October 2023

Gender Differences in Episodic Memory in Later Life: The Mediating Role of Education

Sara Robinson
University of South Florida

Gender Differences in Episodic Memory in Later Life: The Mediating Role of Education

by

Sara Robinson

A thesis defense submitted in partial fulfillment
of the requirements for the degree of
Master of Science in Public Health
Department of Epidemiology and Biostatistics
College of Public Health
University of South Florida

Co-Major Professor: Judith Rijnhart, M.Sc., Ph.D.
Co-Major Professor: Jason L. Salemi, M.P.H, Ph.D.
Hongdao Meng, M.D., M.P.H., Ph.D.

Date of Approval:
October 20, 2023

Keywords: dementia, mediation analysis, sociodemographic factors, immediate recall, delayed recall

Acknowledgments

To the people who made this possible, I am so incredibly thankful. I have learned alongside the most incredible scholars. To Dr. Salemi, thank you for the countless hours you worked with me, and all I’ve learned from you. You inspired my love for epidemiology and taught me more than I could ever put into words. Dr. Rijnhart, thank you for being the most incredible mentor. In you, I have found a role model, a colleague, and a friend. To have had the opportunity to work with you, is something I will never take for granted. I sincerely look forward to all our future collaboration. And to Dr. Meng, thank you for your words of encouragement, assistance, and teaching me more about this important field of research.

To my friends and my family, thank you for being the most incredible support system, I would have never been able to do this without you. I am so incredibly lucky for the people in my life. You make every day beautiful.

Table of Contents

List of Tables

List of Figures

Abstract

In the United States (U.S.), 14 million individuals aged 65+ are expected to be diagnosed with dementia by 2060, and women are nearly twice as likely to be diagnosed. Low education is a well-established risk factor for dementia and is hypothesized to partly explain the gender differences in late-life cognition. However, few studies have investigated education as a mediator of these gender differences. This study aims to investigate education as a mediator of gender differences in episodic memory using longitudinal data from the U.S. Health and Retirement Study (HRS). I used a sample of 35,721 respondents (20,190 women and 15,531 men) with episodic memory data available between 1998 and 2018 and data on self-reported education (median = 12, interquartile range = 12, 15). Analyses were adjusted for confounders (ethnicity, race, childhood SES, childhood immigration status, and birth year) and effect modification by race, ethnicity, childhood SES, and birth year was assessed. Episodic memory was measured as immediate and delayed recall. Linear and linear mixed-effects models were used to estimate the associations between gender and years of education and years of education and episodic memory. Education was a significant mediator of the association between gender and episodic memory. Race was an effect modifier of the association between gender and years of education, and race, ethnicity, and birth year were effect modifiers of the association between education and episodic memory. All direct and total effects were positive, indicating that women had higher episodic memory scores across all racial and ethnic groups for all birth years, both before and after adjustment for education. The indirect effects were negative in those who identified as

White and other race, indicating that women recalled fewer words in comparison to men, because they had fewer years of education. The indirect effects were positive in those who identified as Black and African American, indicating that women recalled more words in comparison to men, because they had more years of education. These findings indicate that the gender difference in episodic memory would have been larger if, on average, women had the same educational level as men, and this level of protectiveness varies across levels of race, ethnicity, and birth year.

Chapter One: Introduction

Background

Alzheimer's Disease and Related Dementias (ADRD) are characterized by impairments in memory, attention, communication, reasoning, judgement, and problem solving, resulting in significant changes in cognitive function and behavior (Centers for Disease Control and Prevention [CDC], 2019; Duong et al., 2017). Dementia is a growing global problem with the number of individuals affected by dementia worldwide increasing by 117% between 1990 and 2016 (GBD 2019 Dementia Forecasting Collaborators, 2022). To date, dementia affects approximately 57.4 million individuals worldwide and the prevalence rate is projected to increase to 152.8 million by 2050 (GBD 2019 Dementia Forecasting Collaborators, 2022). In the United States (U.S.) projections follow that of global concern, as research projects that nearly 14 million U.S. individuals aged 65+ will be diagnosed with dementia by 2060 (Beydoun et al., 2022; CDC, 2019). However, the actual prevalence may be higher, as dementia often remains undiagnosed, leading to underestimated statistics (Bennett et al., 2021). Due to the challenges associated with classifying and diagnosing dementia, several studies have utilized cognitive function, cognitive decline, or episodic memory as primary outcome measures (Clousten et al., 2019; Ding et al., 2019; Hale et al., 2021; Marden et al., 2016; Stern et al., 2020).

There is a significant gender gap in global incidence rates of dementia with a global female-to-male ratio of 1.69 in 2019 (GBD 2019 Dementia Forecasting Collaborators, 2022).

This gap is expected to persist through 2050, with an estimated global female-to-male ratio of 1.67 (GBD 2019 Dementia Forecasting Collaborators, 2022). In the U.S., females are nearly twice as likely as males to be affected by dementia (CDC, 2019). This gender difference may be partially attributed to varying life expectancies, as females in the U.S., have a longer average lifespan than males (Zarulli et al., 2018).

Above and beyond the impact of age, gender differences in later life cognition may also be driven by differences in educational attainment (Ford & Leist, 2021; Hale et al., 2020; Hasselgran et al., 2020; Rocca et al., 2014). On average, older women have lower levels of education than older men (Rocca et al., 2014). Moreover, numerous studies have emphasized the importance of education as a significant risk factor for the onset of dementia and cognitive decline (GBD 2019 Dementia Forecasting Collaborators, 2022; Hale et al., 2020; Langa et al., 2017; Walsemann & Ailshire, 2019). Education is hypothesized to be a proxy for cognitive reserve, which is defined as the adaptability of cognitive processes (Clousten et al., 2020; Stern et al., 2020). Individuals with higher levels of cognitive reserve may be better equipped to handle increased pathological insults on the brain and may therefore reach dementia thresholds later in life than those with lower levels of education (Mielke et al., 2014; Stern et al., 2020).

Understanding the potential mediating role of education in the association between gender and cognitive function could shed light on the underlying reasons for the widening gap between women and men in terms of dementia onset (Rouanet et al., 2021). Examining the aging population in the U.S. requires considering education rates within pivotal time periods. During the early-to-mid 1900s, men had more opportunities to pursue higher education than women, who faced legal restrictions, quotas, and administrative regulations (Mielke et al., 2014; Parker, 2015). Universities often accepted more male applicants, contributing to gender inequality in access to college education (Parker, 2015). Additionally, women held more domestic responsibilities; leading them to choose jobs that required less education (Parker, 2015). Consequently, women currently over 50, on average, have lower levels of education than men of the same age, increasing their risk of developing dementia (Mielke et al., 2015; Parker, 2015; Rouanet et al., 2021).

