despite these inconsistencies, researchers continue to search for biological explanations for potential sex/gender differences in the risk and development of AD (Burke et al., 2019; Koran, Wagener, Hohman, & Initiative, 2017; Liesinger et al., 2018; L. Zhao, Mao, Woody, & Brinton, 2016)

The lack of consistent findings regarding differences in rates of incident dementia between men and women should not preempt investigation of sex/gender differences in risk factors associated with the development, onset, and maintenance of AD or sex/gender differences in the clinical presentation and neuropathology associated with AD. However, the research currently being conducted is limited for several reasons. First, most of the

sex/gender research conducted in Europe and the U.S. is based on predominantly NHW samples. Our findings show that sex/gender differences and determinants of such differences vary as a function of race/ethnicity. Thus, findings from these studies lack generalizability to racial/ethnic minority populations, who are most at risk for AD. Second, many of the studies linking biological mechanisms to sex/gender differences do not account for selective survival, which interferes with the ability to make valid conclusions about the explanatory power of such biological mechanisms. Third, socio-cultural explanations of sex/gender differences have largely been ignored. Simply adding a 'sex' variable into an analysis and finding differences between men and women on an outcome and a biological indicator of that outcome does not necessarily mean that the demonstrated differences are then due to differences in sex hormones and sexual dimorphism of the brain (Springer, Mager Stellman, & Jordan-Young, 2012). Based on findings from the current study, it is likely that what is being attributed to biological differences can be explained by socio-cultural differences between men and women. That is not to say that sex-specific hormones and biological differences do not play a role in brain development, expression of certain genes, and brain pathology associated with AD, but solely focusing on hormones/biological differences and continuing to ignore socio-cultural explanations of sex/gender differences will do little to further our understanding of AD disparities.

Our findings also have important clinical implications, especially in regard to the use of norms. We found substantial racial/ethnic differences within each sex/gender group that were not accounted for by educational attainment. Thus, when comparing racial/ethnic minorities to a normative sample that is predominantly NHW, regardless if these norms are stratified by sex/gender, education, or sex/gender and education, it is likely that their true

level of cognitive functioning will be underestimated and the risk of misclassification of cognitive impairment will increase. Clinicians should also be mindful of differences in socio-cultural/health indicators across sex/gender by racial/ethnic subgroups and how each indicator may differentially influence cognitive test performance and dementia risk across certain groups of people. Thorough clinical interviews that gather information about life-course socio-cultural experiences and current risk/protective factors will better guide and inform the interpretation of neuropsychological test performance and diagnostic decision-making process (Torres et al., 2016).

The new NIA-AA biomarker diagnostic criteria research framework proposed by Jack et al., (2018), although not yet successfully implemented or validated, may be adopted in clinical practice in the future (Lancet Neurology, 2017). Clinicians, and researchers alike, should stay informed of the major limitations of biomarker based diagnostic criteria. In addition to issues surrounding the devaluation of neuropsychological assessment and expensive blood-based biomarker measures, the proposed criteria fails to acknowledge potential sex/gender or racial/ethnic variability in AD biomarkers. Recent research demonstrated differences in CSF levels of tau pathology between NHWs and Blacks, with levels being lower for Blacks (Morris et al., 2019), as well as mixed vascular and AD pathology being more common in Blacks than NHWs (Barnes et al., 2015). Our findings that socio-cultural/health indicators are differentially related to dementia across groups raises the likelihood of differential expression of biomarkers and brain pathology across sex/gender by racial/ethnic groups. Before biomarker criteria is adopted in clinical practice, more research must be done to identify specific biomarker profiles across sex/gender by racial/ethnic groups and determine the influence of specific socio-cultural/health

experiences on the expression of such biomarker profiles. Failure to do so will result in an under-diagnosis of those most at risk for AD.

Regarding policy implications, racial/ethnic disparities in AD have been well-documented, yet little has been done at the policy level to address these disparities. The money and resources put toward AD prevention research targeting amyloid burden (Yiannopoulou & Papageorgiou, 2013) will do nothing to reduce the impact of life-course disadvantage on cognitive health. Efforts to reduce AD disparities should begin early in life, as cognitive trajectories likely being to diverge in childhood. Investing in early, good quality, educational programs and increasing access to good nutrition and pediatric medical care will likely have a profound effect on adult health (Williams & Purdie-Vaughns, 2016). Community-based participatory research (CBPR) is another promising approach to addressing health disparities and influencing health policy (Minkler, 2013). CBPR involves community partners, or stakeholders, in all aspects of the research process, from defining the problem to analysis, dissemination, and application of findings. This allows for individuals most at risk for health disparities to gain a seat and the table and exercise their voice in decision making. In WHICAP, engaging community stakeholders has increased participant retention and allowed research findings to be communicated to the community at large. Other studies have used this approach to address diesel bus pollution (Brechwich Vasquez, Minkler, & Shepard, 2006) and food insecurity (Brechwich Vasquez et al., 2007) in New York City.

Congress recently passed the Building Our Largest Dementia (BOLD) Infrastructure for Alzheimer's Act (P.L. 115-406), which includes funding for establishing "Centers of Excellence" that aim to "expand innovative public private partnerships that

focus on addressing cognitive impairment and health disparities" (Alzheimer's Association, 2018). At face value, this initiative seems to be a step in the right direction; however, it gives much discretion to the Department of Health and Human Services (DHHS) Secretary to decide what programs are allocated money (Gleckman, 2019). This raises the potential that highly influential organizations that primarily focus on drug research will receive funding priority. Influencing policy through the National Institute on Aging (NIA), and similar organizations, will help make AD disparities a priority by impacting how research is conducted and how information is disseminated to the public. Hill and colleagues (2015) proposed a NIA health disparities research framework, whereby they encourage researchers to examine multiple levels of analysis (environmental, socio-cultural, behavioral, and biological) to broaden the scope of intervention targets. Future research frameworks should also encourage researchers to increase community engagement and provide strategies to improve racial/ethnic minority enrollment and retention. As a field, we should work toward developing specific guidelines for conducting AD disparities research and encourage research infrastructures, like NIA and the Alzheimer's Association, to adopt and implement these guidelines with the research they are funding. Finally, relying on policymakers to bridge the gap between science and policy often leads to misappropriation of research findings. We should work toward incorporating more specific policy implications and, perhaps, policy proposals in the dissemination of research findings to more directly influence policy change.

In conclusion, this study improves our understanding of how race/ethnicity and sex/gender intersect to define cognitive health in older adults. Examining race/ethnicity and sex/gender separately will obscure important differences in the onset and maintenance

of AD and can hinder efforts to eliminate disparities. Widespread adoption of this intersectionality approach across cognitive aging studies will provide a more nuanced understanding of mechanisms of AD disparities and may lead to the development of new strategies to prevent or slow AD-related cognitive decline.

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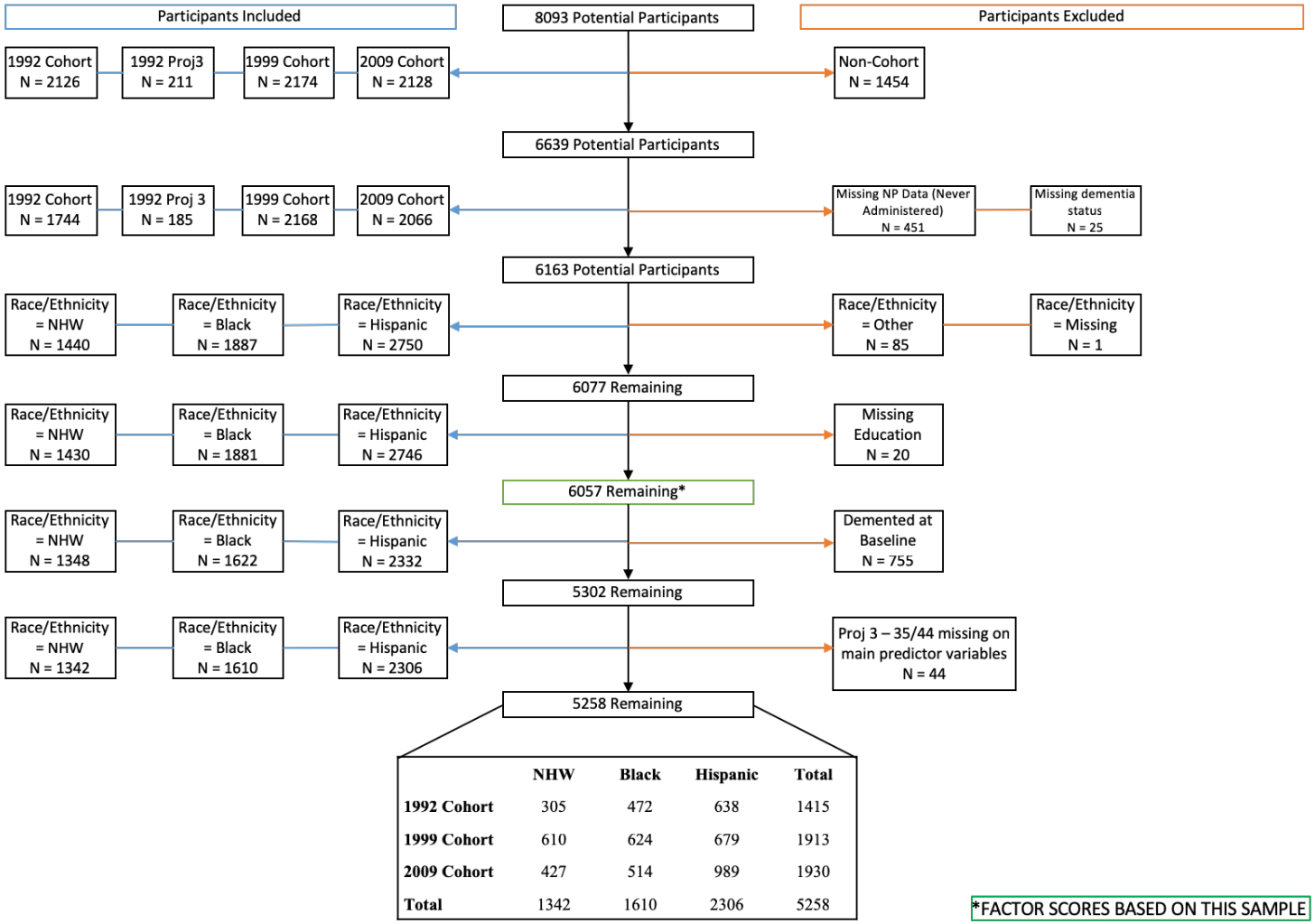
Figure 1. Sample Selection Procedures



	NHW	Black	Hispanic	Total
1992 Cohort	305	472	638	1415
1999 Cohort	610	624	679	1913
2009 Cohort	427	514	989	1930
Total	1342	1610	2306	5258

Figure 2. Confirmatory Factor Analysis Model of the WHICAP Neuropsychological Battery

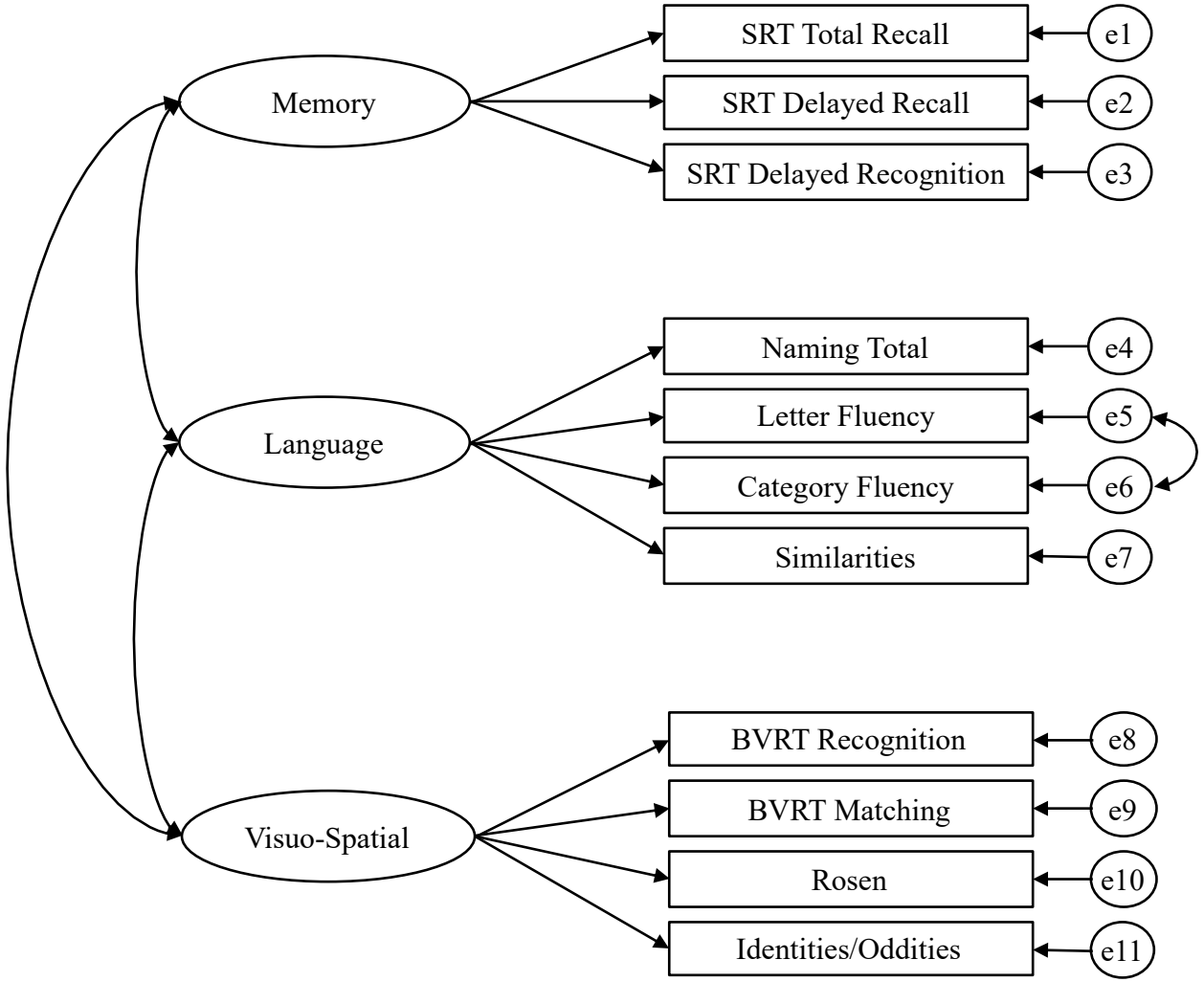


Figure 3. Estimated Memory, Language, and Visuo-Spatial Trajectories for the Unadjusted Multiple-Group Latent Growth Models Across Sex/Gender Subgroups (Model 1)

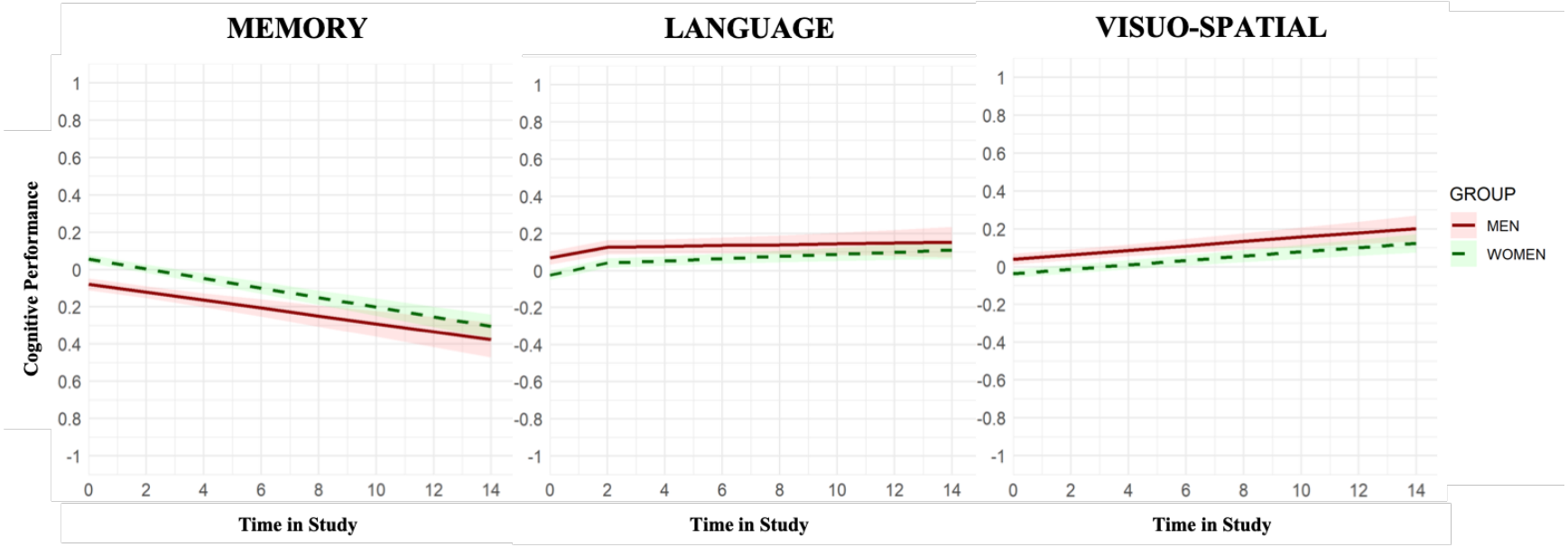


Figure 4. Estimated Memory, Language, and Visuo-Spatial Trajectories for the Unadjusted Multiple-Group Latent Growth Models Across Racial/Ethnic Subgroups (Model 2)