Previous Research and Gaps in Knowledge

Previous research has investigated the role of education as a mediator between gender and cognitive performance and dementia (Ford & Leist., 2021; Hasselgren et al., 2020). One study used data from South Korean adults aged 45-65 to examine whether education and occupation mediate the association between gender and cognitive performance (Ford & Leist, 2021). These authors used quantile regression decompositions and found evidence that education was a mediator of the gender differences in cognitive performance, as measured by differences in rates of educational attainment. Potential mechanism may include the fact that women had fewer opportunities throughout life to pursue formal education and therefore had less cognitive reserve, ceteris paribus. A Swedish study used data from two longitudinal cohorts of women, born in 1908, 1914, 1918, 1922, and 1930, and men born in 1930: the H70 Birth Cohort Study and the Prospective Populations Study of Women (Hasselgren et al., 2020) to examine whether education and psychological distress mediate the association between sex and dementia. This study did not find that education mediates the effect of sex on dementia.

Although these previous studies provide some first insights into the mediating role of education, they also have important limitations. Ford & Leist's (2021) use of cross-sectional data means that their effect estimates only reflect a difference in cognitive level, rather than cognitive decline. To assess whether education mediates sex differences in cognitive decline, longitudinal data are necessary. Furthermore, neither study investigated possible interactions with birth year, which is crucial to consider, given that gender differences in education have diminished over time (GBD 2019 Dementia Forecasting Collaborators, 2022). Finally, the extent to which the findings from studies on Swedish and South Korean elderly populations are generalizable to the U.S. context is uncertain. To better understand the heterogeneity of the mediation effect estimates within a population, it is important to investigate the impact of effect modifiers such as race, ethnicity, and childhood socioeconomic status (SES). By including childhood SES, race, and ethnicity, the size of the indirect effect of gender on cognitive functioning through education as a mediator of the association between gender and cognitive function may vary substantially between different levels of these effect modifiers.

Research Objectives and Hypotheses

To address the limitations in previous research, the aim of this project was to investigate education as a mediator of gender differences in cognitive functioning using longitudinal data from the U.S. Health and Retirement Study (HRS). I used repeated measurements of episodic memory to model cognitive functioning over time. Episodic memory was selected as a measure of cognitive performance, representing early risk for cognitive decline and dementia (Boraxbekk et al., 2015). Furthermore, I investigated birth year, race, ethnicity, and childhood SES as potential effect modifiers. Insight into effect modification by these factors will improve overall knowledge of the size of the indirect effect of gender on episodic memory through education across intersections of these factors.

The primary research hypothesis is that education will partially explain gender differences in episodic memory among middle-aged and older adults in the U.S, after controlling for sociodemographic factors. The secondary hypotheses are that the size of at least one of the pathways in the mediation model differs between levels of race, ethnicity, birth year, and childhood SES subgroups. The decision to include these variables as effect modifiers is further explained in the theoretical model section of this thesis.

Specifically, I hypothesized that the exposure-mediator effect will be largest for Hispanic individuals in comparison to White and Black and African American individuals, and that the gender differences in this subgroup may be more negative than those observed in White and Black and African American individuals. In Black American racial-ethnic groups, it is theorized that females have higher education, so the exposure-mediator effect may be more positive than those observed in Hispanic and White individuals (Diaz-Venegas et al., 2016). I also hypothesize that the exposure-mediator effect will be largest for individuals of low childhood SES, with larger gender differences observed as years of parental education decrease.

It is expected that higher education will be associated with better episodic memory, so the effect is positive (Ford & Leist, 2021; Hale et al., 2020; Hasselgran et al., 2020; Rocca et al., 2014). The effect of education on episodic memory might be less pronounced, so less positive, in historically marginalized racial-ethnic groups in comparison to White individuals. It is also hypothesized that the mediator-outcome effect will be largest for individuals of high childhood SES (Cha et al., 2021). Thus, the effect of education on episodic memory might be less pronounced, so less positive, as years of parental education decreases.

From these hypotheses, childhood SES, race, and ethnicity may modify both the exposure-mediator and mediator-outcome effects. As the years of parental education decrease, the gender difference in education increases, and the effect of education on episodic memory decreases. For those of historically minoritized racial-ethnic groups, the gender difference in education increases, and the effect of education on episodic memory decreases. Thus, it is unclear how the indirect effect will be influenced in the analyses considering both pathways may be affected across levels of the effect modifiers.

Chapter Two: Theoretical Model

Primary Variables

Education is hypothesized to mediate the association between gender and episodic memory. Specifically, women age ≥50 years on average have lower education than men age >50 years+, which can in turn affect their episodic memory. Recent studies have suggested that women may be at a higher risk for developing dementia than men. Investigating education as a mediator in this association may help to elucidate the reasons for this gender difference (GBD 2019 Dementia Forecasting Collaborators, 2022; Rouanet et al., 2021).

Confounding Variables

Using a life-course model, several variables can be identified as possible confounders of the relationship between education and episodic memory, as seen in Figure 1. These are race, ethnicity, childhood SES, birth year, childhood immigration status, childhood adversity, childhood learning problems, childhood health behavior, and childhood health (Gross et al., 2015; Hunt et al., 2017; Ma et al., 2021; McHutchison et al., 2017).

Health disparities are often associated with racial minorities and lower educational attainment (Diaz-Venegas et al., 2016; Gross et al., 2015). Additionally, people from historically minoritized racial-ethnic groups are at higher risk of developing dementia (Diaz-Venegas et al., 2016; Gross et al., 2015).

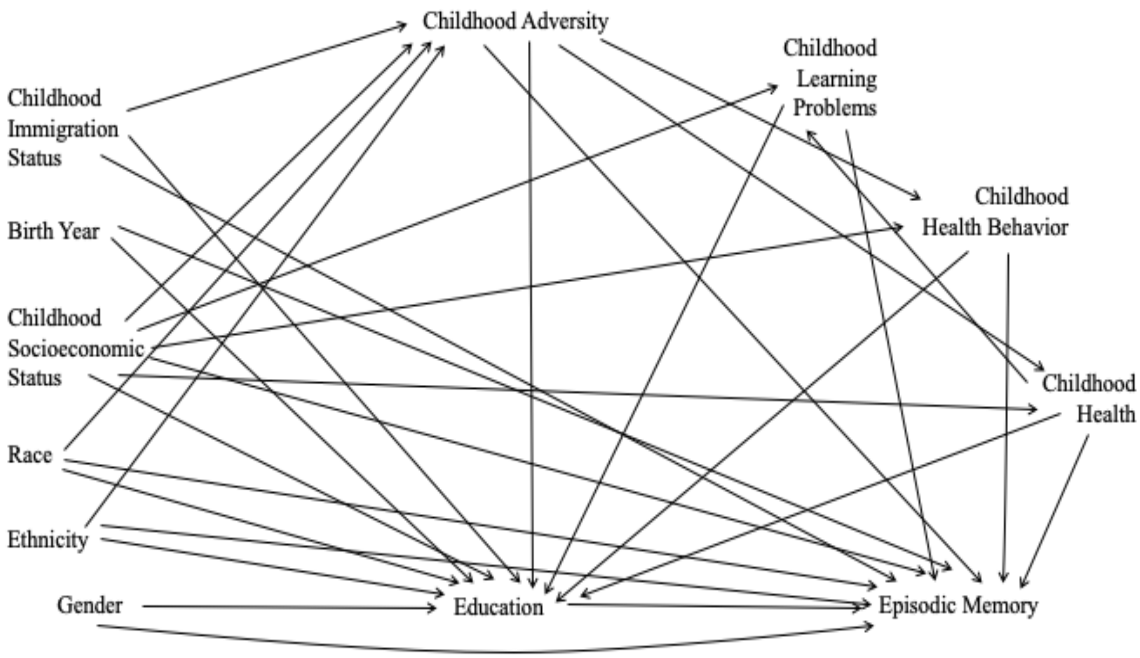

Figure 1: A directed acyclic graph (DAG) used to represent the assumed causal effects among the variables of interest

Low childhood SES is correlated with fewer years of schooling in children; low childhood SES is also associated with increased risk for cognitive decline later in life (Lindberg et al., 2021; McHutchison et al., 2017).

Year of birth is one of the most common predictors for cognitive decline, with the aging population significantly contributing to the increase in the prevalence of dementia (GBD 2019 Dementia Forecasting Collaborators, 2022). In older adult populations, years of education has been shown to be independently and positively associated with cognitive function (Fletcher et al., 2021; Peterson & Shakeel, 2022). The number of years of education increases as birth year increases; in general, older populations, those with an earlier birth year, are at higher risk of dementia and cognitive decline (Fletcher et al., 2021; Peterson & Shakeel, 2022).

Immigrant populations are negatively affected by the social determinants of health, including lower educational attainment; in addition, this population has poorer health outcomes, which may increase the risk of cognitive decline (Chang, 2019). Experiencing childhood adversities is correlated with lower educational attainment, as children who experience adversities are more likely to drop out of school earlier (Rockers et al., 2023). In addition, childhood adversities have been negatively associated with cognitive capability in later life (Ma et al., 2021). Childhood learning problems have been shown to pose a risk for education, with affected children experiencing difficulties attaining educational degrees (Aro et al., 2019). In addition, childhood learning problems were identified as significant predictors of cognitive performance (LaRue et al., 2008). Childhood health behavior, specifically drug or alcohol use, can result in decreased school attendance; children who suffer from health consequences of drug or alcohol use, may also suffer from decreased educational attainment (Reynolds et al., 2015). Childhood health behavior, specifically drug or alcohol use, has a relationship with lower cognitive performance in older age (Corley et al., 2012). There are also associations between childhood health and education, with the health of a child impacting education received (Aro et al., 2019). In addition, mental and physical health in childhood is associated with cognitive function and memory performance in later life (Wan et al., 2022; Wang et al., 2018).

These confounders may bias the association between education and cognitive performance, resulting in over- or under- estimation of the associations; therefore, adjusting for these variables is crucial for the mediation analyses. Considering sex was used as a proxy for gender, sex is randomly assigned at birth. Hence, no confounders were identified for the associations between gender and education, and gender and episodic memory.

Effect Modifiers

Birth year, race, ethnicity, and childhood SES may moderate the relationship between gender and education, and education and episodic memory. Gender disparities in education often lead to significant differences in years of educational attainment between men and women (Zeng et al., 2014; Diaz-Venegas et al., 2016). Furthermore, race and ethnicity can further compound these disparities (Diaz-Venegas et al., 2016; Zeng et al., 2014). Therefore, gender differences in educational attainment may differ across racial-ethnic groups (Diaz-Venegas et al., 2016; Zeng et al., 2014). Using data from HRS, one study found that, on average, White men had 13.8 years of education, Black men had 12.4 years of education, and Hispanic men had 10.4 years of education (Diaz-Venegas et al., 2016). In contrast, White women had an average of 13.5 years of education, Black women had 12.7 years of education, and Hispanic women had 9.8 years of education. Hence, the gender gap in educational attainment differed across racial-ethnic groups, with White and Hispanic men having higher educational attainment than White and Hispanic women, respectively. For Blacks, women had higher educational attainment than men. The gender gap in educational attainment was greatest in Hispanic individuals.

Childhood SES may also moderate the association between gender and education (Diaz-Venegas et al., 2016; Zeng et al., 2014). In childhood, gender differences in education are more prominent in those with low childhood SES (Amao & Gbadamosi, 2015; Cha et al., 2021). Using HRS data, one study measured how SES advantages affected educational attainment in both men and women (Cha et al., 2021). A summary score for socioeconomic disadvantages was created for each respondent and ranged from 0-3. The summary score was created based on paternal education level, maternal education level, and the respondent's perception of whether their family was well-off financially, average, or poor. Having no socioeconomic disadvantages was coded as 0, one socioeconomic disadvantage was coded as 1, two socioeconomic disadvantages was coded as 2, and three socioeconomic disadvantages was coded as 3. Among those with three SES disadvantages, only around 9% of women attended college, compared to approximately 26% of men. Conversely, in those with no SES disadvantages, around 87% of women and 92% of men attended college. One possible hypothesis stated that women of lower childhood SES may not have had the opportunity to pursue higher education due to gender norms that may have implicitly or explicitly influenced women's abilities to pursue education, including less familial support, lack of information, and insufficient academic support (Psaki et al., 2022).

The expansion in educational opportunities for women in recent decades has resulted in a significant decrease in the gender gap in education (Esteve et al., 2012). Therefore, considering HRS includes several generations, a respondent's birth year greatly impacts the size of the gender difference in educational attainment.