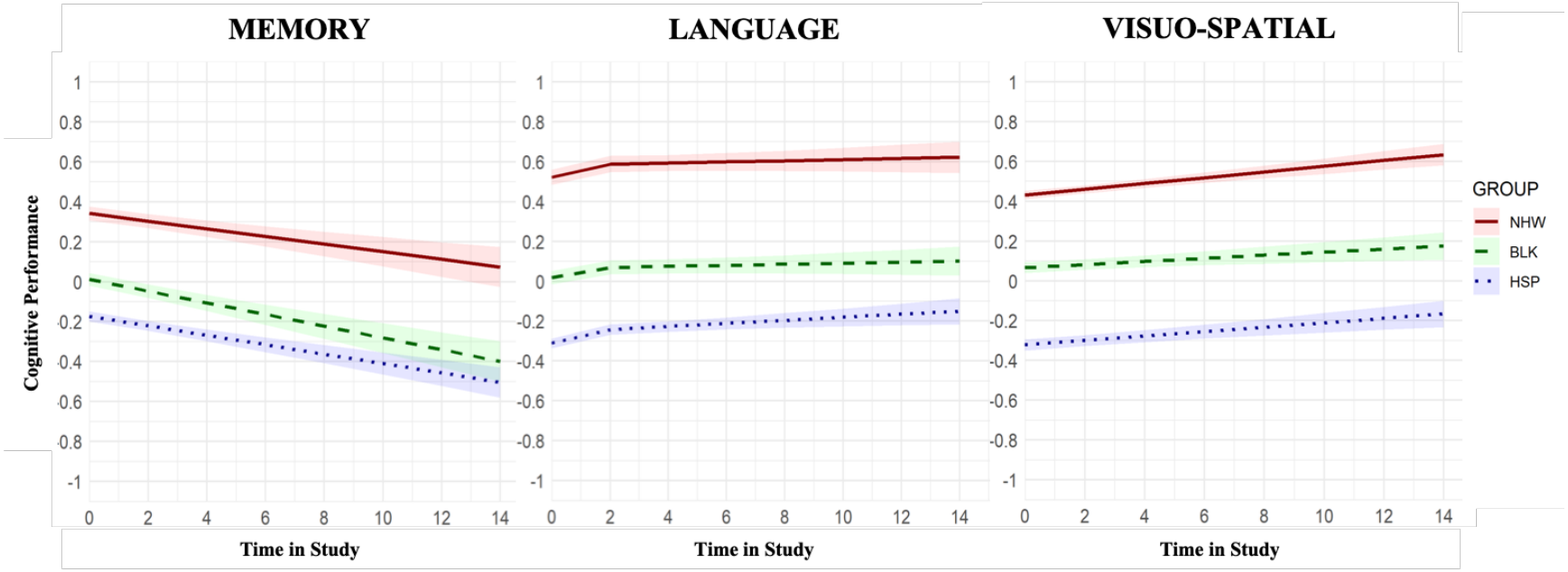


Figure 5. Estimated Memory, Language, and Visuo-Spatial Trajectories for the Unadjusted Multiple-Group Latent Growth Models Across Sex/Gender by Racial/Ethnic Subgroups (Model 3)

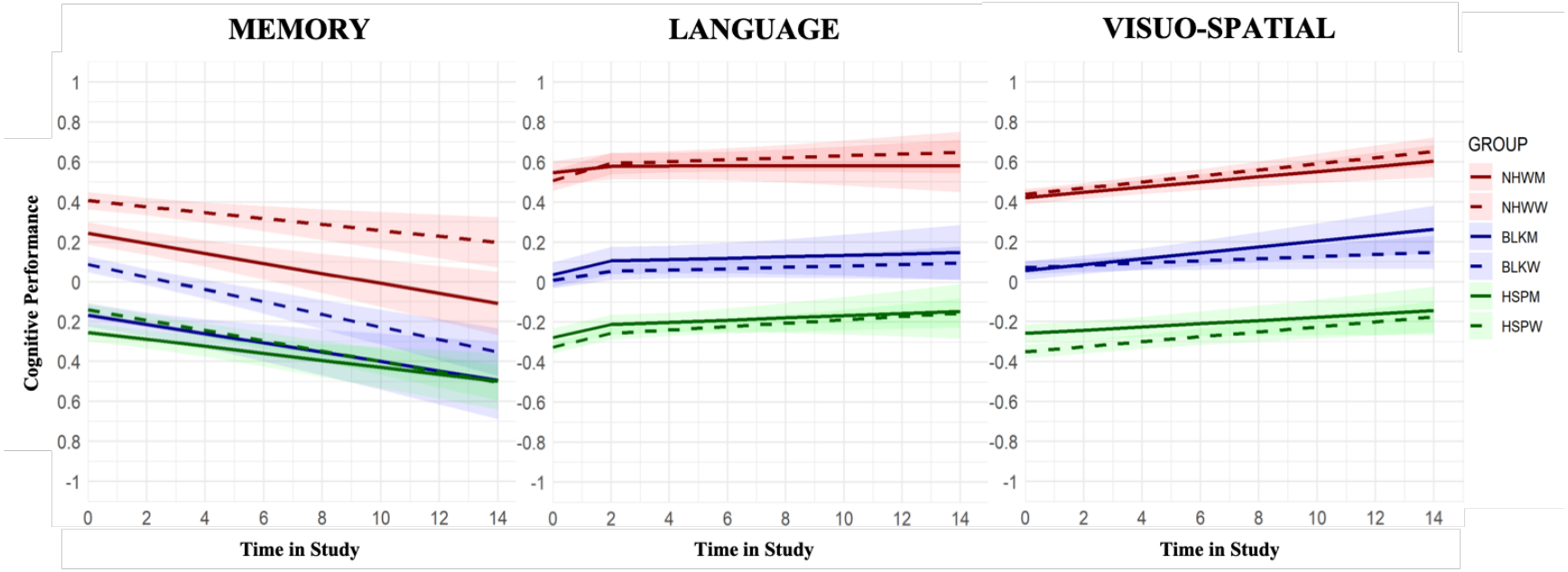


Figure 6. Summary of Selective Attrition Across the Entire Sample

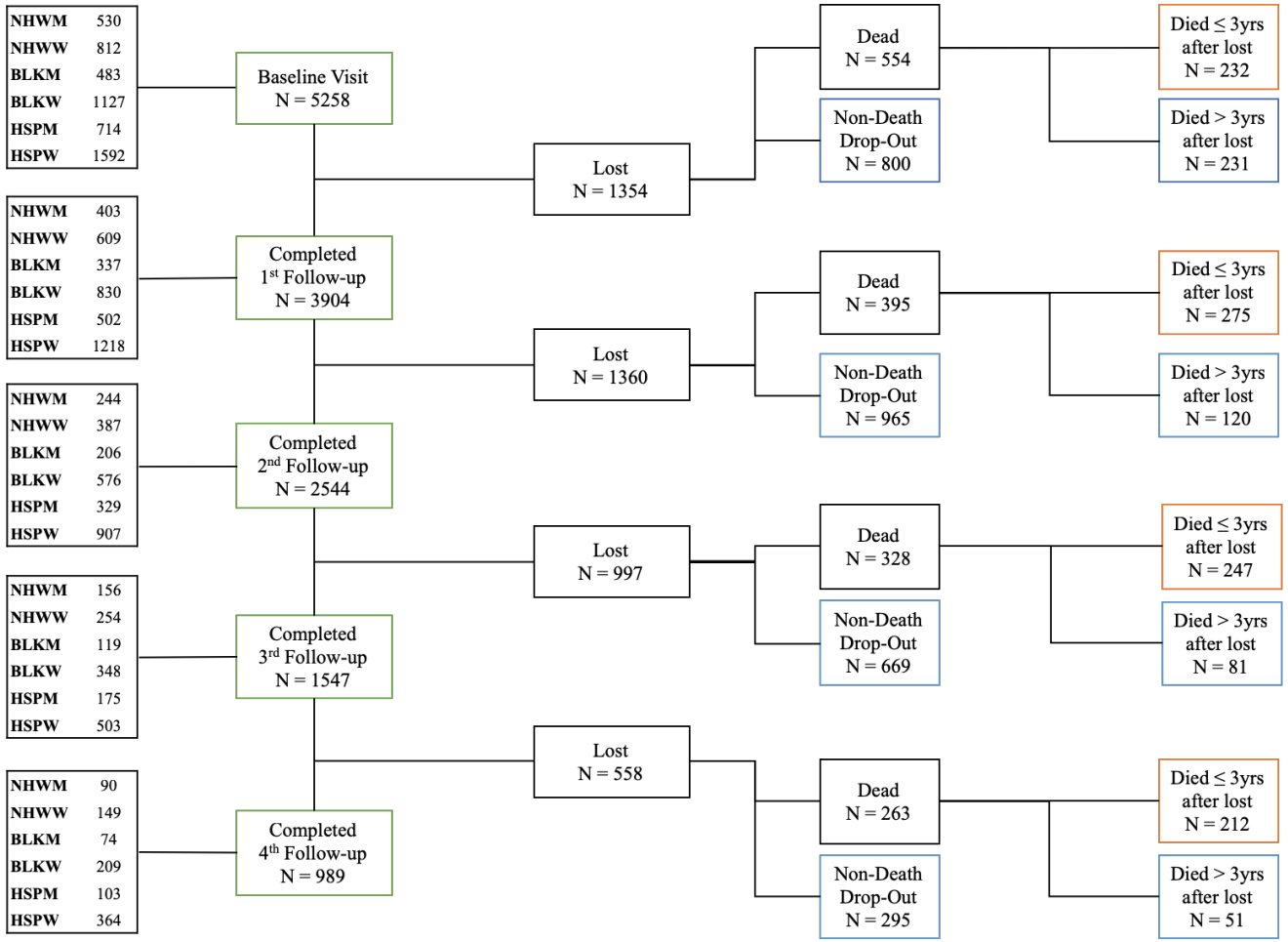


Figure 7. Survival Curves from the Cox Regression Models for Death Across Sex/Gender by Racial/Ethnic Subgroups

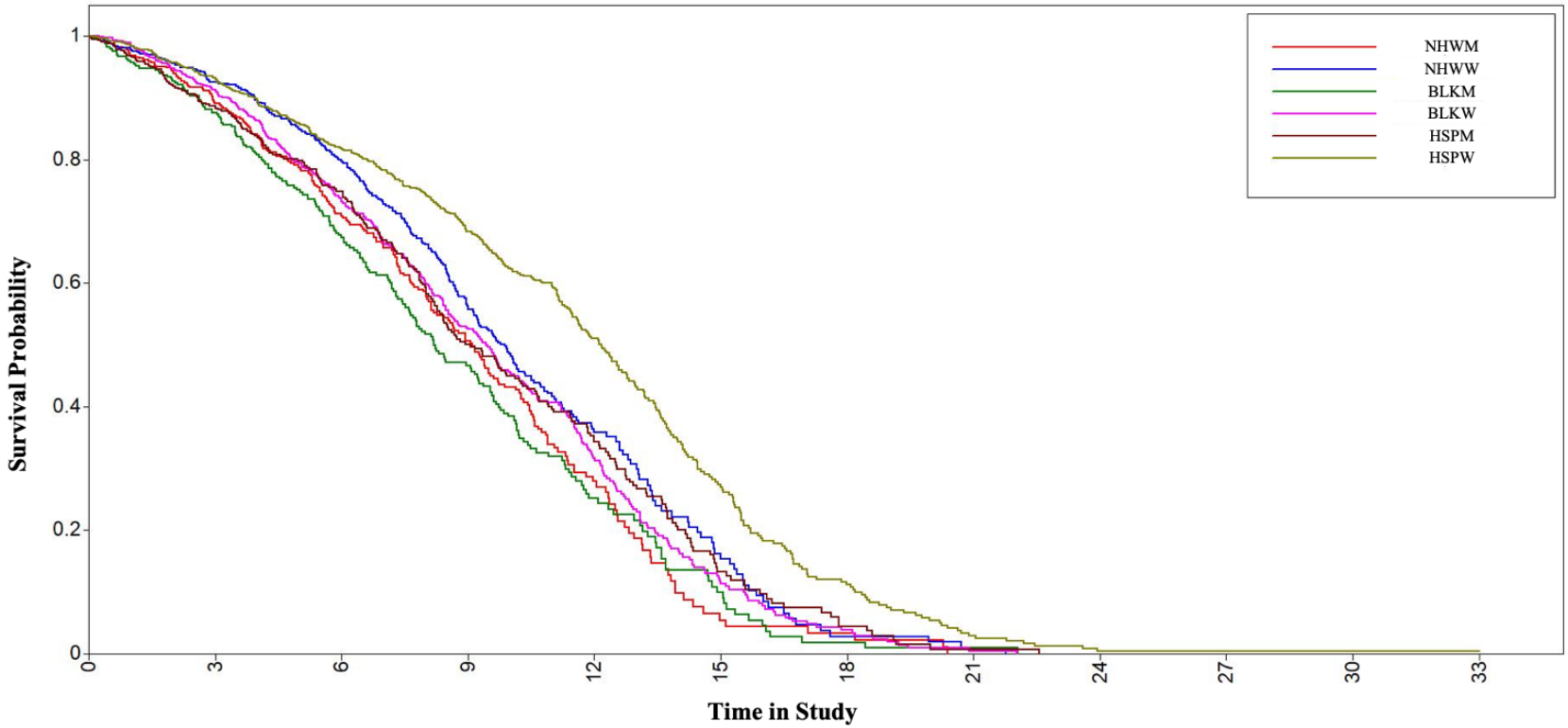


Figure 8. Estimated Memory, Language, and Visuo-Spatial Trajectories for the Unadjusted Multiple-Group Joint Models Across Sex/Gender Subgroups (Model 4)

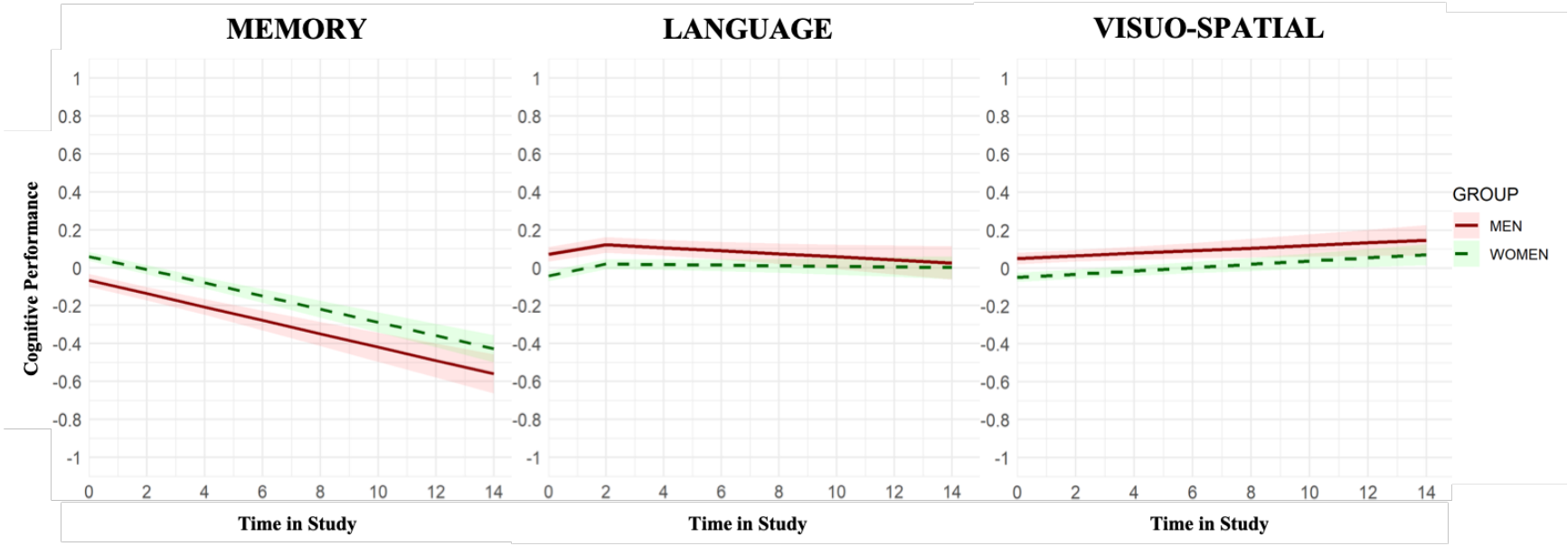


Figure 9. Estimated Memory, Language, and Visuo-Spatial Trajectories for the Unadjusted Multiple-Group Joint Models Across Racial/Ethnic Subgroups (Model 5)

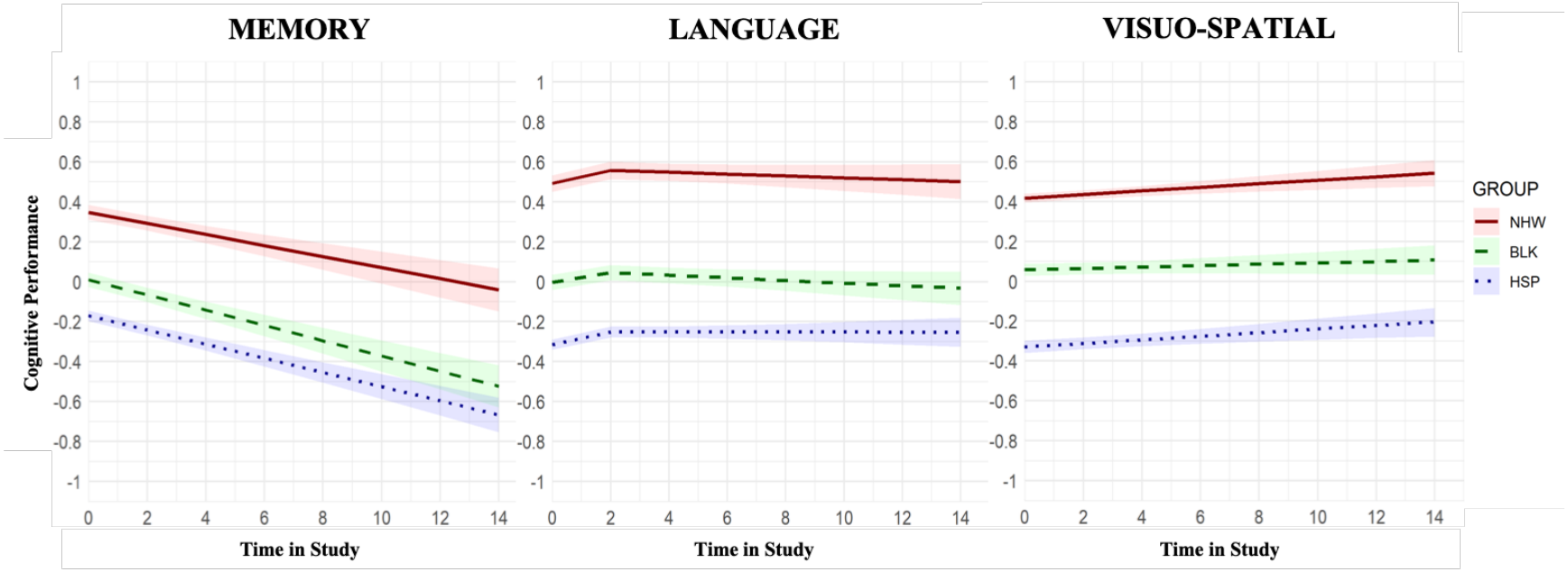


Figure 10. Estimated Memory, Language, and Visuo-Spatial Trajectories for the Unadjusted Multiple-Group Joint Models Across Sex/Gender by Racial/Ethnic Subgroups (Model 6)