The size of educational inequalities in episodic memory may vary across levels of race, ethnicity, childhood SES, and birth year (Eagan & Etowa, 2009; Greenfield et al., 2021; Peterson & Shakeel, 2022). The effect of education on episodic memory has been found to be larger for certain racial-ethnic groups (Diaz-Venegas, 2016; Eagan & Etowa, 2009). It has been hypothesized that everyday racism affects occupational opportunities in historically minoritized racial-ethnic groups, even in those of similar educational attainment to White individuals; this may result in less cognitively engaging activities throughout life, thus increasing the onset of dementia (Eagan & Etowa, 2009). Diaz-Venegas et al. (2016) measured cognitive functioning in HRS by using the modified Telephone Interview for Cognitive Status (TICS-M). The score ranged between 0-35 points, and consisted of tests for immediate recall, delayed recall, serial 7's, and counting backwards. When controlling for age, gender, and years of education, each racial-ethnic group benefited cognitively from increased years of education. However, the beneficial effect of education on cognition was less strong in Hispanic individuals when compared to other racial-ethnic groups. White individuals had the highest predicted total cognition score of respondents across all years of education, and these trends persisted across values of age and years of educational attainment.

In addition, the effect of education on episodic memory is larger in certain subgroups of childhood SES (Cha et al., 2021; Greenfield et al., 2021; McHutchison et al., 2017). Using HRS data, Cha et al. (2021) evaluated the differences of childhood SES and the numbers of years spent with dementia. For those individuals with less than high school education, both men and women with three SES disadvantages had more years spent with dementia in comparison to those who had less than three SES disadvantages with less than high school education. This trend was also observed for those with college-level education. Therefore, the magnitude of the increased rate of dementia was larger for individuals who had less than a college education compared to those individuals who had college education. Thus, when assessing the interaction between education and childhood SES, those of low childhood SES had increased dementia risks based on low cognition than those of high childhood SES, even when educational attainment was identical. This could be due to individuals with higher SES status in childhood being more likely to have a higher status occupation in adulthood, which can result in increased cognitive engagement throughout life, as well as higher income which may improve access to care (Greenfield et al., 2021; McHutchison et al., 2017).

Lastly, educational programs have changed over the years; thus, an individual's birth year may contribute to the education received, impacting future cognitive function (Peterson &

Shakeel, 2022). Thus, the magnitude of the education-cognition effect would be stronger for those of later birth-years in comparison to those of earlier birth-years.

Exposure-Mediator Interaction

An exposure-mediator interaction implies that education not only mediates the association between gender and episodic memory, but also is an effect modifier of the same association. This interaction also implies that gender is an effect modifier of the association between education and episodic memory. The gender difference in the risk of cognitive impairment varied across levels of educational attainment (Kim & Chung, 2022). The gender differences on cognitive impairment were smaller as educational attainment increased (Kim & Chung, 2022). Additionally, the protective effect of education on cognitive decline is larger in women compared to men (Cha et al., 2021; Maccora et al., 2015). Hence, based on research, it is important to test this interaction in the analyses (Maccora et al., 2015).

Assumptions of Mediation Analysis

The four assumptions for causal mediation analysis are: there are no (unmeasured) confounders of the exposure-outcome effect, mediator-outcome effect, exposure-mediator effect, and no confounders of the mediator-outcome effect that are affected by the exposure. Adjusting for the confounders described in the previous section addresses the first three no (unmeasured) confounder assumptions of the mediation analyses. The described confounders affect both education and episodic memory. Considering education is used in this research as an early life exposure, educational attainment would likely precede other possible mediators of the relation between gender and episodic memory, like occupation. Therefore, education is likely the first mediator within the causal chain between gender and episodic memory decline, which satisfies the fourth assumption that there are no confounders of the mediator-outcome effect that are affected by the exposure.

Chapter Three: Methods

Study Design

This research used data from the ongoing University of Michigan Health and Retirement Study, which consists of individuals aged ≥51 years who live in private residences across the U.S., as well as their spouses regardless of age (Sonnega et al., 2014). The HRS (Health and Retirement Study) is sponsored by the National Institute on Aging (grant number NIA U01AG009740) and is conducted by the University of Michigan. HRS is a prospective longitudinal cohort study composed of several cohorts. The initial 1992 cohort consists of individuals born between 1931 and 1941 (Sonnega et al., 2014). The Asset and Health Dynamics Among the Oldest Old (AHEAD) cohort was added in 1993, consisting of those born before 1924 (Sonnega et al., 2014). In 1998, the HRS and AHEAD cohorts were merged, and two new cohorts were enrolled to include individuals older than 50 (Sonnega et al., 2014). These include the Children of the Depression (CODA), for those born between 1924 and 1930 and the War Babies, for those born between 1942 and 1947 (Sonnega et al., 2014). Currently, the HRS replenishes the sample every six years with younger cohorts (Sonnega et al., 2014). Data are collected through extensive in-person and telephone interviews that cover measurements of cognitive function, health behaviors, overall health, and labor force participation (Sonnega et al., 2014).

This study utilized sample data collected from 1998 to 2018, starting with 21,380 individuals in 1998. The RAND Center for Study of Aging creates data products that are more accessible for researchers, consisting of cleaned and processed variables to assist in research analyses; these are derived from HRS datafiles (RAND Corporation, 2022). The RAND 2018 Longitudinal File is a cleaned, easily accessible, and streamlined data product containing information from the Core and Exit Interviews of the HRS and therefore were used for these analyses (RAND Corporation, 2022).

Participants

Individuals who were included in the analyses were aged ≥51 years at any point between 1998-2018 and had available data on education and at least one measurement of episodic memory (delayed or immediate recall) in at least one wave. The delayed and immediate recall tests in the first two waves of HRS included 20 words instead of 10; due to this, cognition data from 1992 and 1994 are not included (McCammon et al., 2019). In addition, in 1998 the HRS age inclusion criterion was altered to include a broader age range, encompassing both those born between 1924-1930 and 1942-1947; this created a U.S. representative sample for ages ≥51 years beginning in 1998 (Sonnega et al., 2014). Data up until 2018 are utilized, as HRS is making updates to the data collected through cognition tests in 2020. To stay consistent across age range, tests and scoring measures, these inclusion criteria are applied.

Variable Measures

Variables included in the analyses that come from the RAND 2018 Longitudinal File are immediate and delayed recall, gender, birth year, education, race, ethnicity, and parent's years of education. Variables from the HRS 2020 Early Release Tracker File Version 2 include year immigrated to the U.S and if a respondent is U.S. born. For cognition data in 2018, delayed and immediate recall, as well as a cognition test mode indicator (web-based versus oral presentation), were also taken from the HRS tracker file due to HRS updates with cognition tests and RAND reforming these variables in their datasets.

Due to levels of variable missingness and unclear timing in relation to education, childhood adversity, childhood health behavior, childhood health, and childhood learning problems were not included as confounders in the analyses. In HRS, these variables were asked in optional surveys beginning in 2008. Considering variables for the exposure, mediator, and outcomes used in the sample were asked beginning in 1998, the levels of missingness for these additional confounders would have resulted in selection bias in my results. Figure 2 includes a DAG encompassing the variables used for the analyses.

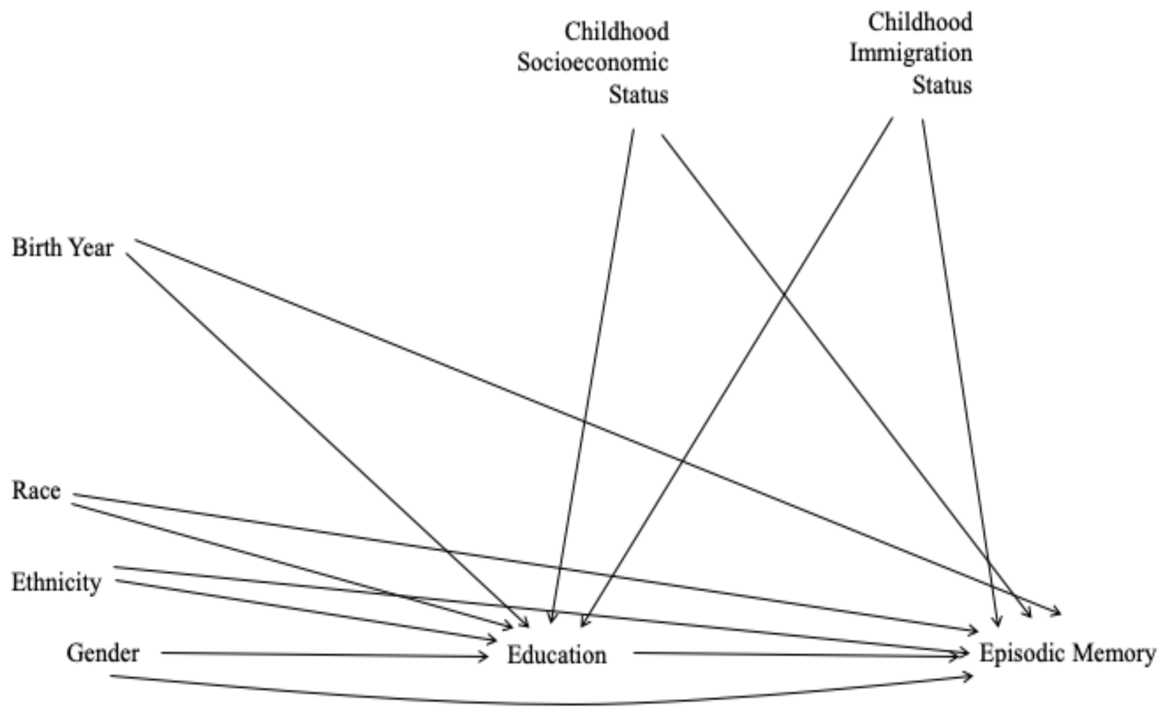

Figure 2: A DAG of confounders used in the analyses of the association between education and episodic memory

Gender

HRS measures gender by asking if respondents identify as male or female. Sex is used as a proxy for gender, referring to men and women (Williams et al., 2021). Considering the phrasing of this question in HRS, this left room for gender interpretation, pertaining to if a respondent identifies as male or female. In this study, gender is a binary variable, with men coded as 0 and women coded as 1. Men are the reference group, considering I hypothesize that women experience more rapid cognitive decline than men, and the extent to which women experience more rapid cognitive decline compared to men is of study interest (CDC, 2022; GBD 2019 Dementia Forecasting Collaborators, 2022). Gender was used as the exposure in statistical analyses.

Episodic Memory

In HRS, a modified version of the Telephone Interview for Cognitive Status (TICS-M) was conducted at each wave (Crimmins et al., 2011). The TICS-M included two tests of episodic memory: immediate recall and delayed recall. Immediate recall was measured by interviewee presentation of a 10-word list and requests that respondents repeat the words back in any order immediately after presenting the list. Delayed recall was measured by asking respondents to repeat the previously presented words after approximately five minutes of asking other survey questions (Ofstedal et al., 2005). Between 1998 and 2016, all recall tests were conducted orally. In 2018, respondents were offered oral or web interviews for recall measures. The repeatedly measured immediate and delayed recall scores will be used as outcomes in statistical analyses. In this study, immediate and delayed recall are measured at 12 waves, between the years of 1998 and 2018. These variables are both continuous and consist of values ranging from 0-10. Each correctly recalled word is equivalent to one-point.

Education

HRS measures the number of years in school by asking respondents how many years of school they completed. This variable is measured at study entry and is defined as years of formal schooling. It is a continuous variable consisting of numeric values between 0 and 17 and was used as the mediator in statistical analyses.

Confounders and Effect Modifiers

In HRS, race and ethnicity were measured by asking respondents which racial-ethnic group they identify with upon study entry. Race was measured by asking if respondents identify with White/Caucasian, Black or African American, or other racial groups. White/Caucasian is coded as 0. Black/African American is coded as 1. Other reported racial groups are coded as 2. The second question asked if respondents identified as Hispanic. For ethnicity, if respondents identified as Hispanic (either Mexican, other, or unknown), they will be classified as Hispanic, which will be coded as 1. Non-Hispanic ethnic groups indicated by respondents will be coded as 0. Race and ethnicity were used as effect modifiers and confounders in the analyses.

Father's years of education was used as a proxy for childhood SES; if this value was unknown, the mother's years of education was used instead. In HRS, paternal years of education is measured by asking respondents for the highest grade of school that their father completed. Maternal years of education is measured by asking respondents for the highest grade of school that their mother completed. The completed grade is transformed into years of education, and these variables are continuous and encompass a numeric range between 0 and 17. Childhood SES was used as an effect modifier and confounder in the analyses and is measured upon study entry.

Upon study entry, HRS measures year of birth by asking respondents for the year they were born. Year of birth, which was also used as a confounder and effect modifier, is a continuous variable consisting of numeric values between 1892 and 1972. To enhance the interpretability of the coefficients in the analyses, birth year was centered by subtracting 1892 from the respondent's birth year.