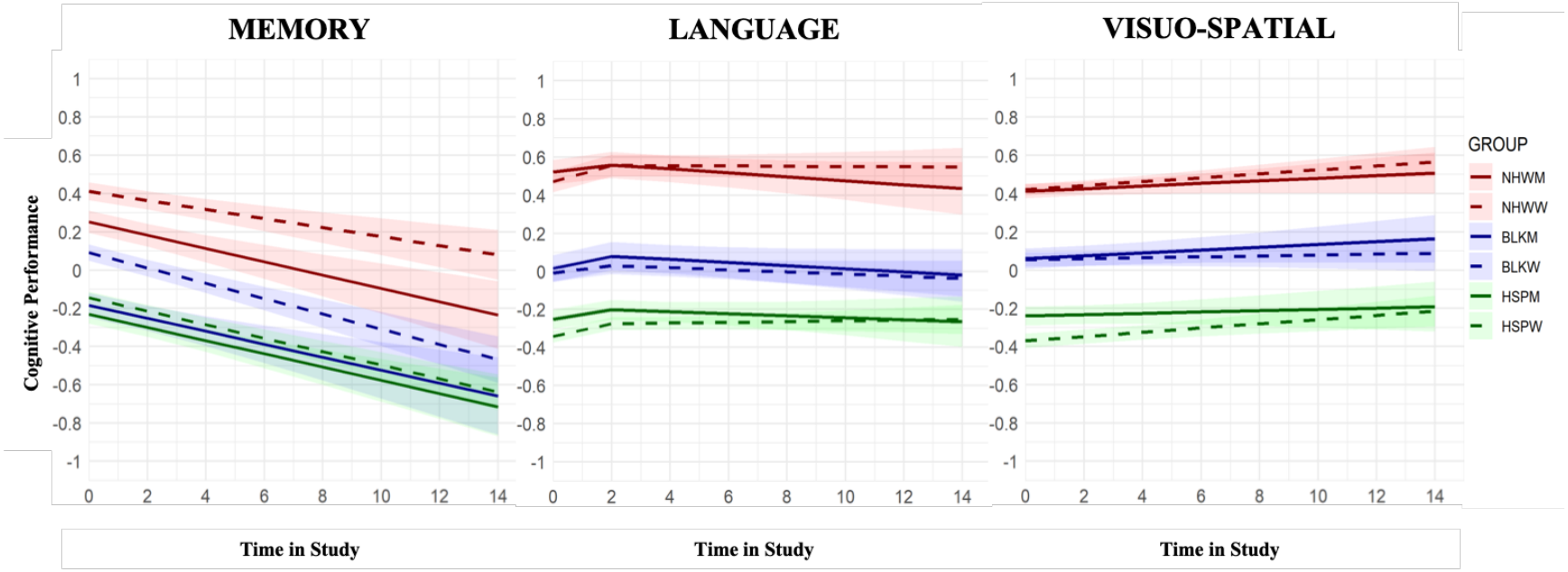


Figure 11. Comparison of Unadjusted Multiple-Group Latent Growth and Joint Models for the Memory Domain Across Sex/Gender Subgroups

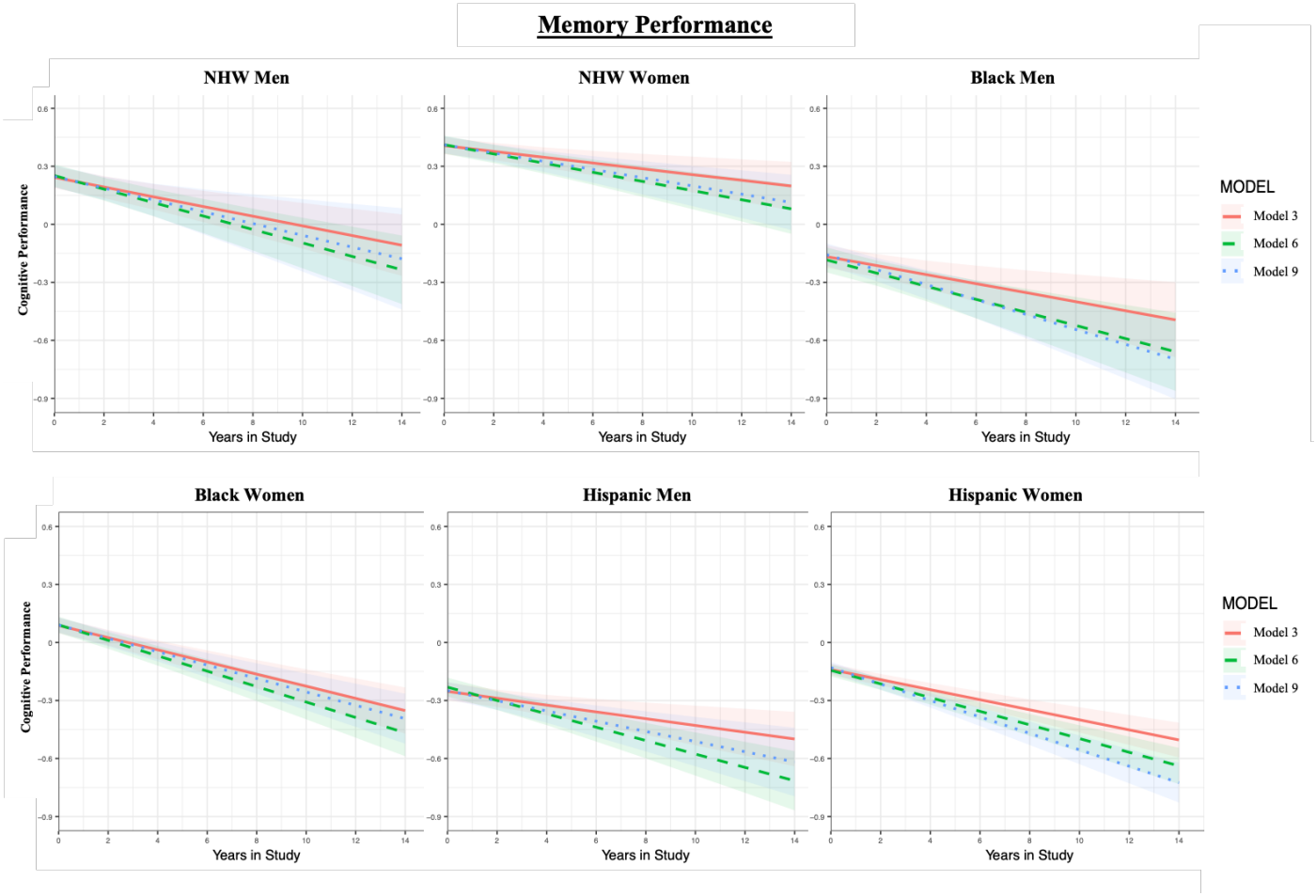


Figure 12. Comparison of Unadjusted Multiple-Group Latent Growth and Joint Models for the Language Domain Across Sex/Gender Subgroups

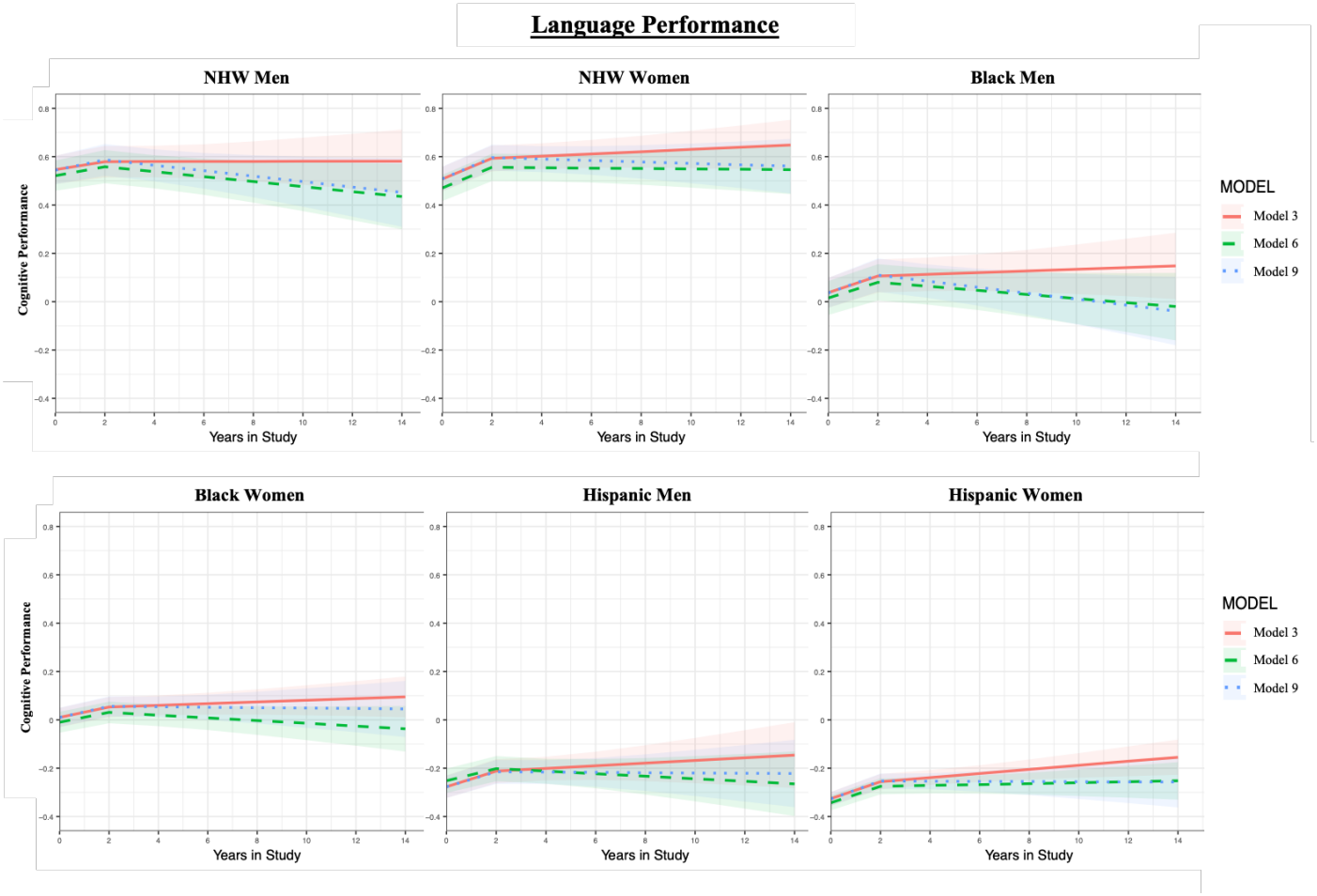


Figure 13. Comparison of Unadjusted Multiple-Group Latent Growth and Joint Models for the Visuo-Spatial Domain Across Sex/Gender Subgroups

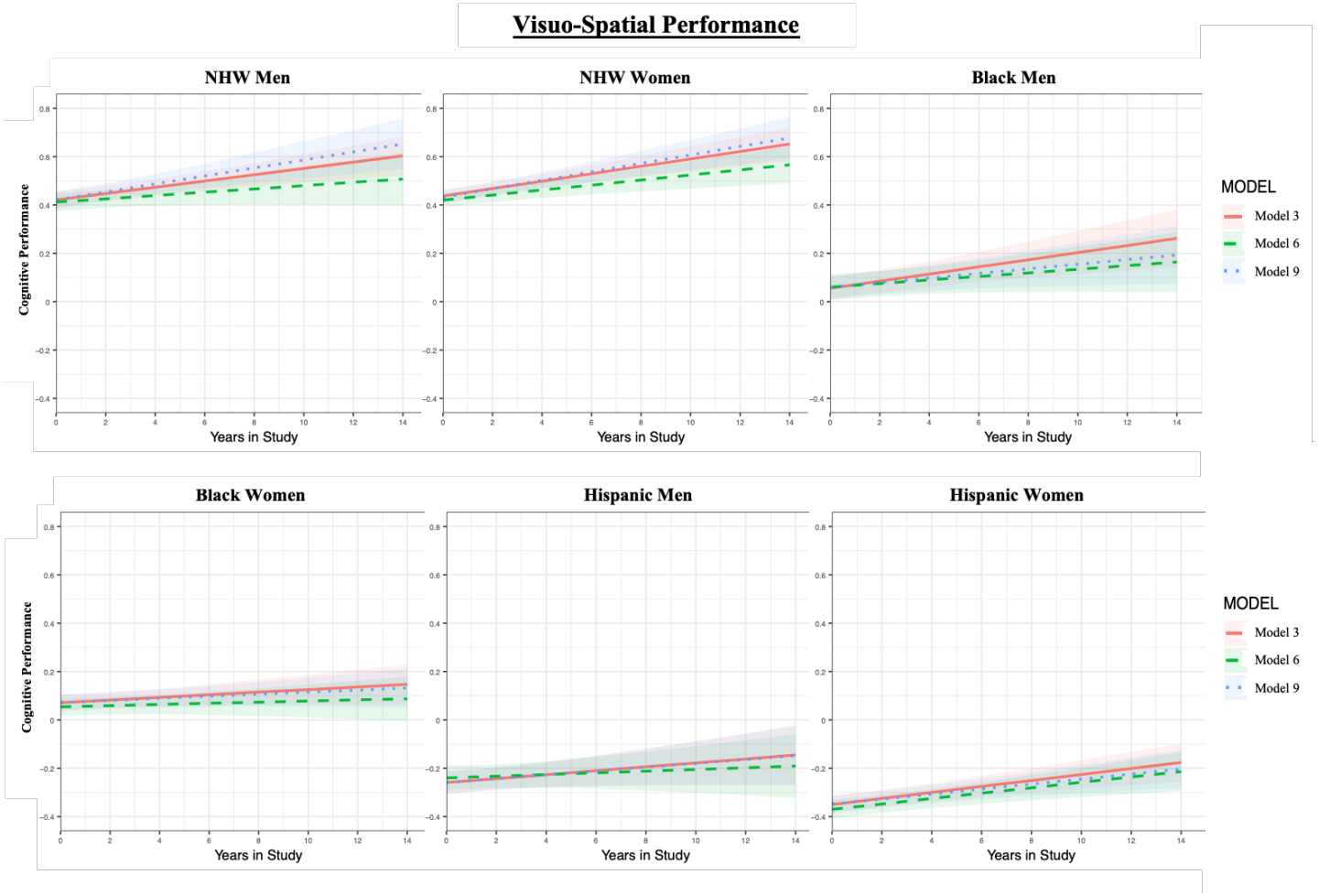


Figure 14. Differences in Average Baseline Memory Performance from Models 6 through 6G Across Sex/Gender Subgroups

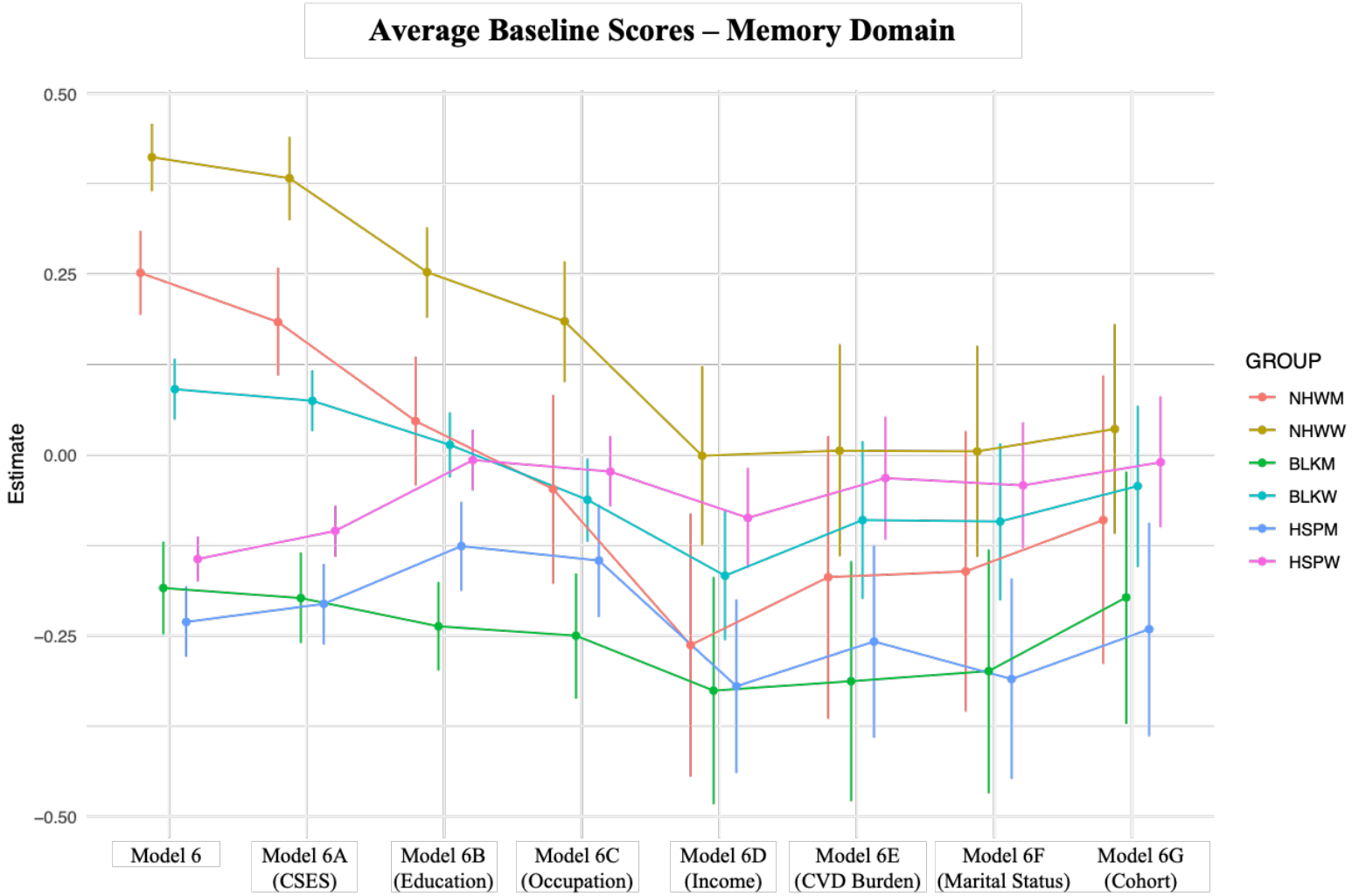


Figure 15. Differences in Average Baseline Language Performance from Models 6 through 6G Across Sex/Gender Subgroups