Upon study entry, HRS measured immigration status by asking respondents if they immigrated to the U.S., and if so, then what year this occurred in. First, to assess if the respondent was born in the U.S., a binary variable indicated either they were born in the U.S. or in a foreign country. The second, continuous variable consisted of date ranges between 1905 and 2019, which stated which year the respondent immigrated to the U.S, if immigration did occur. In the analyses, childhood immigration was computed using these two variables. To account for childhood immigration, year of birth was used to identify the year in which individuals turned 18 years old, and the immigration year then identifies if childhood immigration occurred. Creation of this new binary variable identified if childhood immigration did occur. Childhood immigration was coded as yes when the immigration year was before the year in which an individual turned 18. Childhood immigration was coded as no when immigration year was after the year in which an individual turned 18, or if childhood immigration did not occur. Yes was coded as 1 and no was coded as 0.

Statistical Analyses

Demographics of the Sample

To determine the demographics of the sample participants, descriptive statistics were obtained. Means and standard deviations (SD) were reported for normally distributed variables. Medians and interquartile ranges (IQR) were reported for continuous variables with skewed distributions. I did not use sampling weights, because I used data from multiple HRS cohorts. There is not one specific time point at which all participants entered my analytic sample, therefore making it impossible to weight the sample back to a reference population. Frequencies and percentages were reported for categorical variables. These statistics were included for the complete sample and stratified by gender. To determine statistically significant differences between men and women, chi-square tests were used for categorical variables, t-tests were used for continuous variables with normal distributions, and Wilcoxon rank sum tests were used for continuous variables with non-normal distributions. Respective p-values were reported.

Pathways of the Mediation Model

Multiple regression was used to estimate the associations between gender, education, and episodic memory. First, a linear regression model (model 1) was used to estimate the path between gender and education, resulting in an estimate of the *a* path. Second, a linear mixed-effects model (model 2) was used to estimate the path between education and episodic memory (b) and between gender and episodic memory (c'). The *c'* path was used to explain the difference in episodic memory between men and women when adjusted for education. The *b* path was used to explain how education impacts episodic memory, while adjusted for gender. These paths were used to estimate the mediation effects.

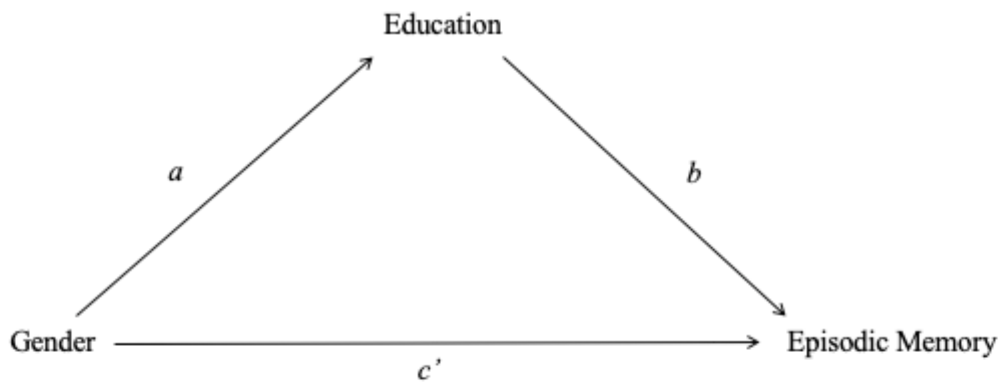

Figure 3: Diagram of the *a* path, *b* path, and *c'* path estimated in the mediation analyses

To address the dependence of the repeated measurements of episodic memory, a linear mixed-effects model was used in the analyses. This model, when including the interaction with age, allows distinguishment between cognitive level and cognitive decline. Considering interactions with age were assessed in the mixed-effects model, the coefficient for the interaction term provides insight into trajectories of episodic memory over time. These curves were used to measure how steep the decline in episodic memory is. It is hypothesized that higher education will produce a delayed and less steep decline in the episodic memory curves. If a mixed-effects model was not used within this research, the clustering of repeated measures of episodic memory would result in a violation of the independence of observations/measurements assumption. The result of this violation would be underestimated standard errors and increased likelihood of type 1 error.

Exposure-Mediator Interaction

An exposure-mediator interaction term is included in model 2 to test for a statistically significant interaction between gender and education ($p<0.05$).

Effect Modification and Confounding

Both models 1 and 2 were adjusted for confounding by birth year, race, ethnicity, childhood SES, and childhood immigration status. Quadratic and cubic terms were added to the models to assess if the effect of the continuous variables on education and episodic memory are non-linear; if $p<0.05$, these terms remain in the models. To assess potential effect measure modification of the *a* path, *b* path, and *c'* path, by birth year, race, ethnicity, and childhood SES, interaction terms were included in the models and were retained if $p<0.05$.

When significant interactions were present with birth year, the estimates of the effects were reported separately for participants born in 1920, 1940, and 1960, considering relatively few individuals in the sample were born before 1920. If an interaction was present for race, the effect estimates for Black and African American, White, and other racial groups were reported. If an interaction was present for ethnicity, the estimate of the effects for Hispanic and other ethnic groups were reported. If an interaction was present for childhood SES, the estimated effects were reported in 5-year increments pertaining to years of parental education.

The Mediation Model

The final versions of model 1 and model 2 included any statistically significant interaction and higher-order terms and these models were used as input for the mediation analyses. Considering this study used longitudinal episodic memory data, the effect estimates have both between-person and within-person interpretations. The model includes time, as this model is used over various ages. Total, indirect, and direct effects are reported. The total effect – of gender on episodic memory – is the sum of the direct and indirect effects. Considering the indirect effect has a skewed sampling distribution, 95% Monte-Carlo confidence intervals were reported for indirect effect estimates. Normal-theory 95% confidence intervals were reported for direct and total effect estimates. All descriptive statistics were conducted in SAS Version 9.4, and the regression and mediation analyses were conducted in RStudio Version 2022.12.0+353. The R package titled ‘lme4’ was used for the linear mixed-effects models and the R package titled ‘Rmediation’ was used for creating the confidence intervals of the mediation effect estimates.

Statistical Assumptions

Linearity, homoscedasticity, independence, and normality were assessed in the analyses. Prior to analyses, each variable was plotted to determine normal or skewed distributions.

To address the assumption of normality, the variable and residual-term distributions were plotted. For the residual-terms, the residual was calculated for each observation using the regression analyses. Variables were plotted using histograms; to check for normality, histograms were visualized for a symmetrical bell shape. In addition, means and medians were compared to determine normality.

To address the assumption of homoscedasticity, a standardized residuals versus predicted values plot was used to check if the data was homoscedastic.