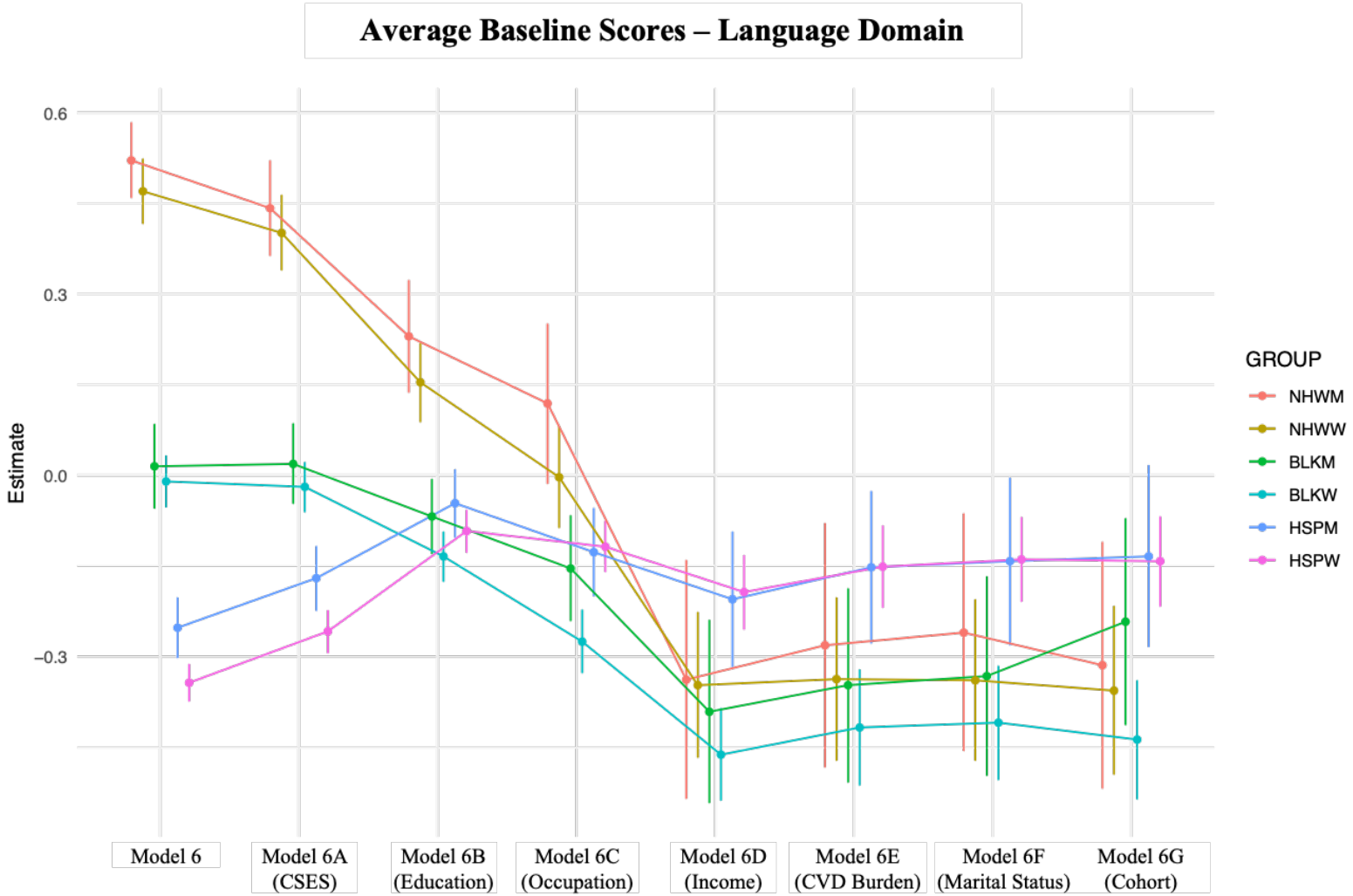


Figure 16. Differences in Average Baseline Visuo-Spatial Performance from Models 6 through 6G Across Sex/Gender Subgroups

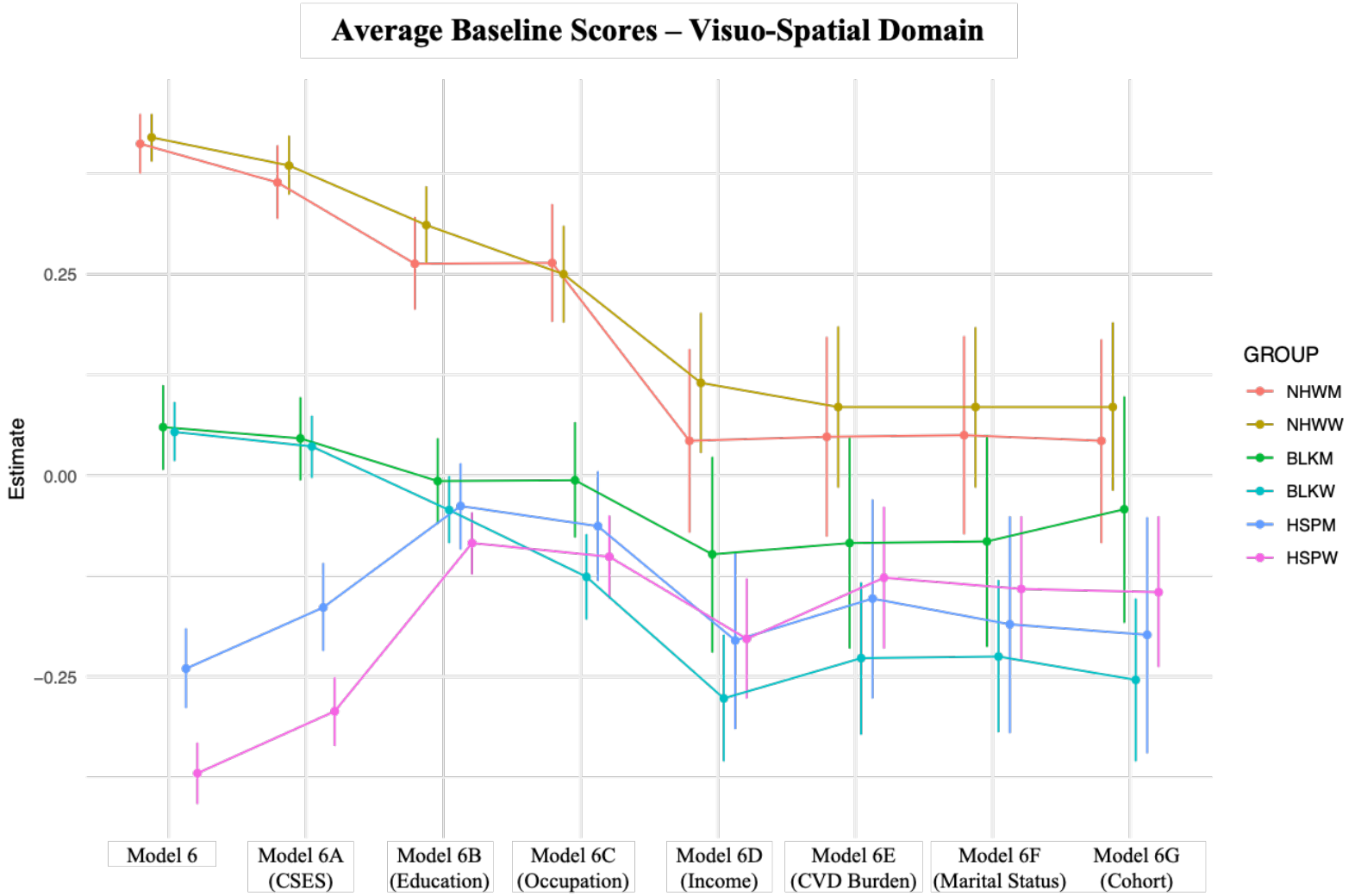


Figure 17. Differences in Average Rate of Decline in Memory Performance from Models 6 through 6G Across Sex/Gender Subgroups

Figure 18. Differences in Average Rate of Decline in Language Performance from Models 6 through 6G Across Sex/Gender Subgroups

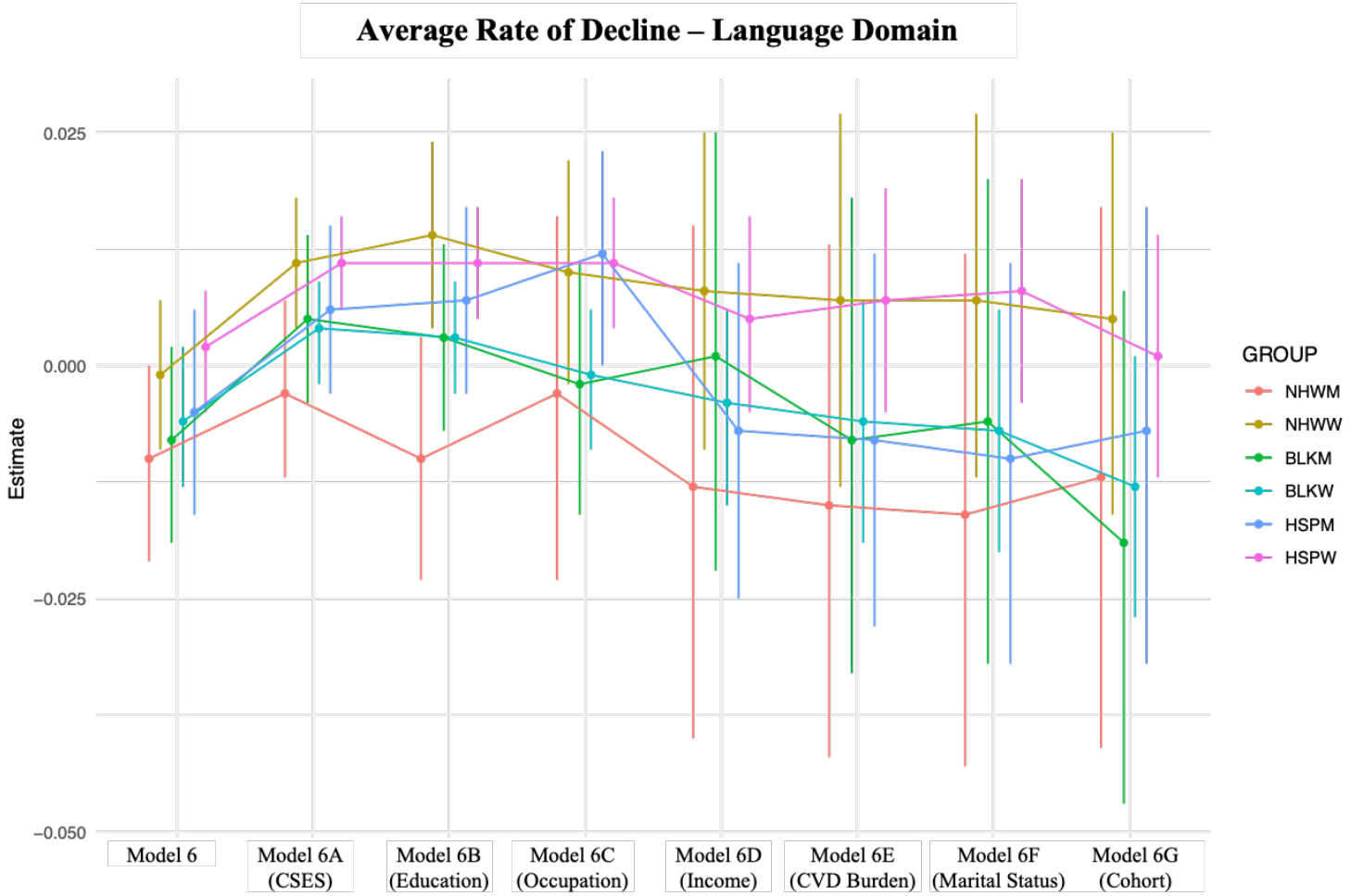


Figure 19. Differences in Average Rate of Decline in Visuo-Spatial Performance from Models 6 through 6G Across Sex/Gender Subgroups

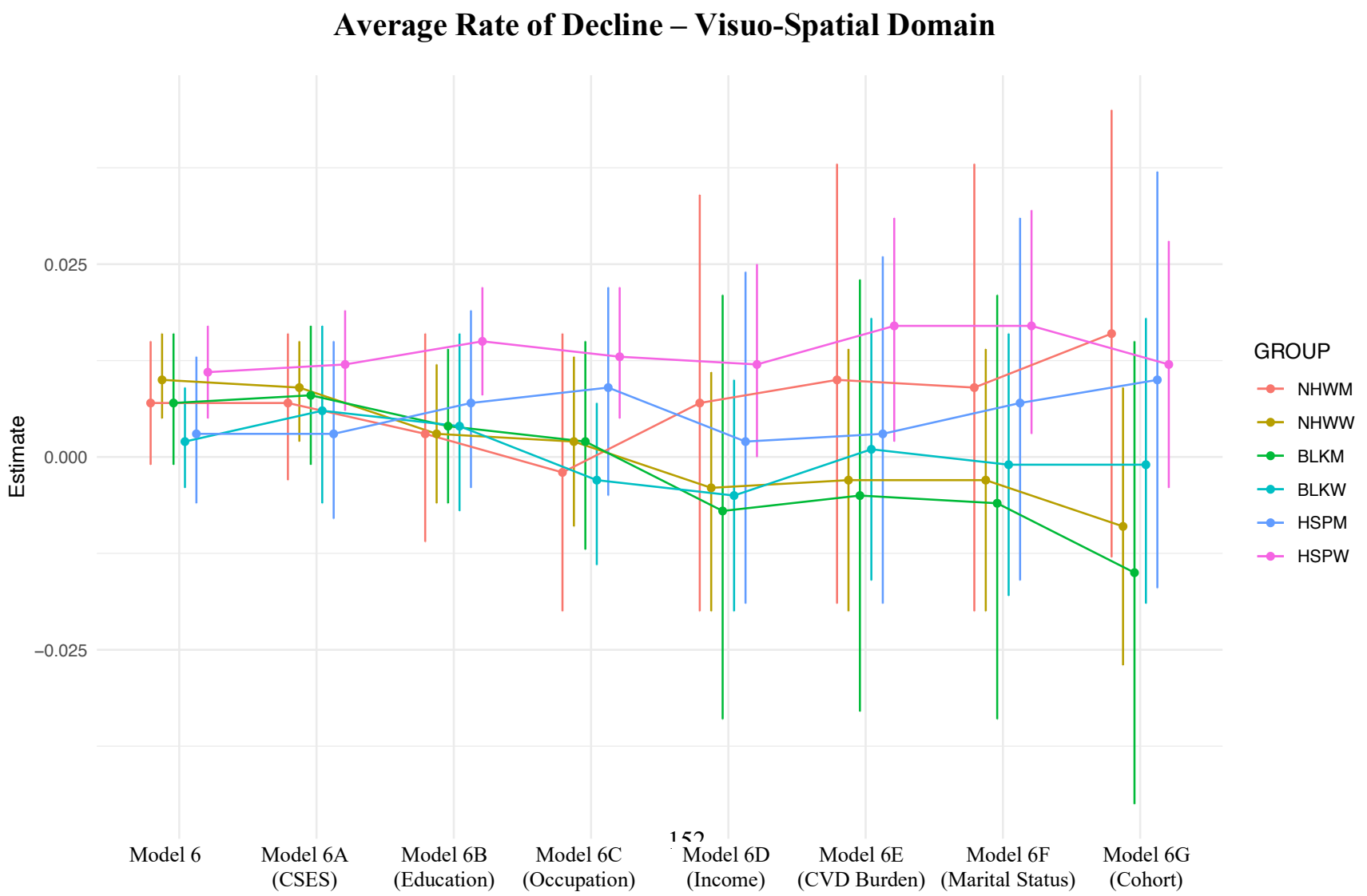


Figure 20. Survival Curves from the Cox Regression Models for Dementia Conversion Across Sex/Gender by Racial/Ethnic Subgroups

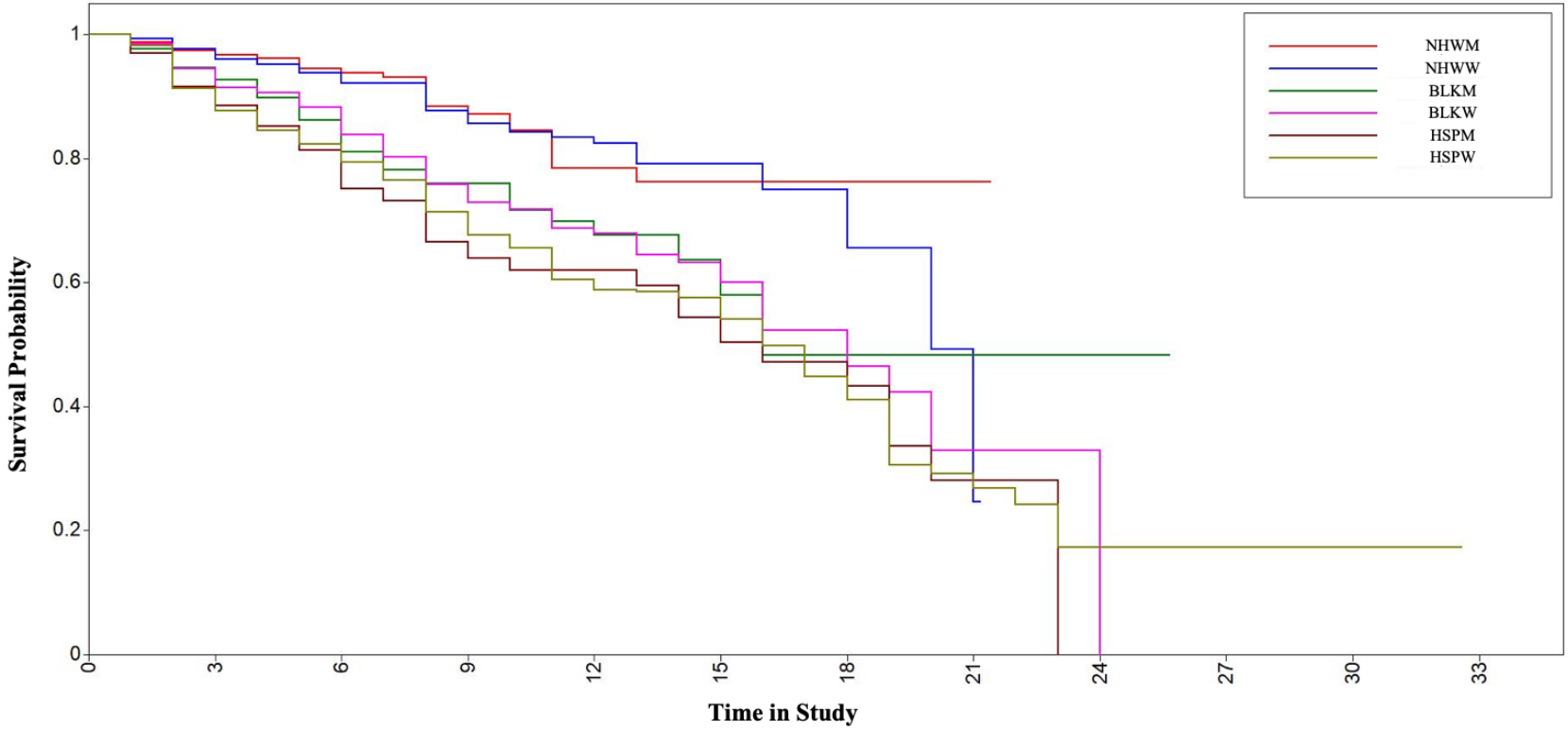


Figure 21. Comparison of Survival Curves Between the Cox Regression Model and Competing Risk Model for Dementia Conversion Across Sex/Gender by Racial/Ethnic Subgroups

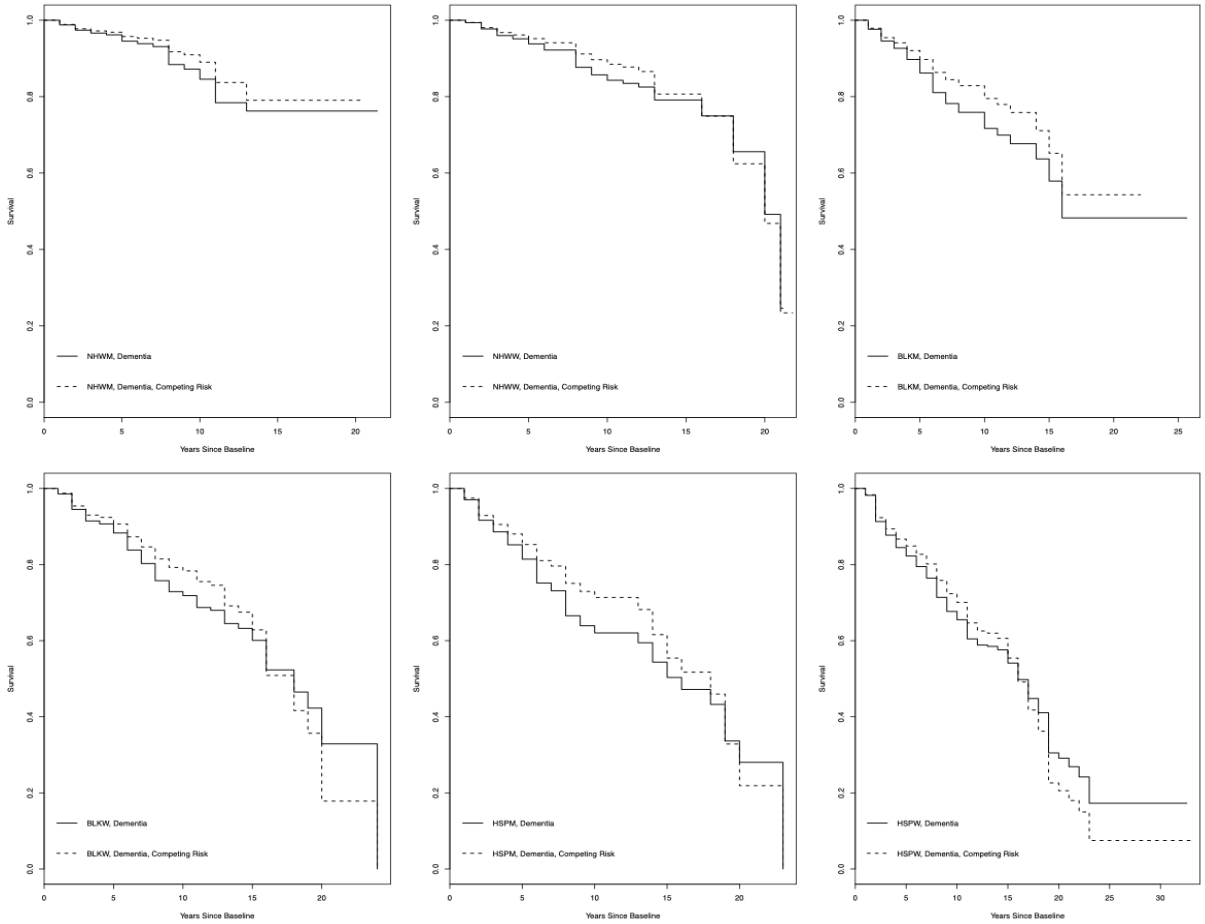


Table 1

Characteristics of Sample Used in Aim 1 Across Sex/Gender by Racial/Ethnic Subgroups

Characteristics	**NHW Men (n = 554)**	**NHW Women (n = 876)**	**Black Men (n = 549)**	**Black Women (n = 1332)**	**Hispanic Men (n = 834)**	**Hispanic Women (n = 1912)**
Age, mean (SD)	75.7 (6.7)	77.2 (7.6)	75.4 (6.9)	77.3 (7.3)	76.4 (6.5)	76.6 (6.7)
Education, mean (SD)	14.2 (4.0)	13.4 (3.6)	10.9 (4.1)	11.3 (3.8)	7.0 (4.4)	6.5 (4.4)
English Language Administration, No. (%)	547 (99%)	864 (99%)	548 (99%)	1331 (99%)	47 (6%)	97 (5%)
Initial Diagnostic Status, No. (%)						
MCI	94 (17%)	149 (17%)	91 (17%)	200 (15%)	149 (18%)	360 (19%)
Dementia	22 (4%)	60 (7%)	64 (12%)	195 (15%)	116 (14%)	298 (16%)
Incident Dementia	35 (6%)	67 (7%)	55 (10%)	166 (13%)	126 (15%)	341 (18%)

Note. NHW = Non-Hispanic White; SD = Standard Deviation.

Table 2

Characteristics of Sample Used in Aims 2 through 4 Across Sex/Gender by Racial/Ethnic Subgroups

Characteristics	**NHW Men (n = 530)**	**NHW Women (n = 812)**	**Black Men (n = 483)**	**Black Women (n = 1127)**	**Hispanic Men (n = 714)**	**Hispanic Women (n = 1592)**
Age, mean (SD)	75.3 (6.3)	76.4 (7.2)	74.6 (6.4)	76.2 (6.6)	75.7 (6.1)	75.7 (6.2)
Childhood SES, mean (SD)	0.46 (0.7)	0.43 (0.7)	0.09 (0.6)	0.10 (0.5)	-0.38 (0.6)	-0.32 (0.6)
Education, mean (SD)	14.3 (3.9)	13.7 (3.5)	11.3 (3.9)	11.8 (3.5)	7.2 (4.4)	6.9 (4.4)
Occupational Status, No. (%)						
Unskilled/Semi-Skilled	82 (16)	154 (19)	213 (44)	482 (43)	495 (69)	1234 (78)
Skilled/Clerical	122 (23)	265 (33)	118 (24)	316 (28)	128 (18)	180 (11)
Professional/Managerial	304 (57)	358 (44)	124 (26)	295 (26)	70 (10)	118 (7)
Missing data	22 (4)	35 (4)	28 (6)	34 (3)	21 (3)	60 (4)
Monthly Income, No. (%)						
$750 and lower	40 (8)	111 (14)	105 (22)	331 (29)	304 (43)	957 (60)
$751to $1550	93 (17)	158 (20)	148 (31)	346 (31)	286 (40)	465 (29)
$1501 to $4000	182 (34)	266 (33)	157 (33)	292 (26)	75 (11)	92 (6)
$4000 and above	138 (26)	115 (14)	35 (7)	48 (4)	6 (1)	13 (1)
Missing data	77 (15)	162 (20)	38 (8)	110 (10)	43 (6)	65 (4)
CVD Count, mean (SD)	0.97 (0.9)	0.84 (0.8)	1.09 (0.9)	1.27 (0.9)	1.31 (1.0)	1.32 (0.9)

Hypertension, No (%)	364 (69)	529 (65)	338 (70)	946 (84)	548 (77)	1345 (85)
Diabetes, No (%)	91 (17)	108 (13)	106 (22)	327 (29)	250 (35)	556 (35)
Heart Disease, No (%)	249 (47)	278 (34)	145 (30)	410 (36)	275 (39)	493 (31)
Stroke, No (%)	11 (4)	23 (5)	19 (7)	37 (6)	19 (6)	45 (6)
Marital Status, No (%)						
Married	309 (58)	236 (29)	194 (40)	156 (14)	440 (62)	330 (21)
Widowed	60 (11)	320 (39)	109 (23)	560 (50)	100 (14)	600 (38)
Never married	100 (19)	139 (17)	80 (17)	169 (15)	32 (5)	162 (10)
Divorced	48 (9)	102 (13)	60 (12)	165 (15)	80 (11)	351 (22)
Separated	9 (2)	12 (2)	38 (8)	73 (7)	54 (8)	128 (8)
Missing data	4 (1)	2 (0)	2 (0)	4 (0)	8 (1)	21 (1)
Diagnostic Status, No. (%)						
MCI at Baseline	94 (18)	149 (18)	91 (19)	200 (18)	149 (21)	360 (23)
Incident Dementia	31 (6)	53 (6)	50 (10)	143 (13)	111 (11)	299 (19)
Baseline Factor Scores[a]						
Memory, mean (SD)	0.40 (0.7)	0.52 (0.7)	0.03 (0.7)	0.22 (0.7)	-0.08 (0.6)	0.04 (0.6)
Language, mean (SD)	0.75 (0.7)	0.68 (0.8)	0.25 (0.7)	0.16 (0.7)	-0.12 (0.6)	-0.16 (0.6)
Visuo-Spatial, mean (SD)	0.59 (0.4)	0.58 (0.4)	0.24 (0.5)	0.22 (0.6)	-0.10 (0.7)	-0.21 (0.7)

Note. NHW = Non-Hispanic White; SD = Standard Deviation; CVD = cardiovascular disease.
[a]Average baseline scores for the current sample are greater than zero because scores were normalized on the entire cohort that included individuals demented at baseline.

Table 3

Model Fit for Confirmatory Factor Analyses of the Three-Factor Model of Baseline Performance by Sex/Gender, Racial/Ethnic, and Sex/Gender by Racial/Ethnic Subgroup

	χ^2	df	CFI	RMSEA	(90% CI)
Sex/gender					
Men	235.00	40	0.980	0.050	0.044, 0.056
Women	665.58	40	0.973	0.062	0.058, 0.066
Race/Ethnicity					
NHW	181.17	40	0.978	0.050	0.042, 0.057
Black	276.29	40	0.976	0.056	0.050, 0.062
Hispanic	408.27	40	0.968	0.058	0.053, 0.063
Race/Ethnicity by Sex/Gender					
NHW Men	78.53	40	0.983	0.042	0.038, 0.055
NHW Women	133.59	40	0.978	0.052	0.042, 0.061
Black Men	96.40	40	0.977	0.051	0.048, 0.064
Black Women	222.04	40	0.976	0.058	0.051, 0.066
Hispanic Men	123.17	40	0.974	0.050	0.040, 0.060
Hispanic Women	336.18	40	0.965	0.062	0.056, 0.068

Table 4

Goodness-of-Fit Indices for the Invariance Models for the Factor Model across Sex/Gender Subgroups

Model	χ^2	df	CFI	RMSEA	(90% CI)	Δ RMSEA	Δ CFI
Configural Invariance	900.58	80	0.975	0.058	0.055, 0.062		
Metric Invariance	938.65	88	0.974	0.056	0.053, 0.060	-0.002	-0.001
Scalar Invariance	981.68	96	0.973	0.055	0.052, 0.059	-0.001	-0.001
Factor Variance Invariance	1034.82	99	0.971	0.056	0.053, 0.059	0.001	-0.002
Factor Covariance Invariance	1042.47	102	0.971	0.055	0.052, 0.058	-0.001	0.000

Table 5

Goodness-of-Fit Indices for the Invariance Models for the Factor Model across Racial/Ethnic Subgroups

Model	χ^2	df	CFI	RMSEA	(90% CI)	Δ RMSEA	Δ CFI
Configural Invariance	865.74	120	0.973	0.055	0.052, 0.059		
Metric Invariance	1256.24	136	0.960	0.064	0.061, 0.067	0.009	-0.013
Scalar Invariance	1819.49	152	0.940	0.074	0.071, 0.077	0.010	-0.020
Partial Scalar Invariance	1473.78	149	0.953	0.066	0.063, 0.069	0.002	-0.007
Factor Variance Invariance	2158.94	155	0.928	0.080	0.077, 0.083	0.014	-0.025
Partial Factor Variance Invariance	1548.78	151	0.950	0.068	0.065, 0.071	0.002	-0.003

Table 6

Goodness-of-Fit Indices for the Invariance Models for the Factor Model across Racial/Ethnic by Sex/gender Subgroups

Model	χ^2	df	CFI	RMSEA	(90% CI)	Δ RMSEA	Δ CFI
Configural Invariance	989.91	240	0.973	0.056	0.052, 0.059		
Metric Invariance	1417.83	280	0.959	0.063	0.060, 0.067	0.007	-0.014
Scalar Invariance	2056.52	320	0.938	0.073	0.071, 0.077	0.010	-0.021
Partial Scalar Invariance	1726.11	316	0.950	0.066	0.063, 0.070	0.003	-0.009
Factor Variance Invariance	2452.95	331	0.924	0.080	0.077, 0.083	0.014	-0.026
Partial Factor Variance Invariance	1873.96	327	0.945	0.068	0.065, 0.071	0.002	-0.005

Table 7

Fit of Most-Constrained Model (Factor Covariance Invariance) Across Time for Each Sex/Gender by Racial/Ethnic Subgroup

Models and Fit Indices	NHW Men	NHW Women	Black Men	Black Women	Hispanic Men	Hispanic Women
Time 1 vs Time 2						
χ^2 (df = 202)	353.87	411.44	389.04	549.59	454.96	961.95
CFI	0.973	0.978	0.965	0.979	0.962	0.959
RMSEA	0.037	0.034	0.041	0.036	0.039	0.044
(90 % CI)	(0.030, 0.043)	(0.030, 0.039)	(0.035, 0.047)	(0.032, 0.040)	(0.034, 0.043)	(0.042, 0.047)
Time 1 vs Time 3						
χ^2 (df = 202)	401.92	497.13	314.96	568.35	408.72	819.01
CFI	0.952	0.961	0.974	0.972	0.962	0.958
RMSEA	0.042	0.041	0.032	0.037	0.035	0.040
(90 % CI)	(0.036, 0.048)	(0.036, 0.045)	(0.025, 0.039)	(0.033, 0.040)	(0.030, 0.040)	(0.037, 0.043)
Time 1 vs Time 4						
χ^2 (df = 202)	374.92	449.36	321.47	510.33	340.68	668.36
CFI	0.946	0.959	0.965	0.971	0.969	0.961
RMSEA	0.039	0.037	0.033	0.034	0.029	0.035
(90 % CI)	(0.033, 0.045)	(0.033, 0.042)	(0.026, 0.039)	(0.030, 0.038)	(0.023, 0.034)	(0.032, 0.038)
Time 1 vs Time 5						
χ^2 (df = 216)	376.73	555.87	435.99	715.99	*	1141.65
CFI	0.942	0.935	0.927	0.946		0.915
RMSEA	0.037	0.042	0.043	0.042		0.047
(90 % CI)	(0.030, 0.043)	(0.038, 0.047)	(0.037, 0.049)	(0.038, 0.045)		(0.045, 0.050)

Table 8

Model Fit Statistics for the Latent Growth Models for Each Cognitive Domain Across the Entire Sample

	BIC's for Each Domain and Model		
Model	**Memory**	**Language**	**Visuo-Spatial**
Linear Slope	24345.63	16648.98	19368.95
Linear and Quadratic Slopes	24728.87	17395.43	20068.74
Linear Slope with Spline	24356.42	16626.73	19388.94

Table 9

Results of the Unconditional Multiple-Group Latent Growth Models for Each Cognitive Domain Across Sex/Gender Groups (Model 1)

Growth Parameters	Men		Women
Memory			
Intercept, mean (SE)	-0.079 (.016)		0.056 (.011)
Slope, mean (SE)	-0.021 (.003)		-0.026 (.002)
BIC		24374.08	
Language			
Intercept, mean (SE)	0.068 (.018)		-0.025 (.012)
Slope, mean (SE)	0.002 (.003)		0.006 (.002)
BIC		16675.79	
Visuo-Spatial			
Intercept, mean (SE)	0.040 (.015)		-0.036 (.012)
Slope, mean (SE)	0.012 (.002)		0.011 (.002)
BIC		19374.37	

Note. NHW = Non-Hispanic White; SE = Standard Error; BIC = Bayesian Information Criterion; Values reflect unstandardized estimates (standard error).