Linearity of the regression coefficients of continuous predictors is assumed. By visualizing the data, and adding higher-order terms, the assumption of linearity was assessed and non-linearity accounted for.

Chapter Four: Results

Descriptive Statistics

The total number of respondents included in the analytic sample was 35,721, as can be seen in Figure 4. Of these, 20,190 (56.5%) were women and 15,531 (43.5%) were men. None of the continuous variables followed a normal distribution, so the medians and interquartile ranges are shown in Table 1, as well as the frequencies and percentages for the categorical variables. Within the sample, there was a median of 12 (IQR=12, 15) years of education for respondents. However, years of education significantly differed between men and women (p<0.001), with men having a median of 12 years of education (IQR=12, 15) and women 12 (IQR=12, 15). The median number of words recalled for immediate recall was 6 (IQR =5, 7) and for delayed recall was 5 (IQR =3, 6). Both immediate and delayed recall showed statistically significant differences between men and women (p<0.001), with men having a median immediate recall score of 5 (IQR=4, 6) and women 6 (IQR=5, 7). Men had a median delayed recall score of 4 (IQR=3, 5) and women 5 (IQR=3. 6). The median number of episodic memory measurements per person was 8 (IQR= 5, 10) with men having a median of 8 (IQR= 5, 10) and women having a median of 8 (IQR= 4, 10).

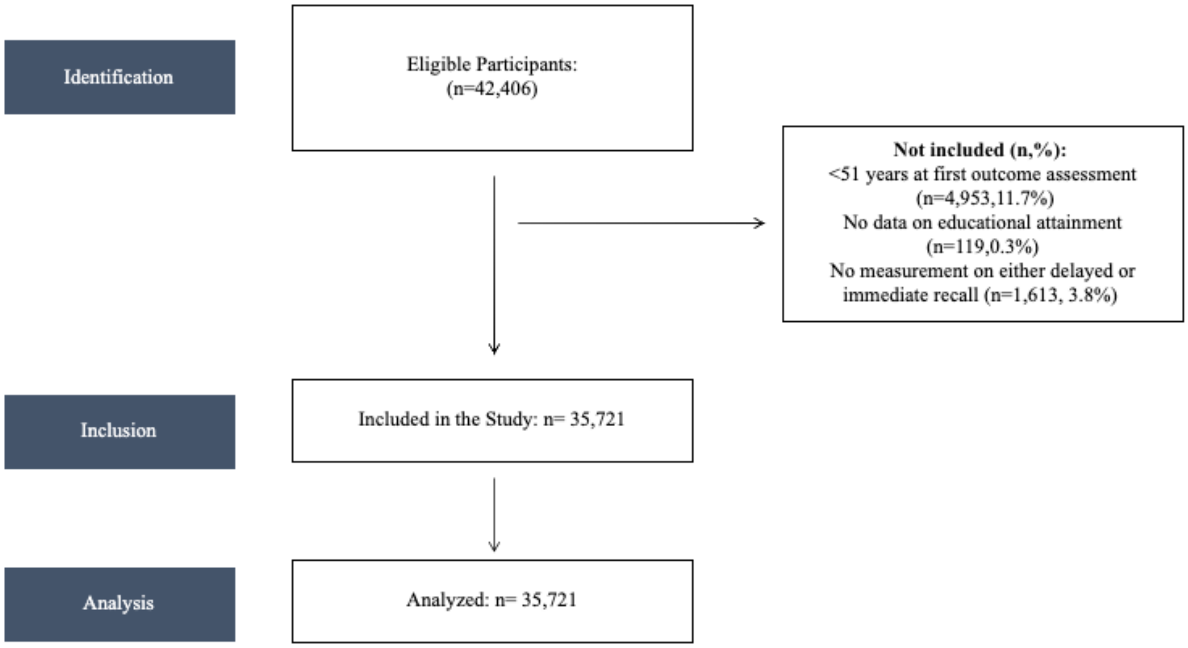

Figure 4: STROBE Flow Diagram for analytic sample

Considering I did not account for missingness in my linear models, there were observations that were included in the unadjusted models but not the confounder-adjusted models. These were removed because respondents had a missing value for at least one of the confounding variables. Thus, the sample size for the confounder adjusted-linear models, which included observations with full information on confounders, was 32,712, 8.4% smaller than the full analytic sample.

In my check for normality of the residuals, the residuals from the regression models approximated bell curves. In addition, I completed linearity checks for the confounders that were continuous variables. I treated birth year as non-linear considering the squared term for birth year was significant. Thus, this was included in confounder-adjusted models.

Table 1: Sample characteristics of participants of the Health and Retirement Study, 1998-2018

		Gender		
Variable	**Overall, N = 35,721**[1]	**Men, N = 15,531**[1]	**Women, N = 20,190**[1]	**p-value**
Birth year, median (Q1, Q3)	1942 (1931, 1955)	1942 (1931, 1955)	1942 (1931, 1955)	0.2728[2]
Number of episodic memory measurements per person	8 (5, 10)	8 (5, 10)	8 (4, 10)	**<0.001**[2]
Baseline immediate recall, median (Q1, Q3)	6 (5, 7)	5 (4, 6)	6 (5, 7)	**<0.001**[2]
Baseline delayed recall, median (Q1, Q3)	5 (3, 6)	4 (3, 5)	5 (3, 6)	**<0.001**[2]
Respondent education in years, median (Q1, Q3)	12 (12, 15)	12 (12, 15)	12 (12, 14)	**<0.001**[2]
Parental education in years, median (Q1, Q3)	8.5 (7.5, 12.0)	9.0 (7.5, 12.0)	8.5 (7.5, 12.0)	**<0.001**[2]
(Missing)	2,695	1,198	1,497	
Race,[4] n(%)				**<0.001**[3]
White	25,654 (72.0%)	11,253 (72.7%)	14,401 (71.5%)	
Black or African American	6,903 (19.4%)	2,783 (18.0%)	4,120 (20.5%)	
Other race	3,073 (8.6%)	1,450 (9.4%)	1,623 (8.1%)	
(Missing)	91	45	46	
Ethnicity[4], n(%)				0.630[3]
Non-Hispanic	31,155 (87.3%)	13,526 (87.2%)	17,629 (87.4%)	
Hispanic	4,521 (12.7%)	1,980 (12.8%)	2,541 (12.6%)	
(Missing)	45	25	20	
Immigration during childhood[4], n(%)				0.078[3]
No	34,514 (97.4%)	14,990 (97.2%)	19,524 (97.5%)	
Yes	939 (2.6%)	435 (2.8%)	504 (2.5%)	
(Missing)	268	106	162	