Table 10

Results of the Unconditional Multiple-Group Latent Growth Models for Each Cognitive Domain Across Racial/Ethnic Groups (Model 2)

Growth Parameters	NHW	Black	Hispanic
Memory			
Intercept, mean (SE)	0.342 (.018)	0.011 (.017)	-0.174 (.013)
Slope, mean (SE)	-0.019 (.004)	-0.029 (.004)	-0.024 (.003)
BIC		23840.34	
Language			
Intercept, mean (SE)	0.522 (.019)	0.018 (.017)	-0.311 (.012)
Slope, mean (SE)	0.003 (.003)	0.003 (.003)	0.008 (.003)
BIC		15428.75	
Visuo-Spatial			
Intercept, mean (SE)	0.430 (.011)	0.066 (.014)	-0.322 (.014)
Slope, mean (SE)	0.015 (.002)	0.008 (.003)	0.011 (.002)
BIC		17467.61	

Table 11

Results of the Unconditional Multiple-Group Latent Growth Models for Each Cognitive Domain Across Sex/Gender by Racial/Ethnic Groups (Model 3)

Growth Parameters	NHW Men	NHW Women	Black Men	Black Women	Hispanic Men	Hispanic Women
Memory						
Intercept, mean (SE)	0.243 (0.028)	0.407 (0.022)	-0.167 (0.029)	0.088 (0.020)	-0.253 (0.023)	-0.140 (0.015)
Slope, mean (SE)	-0.025 (0.006)	-0.015 (0.005)	-0.023 (0.007)	-0.031 (0.004)	-0.018 (0.005)	-0.026 (0.003)
BIC	23982.67					
Language						
Intercept, mean (SE)	0.546 (0.030)	0.507 (0.026)	0.037 (0.031)	0.010 (0.020)	-0.277 (0.024)	-0.326 (0.014)
Slope, mean (SE)	0.000 (0.005)	0.005 (0.004)	0.003 (0.005)	0.004 (0.003)	0.006 (0.006)	0.008 (0.003)
BIC	15695.50					
Visuo-Spatial						
Intercept, mean (SE)	0.421 (0.018)	0.437 (0.014)	0.055 (0.024)	0.071 (0.017)	-0.259 (0.024)	-0.350 (0.018)
Slope, mean (SE)	0.013 (0.003)	0.015 (0.003)	0.015 (0.004)	0.005 (0.003)	0.008 (0.004)	0.012 (0.003)
BIC	17645.52					

Table 12

Results of Cox Regression Analyses for Death, Controlling for Age, Across Sex/Gender by Racial/Ethnic Subgroups

	Reference Group					
	NHW Men	**NHW Women**	**Black Men**	**Black Women**	**Hispanic Men**	**Hispanic Women**
	hOR [95% CI]	hOR [95% CI]	hOR [95% CI]	hOR [95% CI]	hOR [95% CI]	hOR [95% CI]
NHW Men		**1.36 [1.14, 1.61]**	0.93 [0.77, 1.12]	**1.18 [1.00, 1.38]**	1.17 [0.98, 1.39]	**1.87 [1.59, 2.19]**
NHW Women	**0.74 [0.62, 0.88]**		**0.69 [0.58, 0.82]**	0.87 [0.75, 1.00]	0.86 [0.73, 1.01]	**1.38 [1.19, 1.59]**
Black Men	1.08 [0.89, 1.30]	**1.46 [1.23, 1.74]**		**1.27 [1.08, 1.49]**	**1.26 [1.05, 1.50]**	**2.01 [1.71, 2.36]**
Black Women	**0.85 [0.73, 0.99]**	1.15 [0.99, 1.34]	**0.79 [0.67, 0.93]**		0.99 [0.85, 1.15]	**1.59 [1.39, 1.81]**
Hispanic Men	0.86 [0.72, 1.02]	1.16 [0.98, 1.37]	**0.80 [0.67, 0.95]**	1.01 [0.87, 1.17]		**1.60 [1.38, 1.86]**
Hispanic Women	**0.54 [0.46, 0.63]**	**0.73 [0.63, 0.84]**	**0.50 [0.42, 0.59]**	**0.63 [0.55, 0.72]**	**0.63 [0.54, 0.73]**	
Baseline age	**1.88 [1.72, 2.07]**	**1.88 [1.72, 2.07]**	**1.88 [1.72, 2.07]**	**1.88 [1.72, 2.07]**	**1.88 [1.72, 2.07]**	**1.88 [1.72, 2.07]**

Note. Each column represents a separate Cox Regression Model with the group bolded at the top row the reference group. hOR = Hazards odds ratio; CI = Confidence interval.

Table 13

Average Number of Years from Baseline Each Group Was Seen at Each Time Point

	NHW Men	**NHW Women**	**Black Men**	**Black Women**	**Hispanic Men**	**Hispanic Women**
Time 1	0	0	0	0	0	0
Time 2	2.12	2.14	2.03	2.07	2.18	2.14
Time 3	4.27	4.42	3.99	4.14	4.26	4.15
Time 4	6.93	6.96	6.34	6.59	6.39	6.57
Time 5	9.62	9.53	8.79	8.91	8.56	8.99

Note. Time 1 = Baseline visit.

Table 14

Follow-Up Life Table Summarizing Selective Attrition During the Study Across Sex/Gender by Racial/Ethnic Groups

Interval	Entering Interval	Lost to Follow-Up	Number at Risk	Dead	Proportion Dead	Proportion Survive	Survival Probability
NHW Men							
0 to 2	530	126	467	47	0.10	0.90	0.90
3 to 5	357	82	316	60	0.19	0.81	0.73
6 to 8	215	41	194.5	53	0.27	0.73	0.53
9 to 11	121	34	104	45	0.43	0.57	0.30
12 to 14	42	14	35	23	0.66	0.34	0.10
15 to 17	5	0	5	2	0.49	0.60	0.06
18 to 20	3	0	3	3	1.00	0.00	0.00
NHW Women							
0 to 2	812	217	703.5	49	.07	.93	.93
3 to 5	546	121	485.5	61	.13	.87	.81
6 to 8	364	86	321	90	.28	.72	.59
9 to 11	188	58	159	56	.35	.65	.38
12 to 14	74	31	58.5	24	.41	.59	.22
15 to 17	19	1	18.5	15	.81	.19	.04
18 to 20	3	0	3	2	.67	.33	.01
Black Men							
0 to 2	483	144	411	46	.11	.89	.89
3 to 5	293	62	262	56	.21	.79	.70
6 to 8	175	25	162.5	49	.30	.70	.49
9 to 11	101	26	88	38	.43	.57	.28
12 to 14	37	9	32.5	17	.52	.48	.13
15 to 17	11	0	11	9	.82	.18	.02
18 to 20	2	0	2	1	.50	.50	.01
Black Women							

0 to 2	1127	294	980	78	.08	.92	.92
3 to 5	755	169	670.5	125	.19	.81	.75
6 to 8	461	111	405.5	109	.27	.73	.55
9 to 11	241	79	201.5	74	.37	.63	.35
12 to 14	88	14	81	48	.59	.41	.14
15 to 17	26	2	25	16	.64	.36	.05
18 to 20	8	0	8	7	.88	.13	.01
Hispanic Men							
0 to 2	714	187	620.5	65	.10	.90	.90
3 to 5	462	149	387.5	56	.14	.86	.77
6 to 8	257	58	228	69	.30	.70	.53
9 to 11	130	22	119	37	.31	.69	.37
12 to 14	71	16	63	35	.56	.44	.16
15 to 17	20	2	19	12	.63	.37	.06
18 to 20	6	0	6	5	.83	.17	.01
Hispanic Women							
0 to 2	1592	466	1359	85	.06	.94	.94
3 to 5	1041	327	877.5	99	.11	.89	.83
6 to 8	615	174	528	79	.15	.85	.71
9 to 11	362	109	307.5	72	.23	.77	.54
12 to 14	181	49	156.5	65	.42	.58	.32
15 to 17	67	2	66	38	.58	.42	.13
18 to 20	27	0	27	20	.74	.26	.03

Note. Number Entering Interval = Number of participants alive at the beginning of the time interval; Lost to Follow-Up = Number of those lost to follow-up during interval (death or non-death drop-out); Number at Risk = (Number of those event free – number of participants censored) / 2; Dead = Number of deaths during interval; Proportion Dead = Number of participants who died / Number at Risk; Survival Probability = Proportion surviving past the interval.

Table 15

Results of Unconditional Multiple-Group Joint Models for Each Cognitive Domain Across Sex/Gender Groups (Model 4)

Growth Parameters	Men		Women
Memory			
Intercept, mean (SE)	-0.066 (.017)		0.059 (.012)
Slope, mean (SE)	-0.035 (.004)		-0.035 (.003)
Intercept on Death, hOR [95% CI]	0.860 [0.69, 1.03]		0.865 [0.73, 1.00]
Slope on Death, hOR [95% CI]	0.342 [0.22, 0.46]		0.391 [0.26. 0.52]
BIC		41498.01	
Language			
Intercept, mean (SE)	0.070 (.020)		-0.044 (.013)
Slope, mean (SE)	-0.008 (.004)		-0.002 (.002)
Intercept on Death, hOR [95% CI]	0.836 [0.72, 0.95]		0.758 [0.68, 0.85]
Slope on Death, hOR [95% CI]	0.174 [0.05, 0.29]		0.231 [0.09, 0.37]
BIC		33641.85	
Visuo-Spatial			
Intercept, mean (SE)	0.050 (.016)		-0.049 (.013)
Slope, mean (SE)	0.007 (.003)		0.009 (.002)
Intercept on Death, hOR [95% CI]	1.20 [0.92, 1.48]		1.07 [0.88, 1.26]
Slope on Death, hOR [95% CI]	0.119 [-0.05, 0.29]		0.154 [-0.01, 0.32]
BIC		36759.62	

Table 16

Results of Unconditional Multiple-Group Joint Models for Each Cognitive Domain Across Racial/Ethnic Groups (Model 5)

Growth Parameters	NHW	Black	Hispanic
Memory			
Intercept, mean (SE)	0.347 (.019)	0.010 (.018)	-0.170 (.013)
Slope, mean (SE)	-0.028 (.004)	-0.038 (.004)	-0.035 (.003)
Intercept on Death, hOR [95% CI]	0.672 [0.51, 0.84]	0.653 [0.52, 0.79]	0.904 [0.69, 1.12]
Slope on Death, hOR [95% CI]	0.503 [0.27, 0.74]	0.463 [0.32, 0.62]	0.298 [0.16, 0.43]
BIC		44944.66	
Language			
Intercept, mean (SE)	0.491 (.021)	-0.003 (.019)	-0.315 (.013)
Slope, mean (SE)	-0.005 (.004)	-0.007 (.003)	0.000 (.003)
Intercept on Death, hOR [95% CI]	0.691 [0.01, 1.37]	0.683 [-0.36, 1.72]	0.776 [0.77, 0.78]
Slope on Death, hOR [95% CI]	0.278 [-0.55, 1.10]	0.144 [-0.33, 0.62]	0.149 [-0.59, 0.89]
BIC		36718.91	
Visuo-Spatial			
Intercept, mean (SE)	0.417 (.012)	0.057 (.015)	-0.330 (.016)
Slope, mean (SE)	0.009 (.002)	0.004 (.003)	0.009 (.003)
Intercept on Death, hOR [95% CI]	0.581 [0.40, 0.76]	0.858 [0.59, 1.12]	1.25 [0.77, 1.72]
Slope on Death, hOR [95% CI]	0.180 [0.01, 0.35]	0.133 [-0.09, 0.35]	0.101 [-0.10, 0.31]
BIC		39546.14	

Table 17

Results of Unconditional Multiple-Group Joint Models for Each Cognitive Domain Across Sex/Gender by Racial/Ethnic Groups (Model 6)

Growth Parameters	NHW Men	NHW Women	Black Men	Black Women	Hispanic Men	Hispanic Women
Memory						
Intercept, mean (SE)	0.252 (0.03)	0.412 (0.02)	-0.184 (0.03)	0.091 (0.02)	-0.231 (0.03)	-0.144 (0.02)
Slope, mean (SE)	-0.035 (0.01)	-0.024 (0.01)	-0.034 (0.01)	-0.040 (0.01)	-0.035 (0.01)	-0.035 (0.00)
Intercept on Death, hOR [95% CI]	0.91 [0.51, 1.31]	0.56 [0.41, 0.72]	0.53 [0.36, 0.68]	0.74 [0.55, 0.93]	1.03 [0.67, 1.39]	0.88 [0.62, 1.13]
Slope on Death, hOR [95% CI]	0.44 [0.05, 0.83]	0.51 [0.31, 0.72]	0.49 [0.29, 0.68]	0.44 [0.26, 0.62]	0.24 [0.12, 0.36]	0.34 [0.16, 0.51]
BIC			50571.42			
Language						
Intercept, mean (SE)	0.533 (0.03)	0.489 (0.03)	0.032 (0.03)	0.001 (0.02)	-0.241 (0.03)	-0.329 (0.02)
Slope, mean (SE)	-0.001 (0.00)	0.011 (0.00)	0.004 (0.00)	0.002 (0.00)	0.005 (0.00)	0.011 (0.00)
Intercept on Death, hOR [95% CI]	0.91 [0.67, 1.15]	0.57 [0.46, 0.68]	0.65 [0.47, 0.83]	0.67 [0.53, 0.81]	0.87 [0.63, 1.10]	0.68 [0.49, 0.86]
Slope on Death, hOR [95% CI]	0.18 [0.02, 0.34]	0.39 [0.11, 0.66]	0.13 [0.03, 0.23]	0.17 [0.01, 0.33]	0.12 [0.12, 0.36]	0.16 [0.01, 0.30]
BIC			42439.34			
Visuo-Spatial						
Intercept, mean (SE)	0.412 (0.02)	0.420 (0.02)	0.060 (0.03)	0.054 (0.02)	-0.240 (0.03)	-0.370 (0.02)
Slope, mean (SE)	0.007 (0.00)	0.010 (0.00)	0.007 (0.01)	0.002 (0.00)	0.003 (0.01)	0.011 (0.00)
Intercept on Death, hOR [95% CI]	0.72 [0.35, 1.09]	0.50 [0.31, 0.69]	0.94 [0.53, 1.35]	0.78 [0.46, 1.11]	1.58 [0.82, 2.34]	0.99 [0.66, 1.33]
Slope on Death, hOR [95% CI]	0.16 [-0.10, 0.41]	0.22 [0.01, 0.45]	0.07 [-0.05, 0.19]	0.22 [-0.38, 0.82]	0.08 [-0.11, 0.27]	0.17 [-0.11, 0.45]
BIC			45237.33			

Table 18

Results of Unconditional Multiple-Group Joint Models, Accounting for Both Death and Non-Death Drop-Out, for Each Cognitive Domain Across Sex/Gender Groups (Model 7)

Growth Parameters	Men	Women
Memory		
Intercept, mean (SE)	-0.072 (.016)	0.062 (.011)
Slope, mean (SE)	-0.031 (.004)	-0.035 (.003)
Intercept on Death, hOR [95% CI]	0.974 [0.81, 1.14]	0.982 [0.84, 1.12]
Slope on Death, hOR [95% CI]	0.579 [0.38, 0.78]	0.554 [0.37. 0.73]
BIC	42492.15	
Language		
Intercept, mean (SE)	0.068 (.018)	-0.024 (.012)
Slope, mean (SE)	-0.007 (.004)	-0.001 (.003)
Intercept on Death, hOR [95% CI]	0.989 [0.89, 1.09]	1.06 [0.98, 1.15]
Slope on Death, hOR [95% CI]	0.675 [-0.42, 1.77]	1.19 [-0.40, 2.79]
BIC	39930.10	
Visuo-Spatial		
Intercept, mean (SE)	0.044 (.015)	-0.033 (.012)
Slope, mean (SE)	0.008 (.003)	0.008(.002)
Intercept on Death, hOR [95% CI]	2.24 [0.26, 5.73]	2.73 [0.76, 6.21]
Slope on Death, hOR [95% CI]	0.002 [-0.01, 0.02]	0.001 [-0.01, 0.01]
BIC	41767.88	

Table 19

Results of Unconditional Multiple-Group Joint Models, Accounting for Both Death and Non-Death Drop-Out, for Each Cognitive Domain Across Racial/Ethnic Groups (Model 8)

Growth Parameters	NHW	Black	Hispanic
Memory			
Intercept, mean (SE)	0.345 (.018)	0.015 (.017)	-0.166 (.013)
Slope, mean (SE)	-0.024 (.005)	-0.035 (.004)	-0.037 (.004)
Intercept on Death, hOR [95% CI]	0.850 [0.67, 1.03]	0.857 [0.69, 1.02]	1.04 [0.83, 1.24]
Slope on Death, hOR [95% CI]	0.758 [0.44, 1.08]	0.669 [0.43, 0.91]	0.419 [0.25, 0.59]
BIC		50946.20	
Language			
Intercept, mean (SE)	0.522 (.019)	0.018 (.017)	-0.312 (.012)
Slope, mean (SE)	-0.006 (.004)	-0.005 (.004)	0.001 (.004)
Intercept on Death, hOR [95% CI]	1.02 [0.89, 1.15]	1.01 [0.89, 1.13]	1.04 [0.91, 1.16]
Slope on Death, hOR [95% CI]	1.18 [0.06, 2.43]	1.26 [0.08, 2.61]	0.918 [0.20, 1.64]
BIC		43253.84	
Visuo-Spatial			
Intercept, mean (SE)	0.427 (.011)	0.069 (.014)	-0.320 (.015)
Slope, mean (SE)	0.018 (.003)	0.005 (.003)	0.009 (.003)
Intercept on Death, hOR [95% CI]	0.346 [0.08, 0.77]	3.62 [0.91, 8.15]	4.22 [0.27, 9.57]
Slope on Death, hOR [95% CI]	1.19 [0.23, 3.53]	0.000 [-0.01, 0.01]	0.001 [-0.01, 0.01]
BIC		44979.05	

Table 20

Results of Unconditional Multiple-Group Joint Models, Accounting for Both Death and Non-Death Drop-Out, for Each Cognitive Domain Across Sex/Gender by Racial/Ethnic Groups (Model 9)

Growth Parameters	NHW Men	NHW Women	Black Men	Black Women	Hispanic Men	Hispanic Women
Memory						
Intercept, mean (SE)	0.247 (0.03)	0.411 (0.02)	-0.157 (0.03)	0.090 (0.02)	-0.249 (0.02)	-0.130 (0.02)
Slope, mean (SE)	-0.030 (0.01)	-0.021 (0.05)	-0.039 (0.01)	-0.035 (0.01)	-0.026 (0.01)	-0.043 (0.00)
Intercept on Death, hOR [95% CI]	0.99 [0.50, 1.50]	0.80 [0.60, 1.00]	1.02 [0.63, 1.41]	0.85 [0.66, 1.04]	1.01 [0.75, 1.28]	1.16 [0.83, 1.48]
Slope on Death, hOR [95% CI]	0.71 [0.08, 1.49]	0.73 [0.39, 1.07]	0.35 [0.10, 0.60]	0.79 [0.47, 1.10]	0.62 [0.33, 0.90]	0.29 [0.14, 0.45]
BIC	50410.81					
Language						
Intercept, mean (SE)	0.544 (0.03)	0.508 (0.03)	0.036 (0.03)	0.010 (0.02)	-0.277 (0.02)	-0.327 (0.01)
Slope, mean (SE)	-0.011 (0.01)	-0.003 (0.01)	-0.012 (0.01)	-0.001 (0.01)	-0.001 (0.01)	0.000 (0.01)
Intercept on Death, hOR [95% CI]	1.24 [0.97, 1.51]	0.94 [0.79, 1.10]	0.85 [0.66, 1.03]	1.09 [0.94, 1.25]	1.01 [0.80, 1.25]	1.02 [0.85, 1.19]
Slope on Death, hOR [95% CI]	0.32 [0.09, 0.56]	0.45 [0.11, 0.79]	0.19 [0.204, 0.35]	0.63 [0.09, 1.18]	0.49 [0.23, 0.75]	0.33 [0.05, 0.61]
BIC	49823.75					
Visuo-Spatial						
Intercept, mean (SE)	0.421 (0.02)	0.432 (0.01)	0.060 (0.03)	0.072 (0.02)	-0.259 (0.02)	-0.348 (0.02)
Slope, mean (SE)	0.017 (0.00)	0.017 (0.00)	0.010 (0.00)	0.004 (0.00)	0.008 (0.01)	0.010 (0.00)
Intercept on Death, hOR [95% CI]	0.35 [0.17, 0.86]	0.25 [0.08, 0.59]	0.54 [0.05, 0.95]	0.12 [0.09, 0.31]	2.76 [0.16, 5.36]	0.87 [0.22, 0.95]
Slope on Death, hOR [95% CI]	0.81 [0.04, 1.93]	0.73 [0.25, 1.41]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.01 [-0.02, 0.03]	0.00 [0.00, 0.00]
BIC	51514.07					

Table 21

Results of Conditional Multiple-Group Joint Models for the Memory Domain Across Sex/Gender by Racial/Ethnic Groups (Model 6G)

Growth Parameters	NHW Men	NHW Women	Black Men	Black Women	Hispanic Men	Hispanic Women
Memory						
Intercept, mean (SE)	-0.081 (0.10)	0.019 (0.07)	-0.164 (0.09)	-0.034 (0.06)	-0.250 (0.08)	-0.007 (0.05)
Slope, mean (SE)	-0.060 (0.02)	-0.042 (0.02)	-0.064 (0.02)	-0.067 (0.01)	-0.059 (0.02)	-0.030 (0.01)
Covariates on Intercept						
Childhood SES	0.022 (0.03)	-0.043 (0.03)	0.084 (0.05)	0.024 (0.03)	-0.023 (0.03)	0.008 (0.02)
Education	0.032 (0.01)**	0.032 (0.01)**	0.046 (0.01)**	0.029 (0.01)**	0.027 (0.01)**	0.032 (0.01)**
Occupation	0.062 (0.05)	0.055 (0.04)	0.016 (0.05)	0.083 (0.03)*	0.019 (0.04)	0.015 (0.03)
Income	0.049 (0.01)**	0.044 (0.01)**	0.024 (0.01)*	0.035 (0.01)**	0.041 (0.01)**	0.025 (0.01)*
Marital Status	-0.070 (0.06)	0.041 (0.05)	-0.099 (0.01)	0.060 (0.06)	0.099 (0.05)	0.046 (0.04)
CVD Burden	-0.086 (0.03)*	0.014 (0.03)	-0.031 (0.04)	-0.051 (0.02)*	-0.041 (0.02)	-0.044 (0.02)*
Cohort	-0.212 (0.07)*	-0.119 (0.06)*	-0.229 (0.07)**	-0.152 (0.05)*	-0.118 (0.05)*	-0.072 (0.04)*
Covariates on Slope						
Childhood SES	0.011 (0.01)*	0.006 (0.01)	-0.007 (0.01)	-0.006 (0.01)	0.0 (0.01)	0.0 (0.0)
Education	0.0 (0.0)	0.004 (0.0)	0.003 (0.0)	0.002 (0.0)	-0.002 (0.0)	0.0 (0.0)
Occupation	-0.001 (0.0)	0.005 (0.01)	-0.001 (0.01)	0.011 (0.01)	0.018 (0.01)*	0.008 (0.01)
Income	0.001 (0.0)	0.001 (0.0)	-0.001 (0.0)	0.002 (0.0)	0.004 (0.0)	0.001 (0.0)
Marital Status	0.0 (0.01)	0.020 (0.01)*	0.019 (0.01)	0.001 (0.01)	-0.015 (0.01)	-0.006 (0.01)
CVD Burden	0.005 (0.01)	0.0 (0.0)	0.019 (0.01)*	0.0 (0.0)	0.002 (0.01)	-0.001 (0.0)
Cohort	0.015 (0.02)	-0.015 (0.01)	0.003 (0.02)	0.014 (0.01)	0.012 (0.01)	0.002 (0.01)
Intercept on Death, hOR [95% CI]	0.89 [0.57, 1.21]	**0.56 [0.42, 0.70]**	**0.50 [0.33, 0.66]**	**0.70 [0.53, 0.87]**	**0.77 [0.54, 0.99]**	0.83 [0.61, 1.06]
Slope on Death, hOR [95% CI]	0.60 [0.15, 1.04]	**0.60 [0.42, 0.78]**	**0.51 [0.29, 0.73]**	**0.43 [0.27, 0.60]**	**0.32 [0.19, 0.45]**	**0.35 [0.18, 0.52]**
BIC			50754.61			

** $p < .05$. ** $p < .001$.*

Table 22

Results of Conditional Multiple-Group Joint Models for the Language Domain Across Sex/Gender by Racial/Ethnic Groups (Model 6G)

Growth Parameters	NHW Men	NHW Women	Black Men	Black Women	Hispanic Men	Hispanic Women
Language						
Intercept, mean (SE)	-0.314 (0.10)	-0.356 (0.07)	-0.242 (0.09)	-0.437 (0.05)	-0.134 (0.08)	-0.142 (0.04)
Slope, mean (SE)	-0.011 (0.01)	0.005 (0.01)	-0.019 (0.01)	-0.014 (0.02)	-0.007 (0.01)	0.001 (0.00)
Covariates on Intercept						
Childhood SES	0.021 (0.03)	-0.003 (0.03)	0.025 (0.05)	0.023 (0.03)	0.043 (0.03)	0.042 (0.02)
Education	0.043 (0.01)**	0.054 (0.01)**	0.069 (0.01)**	0.044 (0.01)**	0.044 (0.01)**	0.059 (0.0)**
Occupation	0.043 (0.05)	0.153 (0.04)**	0.110 (0.05)*	0.163 (0.03)**	0.143 (0.04)**	0.035 (0.03)
Income	0.078 (0.01)**	0.063 (0.01)**	0.051 (0.01)**	0.047 (0.01)**	0.019 (0.01)	0.022 (0.01)*
Marital Status	-0.094 (0.06)	0.005 (0.05)	-0.063 (0.06)	0.017 (0.05)	0.017 (0.05)	0.018 (0.03)
CVD Burden	-0.069 (0.03)*	0.008 (0.03)	-0.040 (0.03)	-0.045 (0.02)*	-0.061 (0.02)*	-0.046 (0.02)**
Cohort	0.143 (0.08)	0.059 (0.06)	-0.181 (0.06)*	0.093 (0.04)*	-0.017 (0.05)	0.014 (0.03)
Covariates on Slope						
Childhood SES	0.002 (0.0)	0.003 (0.0)	0.005 (0.01)	-0.003 (0.0)	-0.001 (0.01)	-0.003 (0.0)
Education	0.003 (0.0)	-0.002 (0.0)	0.00 (0.0)	-0.001 (0.0)	0.0 (0.0)	0.0 (0.0)
Occupation	-0.009 (0.01)	0.005 (0.01)	0.010 (0.01)	0.006 (0.0)	0.012 (0.01)*	-0.002 (0.01)
Income	0.001 (0.0)	0.00 (0.0)	-0.002 (0.0)	0.0 (0.0)	0.004 (0.0)	0.001 (0.0)
Marital Status	0.010 (0.01)	0.009 (0.01)	0.010 (0.01)	0.005 (0.01)	0.004 (0.01)	-0.007 (0.01)
CVD Burden	0.002 (0.01)	0.001 (0.0)	0.008 (0.01)	0.001 (0.0)	0.002 (0.0)	-0.001 (0.0)
Cohort	-0.011 (0.01)	0.007 (0.01)	0.022 (0.01)*	0.016 (0.01)*	-0.004 (0.01)	0.013 (0.01)*
Intercept on Death, hOR [95% CI]	1.13 [0.80, 1.46]	**0.64 [0.49, 0.80]**	0.82 [0.55, 1.08]	**0.76 [0.58, 0.94]**	0.88 [0.63, 1.13]	0.79 [0.54, 1.05]
Slope on Death, hOR [95% CI]	**0.22 [0.04, 0.41]**	0.74 [0.06, 1.42]	**0.13 [0.03, 0.24]**	**0.17 [0.02, 0.32]**	**0.19 [0.01, 0.37]**	**0.14 [0.01, 0.27]**
BIC			41449.63			

** p < .05. ** p < .001.*

Table 23

Results of Conditional Multiple-Group Joint Models for the Visuo-Spatial Domain Across Sex/Gender by Racial/Ethnic Groups (Model 6G)

Growth Parameters	NHW Men	NHW Women	Black Men	Black Women	Hispanic Men	Hispanic Women
Visuo-Spatial						
Intercept, mean (SE)	0.043 (0.06)	0.085 (0.05)	-0.042 (0.07)	-0.254 (0.05)	-0.198 (0.08)	-0.145 (0.05)
Slope, mean (SE)	0.014 (0.02)	-0.009 (0.01)	-0.016 (0.01)	-0.001 (0.01)	0.013 (0.01)	0.012 (0.01)
Covariates on Intercept						
Childhood SES	0.025 (0.02)	0.003 (0.02)	0.046 (0.04)	0.008 (0.02)	0.068 (0.03)*	0.029 (0.02)
Education	0.027 (0.01)**	0.014 (0.01)*	0.054 (0.01)**	0.030 (0.01)**	0.046 (0.01)**	0.075 (0.01)**
Occupation	-0.041 (0.03)	0.059 (0.03)*	-0.009 (0.03)	0.088 (0.03)**	0.041 (0.04)	0.013 (0.03)
Income	0.037 (0.01)**	0.027 (0.01)**	0.019 (0.01)*	0.037 (0.01)**	0.028 (0.01)*	0.027 (0.01)*
Marital Status	-0.020 (0.04)	0.002 (0.03)	-0.013 (0.05)	-0.044 (0.04)	0.066 (0.05)	0.058 (0.04)
CVD Burden	-0.014 (0.02)	0.024 (0.02)	-0.031 (0.03)	-0.040 (0.02)*	-0.061 (0.05)*	-0.064 (0.02)**
Cohort	0.040 (0.05)	0.013 (0.04)	-0.038 (0.06)	0.094 (0.04)*	0.065 (0.05)	0.041 (0.04)
Covariates on Slope						
Childhood SES	0.0 (0.0)	0.001 (0.0)	-0.007 (0.01)	-0.003 (0.0)	-0.005 (0.01)	0.003 (0.0)
Education	0.001 (0.0)	0.002 (0.0)	0.001 (0.0)	0.0 (0.0)	0.002 (0.0)	0.0 (0.0)
Occupation	0.007 (0.01)	0.001 (0.01)	0.005 (0.01)	0.007 (0.0)	-0.003(0.01)	0.004 (0.01)
Income	-0.001 (0.0)	0.00 (0.0)	0.002 (0.0)	0.0 (0.0)	0.002 (0.0)	0.0 (0.0)
Marital Status	0.006 (0.01)	-0.001 (0.01)	-0.005 (0.01)	0.018 (0.01)*	-0.011 (0.01)	-0.002 (0.01)
CVD Burden	-0.003 (0.0)	0.0 (0.0)	-0.001 (0.0)	-0.004 (0.0)	0.001 (0.0)	-0.004 (0.0)
Cohort	-0.012 (0.01)	0.006 (0.01)	0.016 (0.01)	0.001 (0.01)	-0.005 (0.01)	0.011 (0.01)
Intercept on Death, hOR [95% CI]	0.70 [0.28, 1.12]	**0.51 [0.29, 0.73]**	0.98 [0.55, 1.42]	**0.76 [0.54, 0.98]**	1.18 [0.67, 1.69]	0.98 [0.70, 1.26]
Slope on Death, hOR [95% CI]	**0.16 [-0.16, 0.49]**	**0.733 [-0.06, 0.72]**	**0.06 [-0.07, 0.18]**	**0.08 [-0.11, 0.27]**	0.21 [-0.99, 1.41]	**0.07 [-0.12, 0.26]**
BIC			45237.33			

** p < .05. ** p < .001.*

Table 24

Relationship Between Death and Socio-Cultural/Health Indicators for the Conditional Multiple-Group Joint Models for Each Cognitive Domain Across Sex/Gender by Racial/Ethnic Groups (Model 6G)

Growth Parameters	NHW Men	NHW Women	Black Men	Black Women	Hispanic Men	Hispanic Women
Covariates on Death, hOR [95% CI]						
Memory						
Childhood SES	1.07 [0.88, 1.25]	0.98 [0.85, 1.12]	1.08 [0.88, 1.28]	1.03 [0.86, 1.21]	1.02 [0.86, 1.18]	0.83 [0.61, 1.06]
Education	0.99 [0.95, 1.04]	0.99 [0.94, 1.03]	0.98 [0.93, 1.02]	1.01 [0.97, 1.05]	0.97 [0.93, 1.01]	**0.35 [0.18, 0.52]**
Occupation	0.98 [0.73, 1.23]	1.02 [0.83, 1.21]	1.02 [0.79, 1.24]	0.97 [0.78, 1.17]	**1.70 [1.25. 2.15]**	1.04 [0.89, 1.18]
Income	**0.94 [0.88, 0.99]**	0.96 [0.92, 1.00]	**0.93 [0.88, 0.99]**	1.00 [0.95, 1.06]	1.06 [0.98, 1.14]	0.98 [0.95, 1.01]
Marital Status	0.94 [0.64, 1.24]	**0.74 [0.51, 0.98]**	1.23 [0.83, 1.63]	0.88 [0.61, 1.16]	0.82 [0.57, 1.07]	1.11 [0.86, 1.37]
CVD Burden	**1.30[1.05, 1.55]**	**1.43 [1.24, 1.63]**	**1.31 [1.07, 1.56]**	1.14 [0.99, 1.29]	**1.25 [1.05, 1.45]**	0.96 [0.89, 1.03]
Cohort	1.33 [0.83, 1.83]	0.90 [0.66, 1.15]	0.93 [0.64, 1.23]	1.00 [0.74, 1.26]	1.44 [0.98, 1.89]	0.85 [0.61, 1.09]
Language						
Childhood SES	1.01 [0.83, 1.19]	0.99 [0.87, 1.12]	1.21 [0.87, 1.54]	1.02 [0.82, 1.23]	1.01 [0.81, 1.21]	0.99 [0.85, 1.13]
Education	1.03 [0.97, 1.09]	0.98 [0.93, 1.03]	0.94 [0.87, 1.02]	0.97 [0.93, 1.01]	0.99 [0.94, 1.04]	0.99 [0.95, 1.03]
Occupation	0.84 [0.59, 1.09]	1.03 [0.84, 1.22]	1.26 [0.86, 1.66]	1.04 [0.81, 1.26]	1.17 [0.82, 1.51]	0.96 [0.70, 1.21]
Income	0.94 [0.88, 1.01]	0.96 [0.92, 1.01]	**0.89 [0.82, 0.97]**	0.99 [0.94, 1.05]	1.09 [0.99, 1.19]	0.97 [0.89, 1.04]
Marital Status	1.11 [0.71, 1.52]	**0.67 [0.47, 0.87]**	1.42 [0.85, 1.99]	0.90 [0.55, 1.25]	1.00 [0.65, 1.35]	0.80 [0.55, 1.05]
CVD Burden	**1.30 [1.04, 1.60]**	**1.41 [1.22, 1.59]**	**1.35 [1.04, 1.66]**	**1.19 [1.02, 1.36]**	**1.25 [1.04, 1.47]**	**1.27 [1.08, 1.47]**
Cohort	0.98 [0.54, 1.43]	1.09 [0.79, 1.38]	1.55 [0.88, 2.22]	1.24 [0.86, 1.61]	1.28 [0.79, 1.77]	1.34 [0.96, 1.71]
Visuo-Spatial						
Childhood SES	1.00 [0.79, 1.21]	0.99 [0.85, 1.12]	0.87 [0.49, 1.25]	0.97 [0.70, 1.25]	0.92 [0.63, 1.22]	1.10 [0.84, 1.36]
Education	1.02 [0.96, 1.09]	0.99 [0.93, 1.04]	0.98 [0.87, 1.09]	0.98 [0.92, 1.05]	0.99 [0.89, 1.09]	0.99 [0.93, 1.05]
Occupation	1.07 [0.72, 1.43]	0.99 [0.79, 1.19]	1.13 [0.63, 1.63]	1.14 [0.78, 1.49]	1.31 [0.79, 1.83]	1.10 [0.69, 1.51]
Income	**0.91 [0.83, 0.99]**	0.96 [0.91, 1.01]	0.96 [0.84, 1.08]	0.98 [0.90, 1.06]	1.04 [0.91, 1.18]	0.93 [0.83, 1.03]
Marital Status	1.06 [0.65, 1.46]	**0.66 [0.46, 0.85]**	1.00 [0.41, 1.59]	1.34 [0.50, 2.18]	0.79 [0.24, 1.35]	0.89 [0.51, 1.27]
CVD Burden	1.22 [0.93, 1.50]	**1.45 [1.24, 1.66]**	1.10 [0.81, 1.40]	1.05 [0.83, 1.28]	1.28 [0.97, 1.58]	1.15 [0.91, 1.39]
Cohort	0.99 [0.47, 1.49]	1.25 [0.84, 1.66]	1.66 [0.53, 2.79]	0.97 [0.56, 1.38]	1.29 [0.52, 2.06]	1.36 [0.71, 2.01]

Table 25

Results of Conditional Multiple-Group Latent Growth Model for the Memory Domain Across Sex/Gender by Racial/Ethnic Groups (Model 3G)

Growth Parameters	NHW Men	NHW Women	Black Men	Black Women	Hispanic Men	Hispanic Women
Memory						
Intercept, mean (SE)	-0.042 (.107)	0.006 (.066)	-0.164 (.080)	-0.014 (.054)	-0.275 (.074)	0.007 (.042)
Slope, mean (SE)	-0.050 (.022)	-0.032 (.016)	-0.047 (.023)	-0.061 (.011)	-0.042 (.014)	-0.032 (.009)
Covariates on Intercept						
Childhood SES	0.029 (.029)	-0.034 (.023)	0.088 (.041)	0.003 (.029)	-0.027 (.025)	0.002 (.017)
Education	0.035 (.009)**	0.028 (.009)**	0.048 (.010)**	0.030 (.008)**	0.025 (.006)**	0.031 (.004)**
Occupation	0.060 (.053)	0.047 (.036)	0.000 (.041)	0.067 (.032)*	0.017 (.040)	0.017 (.028)
Income	0.042 (.017)*	0.048 (.009)**	0.023 (.011)*	0.032 (.0009)**	0.041 (.011)**	0.022 (.008)*
Marital Status	-0.092 (.060)	0.010 (.048)	-0.088 (.058)	0.053 (.054)	0.085 (.048)	0.027 (.034)
CVD Burden	-0.100 (.033)*	0.044 (.032)	-0.017 (.038)	-0.057 (.028)*	-0.029 (.024)	-0.050 (.016)**
Cohort	-0.191 (.074)*	-0.144 (.058)*	-0.218 (.065)**	-0.149 (.045)**	-0.138 (.051)*	-0.071 (.034)*
Covariates on Slope						
Childhood SES	0.011 (.005)*	0.006 (.005)	-0.001 (.008)	-0.005 (.006)	0.003 (.006)	0.001 (.004)
Education	0.000 (.001)	0.004 (.002)	0.003 (.003)	0.002 (.002)	-0.001 (.001)	0.000 (.001)
Occupation	-0.002 (.010	0.007 (.008)	0.000 (.010)	0.010 (.008)	0.019 (.008)*	0.010 (.006)
Income	0.001 (.03)	0.000 (.002)	-0.003 (.003)	0.001 (.002)	0.003 (.002)	0.000 (.002)
Marital Status	0.001 (.011)	0.021 (.009)*	0.023 (.014)	0.001 (.011)	-0.010 (.010)	-0.005 (.008)
CVD Burden	0.005 (.006)	-0.002 (.005)	0.020 (.007)*	0.003 (.004)	0.002 (.005)	0.001 (.003)
Cohort	0.015 (.015)	-0.013 (.012)	0.007 (.018)	0.016 (.010)	0.019 (.010)	0.006 (.007)
BIC			23941.16			

** $p < .05$. ** $p < .001$.*

Table 26

Results of Conditional Multiple-Group Latent Growth Model for the Language Domain Across Sex/Gender by Racial/Ethnic Groups (Model 3G)

Growth Parameters	NHW Men	NHW Women	Black Men	Black Women	Hispanic Men	Hispanic Women
Language						
Intercept, mean (SE)	-0.326 (.096)	-0.385 (.067)	-0.216 (.079)	-0.452 (.048)	-0.172 (.074)	-0.190 (.037)
Slope, mean (SE)	-0.010 (.015)	-0.003 (.011)	-0.012 (.013)	-0.011 (.007)	-0.004 (.013)	0.002 (.007)
Covariates on Intercept						
Childhood SES	0.041 (.028)	-0.004 (.028)	0.049 (.054)	0.022 (.026)	0.043 (.025)	0.033 (.016)*
Education	0.044 (.009)**	0.052 (.008)**	0.069 (.009)**	0.043 (.007)**	0.046 (.006)**	0.057 (.004)**
Occupation	0.025 (.047)	0.132 (.037)**	0.093 (.038)*	0.160 (.027)**	0.118 (.033)**	0.060 (.025)*
Income	0.077 (.012)**	0.072 (.010)**	0.043 (.010)**	0.044 (.007)**	0.021 (.010)*	0.026 (.007)**
Marital Status	-0.114 (.055)*	-0.050 (.048)	-0.053 (.054)	0.007 (.042)	0.026 (.043)	0.004 (.029)
CVD Burden	-0.060 (.031)	0.010 (.026)	-0.041 (.032)	-0.041 (.020)*	-0.063 (.022)*	-0.042 (.014)*
Cohort	0.154 (.078)*	0.045 (.060)	-0.149 (.061)*	0.100 (.040)*	-0.022 (.051)	0.013 (.029)
Covariates on Slope						
Childhood SES	0.002 (.004)	0.002 (.003)	0.008 (.005)	-0.004 (.004)	-0.001 (.005)	0.001 (.004)
Education	0.003 (.001)*	-0.002 (.001)	-0.001 (.001)	-0.001 (.001)	0.000 (.001)	-0.002 (.003)
Occupation	-0.008 (.008)	0.005 (.005)	0.013 (.006)*	0.004 (.004)	-0.010 (.007)	0.000 (.001)
Income	0.001 (.002)	0.000 (.001)	-0.002 (.002)	0.000 (.001)	0.004 (.002)*	-0.003 (.005)
Marital Status	0.010 (.009)	0.010 (.006)	0.010 (.008)	0.005 (.007)	0.003 (.008)	-0.001 (.002)
CVD Burden	0.001 (.005)	0.000 (.003)	0.009 (.004)*	0.001 (.003)	0.002 (.004)	0.000 (.001)
Cohort	0.013 (.011)	0.006 (.008)	0.014 (.010)	0.015 (.006)*	-0.006 (.010)	0.013 (.005)*
BIC			14155.17			

** $p < .05$. ** $p < .001$.*

Table 27

Results of Conditional Multiple-Group Latent Growth Model for the Visuo-Spatial Domain Across Sex/Gender by Racial/Ethnic Groups (Model 3G)

Growth Parameters	NHW Men	NHW Women	Black Men	Black Women	Hispanic Men	Hispanic Women
Visuo-Spatial						
Intercept, mean (SE)	0.031 (0.06)	0.067 (0.05)	-0.062 (0.07)	-0.237 (0.05)	-0.199 (0.07)	-0.151 (0.05)
Slope, mean (SE)	0.027 (0.01)	-0.002 (0.01)	-0.009 (0.02)	0.000 (0.01)	0.016 (0.01)	0.014 (0.01)
Covariates on Intercept						
Childhood SES	0.028 (0.02)	0.009 (0.02)	0.053 (0.03)	0.005 (0.02)	0.070 (0.03)*	0.018 (0.02)
Education	0.027 (0.01)**	0.012 (0.01)*	0.048 (0.01)**	0.030 (0.01)**	0.045 (0.01)**	0.075 (0.01)**
Occupation	-0.047 (0.03)	0.068 (0.02)*	0.008 (0.03)	0.075 (0.03)**	0.040 (0.04)	0.030 (0.03)
Income	0.040 (0.01)**	0.030 (0.01)**	0.025 (0.01)*	0.034 (0.01)**	0.033 (0.01)**	0.027 (0.01)*
Marital Status	-0.030 (0.04)	-0.012 (0.03)	-0.040 (0.05)	-0.019 (0.04)	0.056 (0.05)	0.049 (0.04)
CVD Burden	-0.014 (0.03)	0.026 (0.02)	-0.043 (0.03)	-0.035 (0.02)*	-0.070 (0.02)**	-0.067 (0.02)**
Cohort	0.040 (0.05)	0.004 (0.04)	-0.048 (0.05)	0.091 (0.04)*	0.039 (0.05)	0.052 (0.04)
Covariates on Slope						
Childhood SES	0.0 (0.0)	0.000 (0.0)	-0.006 (0.01)	-0.004 (0.0)	-0.005 (0.01)	0.003 (0.0)
Education	0.001 (0.0)	0.002 (0.0)	0.001 (0.0)	0.00 (0.0)	0.002 (0.0)	0.000 (0.0)
Occupation	0.007 (0.01)	0.000 (0.0)	0.003 (0.01)	0.008 (0.0)	-0.002(0.01)	0.003 (0.01)
Income	-0.003 (0.0)	0.000 (0.0)	0.001 (0.0)	0.00 (0.0)	0.001 (0.0)	-0.001 (0.0)
Marital Status	0.008 (0.01)	-0.001 (0.01)	-0.003 (0.01)	0.017 (0.01)*	-0.012 (0.01)	-0.001 (0.01)
CVD Burden	-0.001 (0.01)	0.001 (0.0)	-0.001 (0.0)	-0.003 (0.0)	0.002 (0.01)	-0.003 (0.0)
Cohort	-0.007 (0.01)	0.017 (0.01)*	0.016 (0.01)	0.002 (0.01)	-0.003 (0.01)	0.011 (0.01)
BIC				16707.02		

** $p < .05$. ** $p < .001$.*

Table 28

Results of Cox Regression Analyses for Dementia Conversion, Controlling for Age, Across Sex/Gender by Racial/Ethnic Subgroups

	Reference Group					
	NHW Men	**NHW Women**	**Black Men**	**Black Women**	**Hispanic Men**	**Hispanic Women**
	hOR [95% CI]	hOR [95% CI]	hOR [95% CI]	hOR [95% CI]	hOR [95% CI]	hOR [95% CI]
NHW Men		1.03 [0.66, 1.61]	**0.49 [0.31, 0.76]**	**0.50 [0.34, 0.74]**	**0.35 [0.24, 0.53]**	**0.38 [0.26, 0.55]**
NHW Women	0.97 [0.62, 1.51]		**0.47 [0.32, 0.69]**	**0.48 [0.35, 0.67]**	**0.34 [0.25, 0.47]**	**0.37 [0.27, 0.49]**
Black Men	**2.06 [1.31, 3.22]**	**2.12 [1.44, 3.13]**		1.03 [0.75, 1.42]	0.72 [0.52, 1.01]	0.78 [0.58, 1.05]
Black Women	**1.99 [1.35, 2.94]**	**2.06 [1.51, 2.83]**	0.97 [0.70, 1.34]		**0.70 [0.55, 0.90]**	**0.76 [0.62, 0.93]**
Hispanic Men	**2.84 [1.91, 4.23]**	**2.93 [2.11, 4.07]**	1.38 [0.99, 1.93]	**1.42 [1.11, 1.82]**		1.08 [0.86, 1.34]
Hispanic Women	**2.64 [1.82, 3.82]**	**2.73 [2.03, 3.65]**	1.28 [0.95, 1.73]	**1.32 [1.08, 1.61]**	0.93 [0.75, 1.16]	
Baseline age	**2.90 [2.46, 3.42]**	**2.90 [2.46, 3.42]**	**2.90 [2.46, 3.42]**	**2.90 [2.46, 3.42]**	**2.90 [2.46, 3.42]**	**2.90 [2.46, 3.42]**

Note. Each column represents a separate Cox Regression Model with the group bolded at the top row the reference group. hOR = Hazards odds ratio; CI = Confidence interval.

Table 29

Results of the Multiple-Group Cox Regression Model for Dementia Conversion Across Sex/Gender by Racial/Ethnic Subgroups (Model 10)

	NHWM	NHWW	BLKM	BLKW	HISPM	HISPW
	hOR [95% CI]	hOR [95% CI]	hOR [95% CI]	hOR [95% CI]	hOR [95% CI]	hOR [95% CI]
CSES	1.04 [0.58, 1.50]	0.97 [0.66, 1.27]	0.83 [0.44, 1.21]	0.95 [0.68, 1.22]	1.06 [0.84, 1.29]	1.05 [0.89, 1.21]
Education	1.01 [0.89, 1.12]	0.88 [0.75, 1.00]	**0.92 [0.85, 0.99]**	**0.93 [0.88, 0.97]**	**0.93 [0.97, 0.98]**	**0.93 [0.89, 0.95]**
Occupation	0.79 [0.41, 1.17]	0.89 [0.51, 1.26]	0.73 [0.36, 1.09]	0.85 [0.61, 1.09]	0.92 [0.55, 1.28]	1.18 [0.86, 1.49]
Income	**0.86 [0.73, 0.98]**	0.93 [0.81, 1.05]	**0.87 [0.76, 0.97]**	**0.91 [0.83, 0.98]**	**0.86 [0.76, 0.95]**	**0.94 [0.88, 1.01]**
CVD Burden	1.12 [0.62, 1.63]	1.14 [0.82, 1.46]	0.78 [0.46, 1.09]	**1.28 [1.09, 1.48]**	1.02 [0.81, 1.23]	**1.24 [1.09, 1.39]**
Marital Status	1.16 [0.32, 2.00]	**0.55 [0.12, 0.98]**	1.64 [0.53, 2.74]	1.34 [0.75, 1.93]	1.32 [0.77, 1.86]	1.06 [0.75, 1.38]
Baseline age	**1.09 [1.04, 1.15]**	**1.12 [1.08, 1.16]**	**1.09 [1.05, 1.13]**	**1.11 [1.08, 1.14]**	**1.09 [1.06, 1.12]**	**1.11 [1.09, 1.13]**

Note. hOR = Hazards odds ratio; CI = Confidence interval.

Table 30

Results of the Multiple-Group Cox Regression Model for Death Across Sex/Gender by Racial/Ethnic Subgroups (Model 11)

	NHWM	NHWW	BLKM	BLKW	HISPM	HISPW
	hOR [95% CI]	hOR [95% CI]	hOR [95% CI]	hOR [95% CI]	hOR [95% CI]	hOR [95% CI]
CSES	1.04 [0.90, 1.18]	1.02 [0.88, 1.16]	1.11 [0.89, 1.34]	1.09 [0.93, 1.25]	1.03 [0.88, 1.17]	0.98 [0.86, 1.10]
Education	1.01 [0.98, 1.04]	0.98 [0.93, 1.03]	0.97 [0.92, 1.02]	0.98 [0.95, 1.01]	0.98 [0.95, 1.02]	0.99 [0.97, 1.02]
Occupation	1.03 [0.82, 1.24]	0.99 [0.83, 1.16]	0.91 [0.69, 1.12]	0.93 [0.77, 1.07]	**1.30 [1.01, 1.60]**	0.93 [0.67, 1.19]
Income	**0.93 [0.89, 0.98]**	**0.95 [0.91, 0.98]**	**0.93 [0.88, 0.98]**	0.98 [0.94, 1.02]	1.02 [0.96, 1.09]	0.96 [0.89, 1.02]
CVD Burden	**1.22 [1.02, 1.42]**	**1.38 [1.19, 1.57]**	1.16 [0.97, 1.34]	**1.19 [1.06, 1.31]**	**1.26 [1.10, 1.42]**	1.25 [1.09, 1.41]
Marital Status	0.96 [0.72, 1.20]	0.81 [0.59, 1.04]	1.16 [0.55, 2.77]	0.90 [0.71, 1.27]	0.97 [0.69, 1.25]	1.06 [0.79, 1.32]
Baseline age	**1.09 [1.07, 1.11]**	**1.06 [1.04, 1.08]**	**1.09 [1.05, 1.13]**	**1.07 [1.05, 1.08]**	**1.04 [1.02, 1.07]**	**1.09 [1.07, 1.10]**

Note. hOR = Hazards odds ratio; CI = Confidence interval.

Table 31

Results of the Cox Regression and Competing Risk Models Across Sex/Gender by Racial/Ethnic Subgroups

	NHWM	NHWW	BLKM	BLKW	HISPM	HISPW
Cox Regression						
Baseline age	1.11 [1.05, 1.18]	1.16 [1.11, 1.20]	1.08 [1.04, 1.13]	1.12 [1.09, 1.15]	1.08 [1.05, 1.11]	1.11 [1.09, 1.13]
Education	0.95 [0.87, 1.03]	0.85 [0.77, 0.93]	0.86 [0.81, 0.92]	0.88 [0.85, 0.92]	0.89 [0.85, 0.94]	0.92 [0.89, 0.95]
Cause-Specific						
Baseline age	1.08 [1.02, 1.14]	1.13 [1.09, 1.17]	1.07 [1.03, 1.12]	1.09 [1.06, 1.12]	1.06 [1.03, 1.10]	1.09 [1.07, 1.11]
Education	0.95 [0.88, 1.03]	0.85 [0.78, 0.93]	0.89 [0.84, 0.95]	0.88 [0.85, 0.93]	0.89 [0.85, 0.94]	0.93 [0.90, 0.96]
Subdistribution						
Baseline age	1.04 [0.98, 1.10]	1.08 [1.04, 1.12]	1.05 [1.01, 1.09]	1.05 [1.02, 1.08]	1.04 [1.01, 1.07]	1.05 [1.03, 1.07]
Education	0.95 [0.88, 1.03]	0.87 [0.80, 0.95]	0.90 [0.85, 0.96]	0.89 [0.85, 0.94]	0.89 [0.85, 0.94]	0.94 [0.91, 0.96]

Note. hOR = Hazards odds ratio; CI = Confidence interval.