[1]Median (IQR); n (%)
[2]Wilcoxon rank sum test
[3]Pearson's Chi-square test
[4]Percentages do not add up to 100% due to missingness

Gender Differences in Years of Education

Women, on average, had lower years of educational attainment than men. Effect estimates are reported in Table 2. After adjustment for confounders, women had 0.28 fewer years of education in comparison to men (β= -0.28 (95% CI = -0.36, -0.19)). Childhood SES, ethnicity, and birth year did not significantly moderate the association between gender and years of education. However, race did significantly moderate this association. After adjustment for confounders, White women had fewer years of education than White men (β= -0.37 (95% CI = -0.47, -0.28). The size of the effect of gender on education differed significantly between White individuals and Black or African American individuals (β= 1.01 (95% CI = 0.75, 1.27)), such that in Black or African American individuals, women had more education than men. There was no statistically significant difference in the association between gender and education between White individuals and individuals who identified as a race other than White or Black or African American (β= -0.31 (95% CI = -0.81, 0.19)).

Table 2: Association between gender and years of education in participants of the Health and Retirement Study, 1998-2018

Model[a]	**Independent variable**	***β***	**95% Confidence interval**
Model 1: unadjusted	Gender	-0.3847	(-0.4814, -0.2880)
Model 2: adjusted for confounders	Gender	-0.2769	(-0.3621, -0.1917)
Model 3: model 2 with effect modifiers	Gender	-0.3701	(-0.4650, -0.2752)
	Gender*Race: Black	1.012	(0.7506, 1.2735)
	Gender*Race: Other	-0.3100	(-0.8139, 0.1940)

Models 2 and 3 were adjusted for birth year, birth year^2, race, ethnicity, childhood SES, and childhood immigration status.
[a]Men were treated as the reference group

Gender, Education and Episodic Memory

After adjustment for years of education, women, on average, performed better on immediate and delayed recall tests than men (Table 3). For immediate recall, the adjusted estimate was 0.49 (95% CI = 0.47, 0.52), indicating that women recalled 0.49 more words, on average, than men after adjustment for years of education. This was also true for delayed recall, with the adjusted estimate (β= 0.57 (95% CI = 0.54, 0.60)), indicating that women recalled 0.57 more words than men after adjustment for years of education.

As for the *b* path for recall (Table 3), the adjusted estimate for the effect of years of education on immediate recall was 0.13 (95% CI = 0.13, 0.14) and indicated that, for every one-year increase in years of education, individuals recalled 0.13 more words, after adjustment for gender. Results were similar for delayed recall, with the adjusted estimate (β= 0.14 (95% CI = 0.14, 0.15)), indicating that, for every one-year increase in years of education, individuals recalled 0.14 more words, after adjustment for gender and confounders.

Variables that significantly moderated the relationship between education and both immediate and delayed recall were gender, race, ethnicity, and birth year. Childhood SES did not significantly moderate the relationship between years of education and either outcome. For immediate recall, individuals who identified as racial groups other than White or Black benefited less from additional years of education on recall than White counterparts (β= -0.02 (95% CI = -0.03, -0.01)), as well as those who identified as Hispanic rather than non-Hispanic (β= -0.05 (95% CI = -0.06, -0.04). Those who were born in later birth years also benefited less from additional years of education (β= 0.01 (95% CI = 0.01, 0.01)). However, the effect of education and immediate recall decreased as birth year increased, considering the negative quadratic term (β= -0.0001 (95% CI = -0.0001, -0.00008)). Thus, the amount of protectiveness decreased over time, and those born in later years had less of a benefit from higher education compared to those born in earlier years. The association between education and immediate recall was not significantly different between White and Black individuals (β= 0.0003 (95% CI = -0.01, 0.01)).

For delayed recall, other racial groups in comparison to White counterparts (β= -0.02 (95% CI = -0.04, -0.01)) and those who identified as Hispanic in comparison to non-Hispanic (β= -0.06 (95% CI = -0.07, -0.05)) had less of a protective effect for education on delayed recall. Additionally, with increasing birth year, the protective effect of education on episodic memory also increased (β= 0.01 (95% CI = 0.01, 0.01)). Similarly, those born in later years had less of a benefit from higher education on delayed recall, as the amount of protectiveness decreased over time (β= -0.0001 (95% CI = -0.0001, -0.00008)). The relationship between education and delayed recall was not significantly different between White and Black individuals (β= -0.01 (95% CI = 0.02, 0.01)). However, the education effect is significant in White individuals (β= -0.09 (95% CI = -0.13, -0.05)), so there is still a significant effect of education on delayed recall in both White and Black individuals.

Lastly, I conducted a sensitivity analysis to see if the effect estimates differed depending on the type of cognitive test presented. In 2018, respondents were offered either web-based or oral presentation for the episodic memory assessments. In model 2 for both immediate and delayed recall, there was a significant interaction between education and the indicator for the type of cognitive test (i.e., web-based, or oral presentation). A table with the results from this sensitivity analysis is included in Appendix A, but this interaction was not included in the linear models due to the small subset of observations that completed web-based cognition tests in my sample.

Table 3. Associations between gender, years of education, and episodic memory in participants of the Health and Retirement study, 1998-2018

Dependent variable	Model	Independent variable	β	95% Confidence interval
Immediate recall	Model 1: unadjusted	Gender	0.4544	(0.4292, 0.4796)
		Education	0.1859	(0.1821, 0.1897)
	Model 2: adjusted for confounders	Gender	0.4939	(0.4706, 0.5171)
		Education	0.1337	(0.1295, 0.1379)

Table 3 (continued)

	Model 3: model 2 with effect modifiers	Gender	0.4978	(0.4746, 0.5209)
		Education	-0.0004	(-0.0338, 0.0330)
		Education*Race: Black	0.0003	(-0.0099, 0.0106)
		Education*Race: Other	-0.0159	(-0.0272, -0.0046)
		Education*Hispanic	-0.0530	(-0.0625, -0.0435)
		Education*Birth year	0.0070	(0.0055, 0.0085)
		Education*Birth year^2	-0.00007	(-0.00008, -0.00006)
Delayed recall	Model 1: unadjusted	Gender	0.5101	(0.4790. 0.5413)
		Education	0.2020	(0.1974, 0.2067)
	Model 2: adjusted for confounders	Gender	0.5727	(0.5441, 0.6012)
		Education	0.1426	(0.1374, 0.1477)
	Model 3: model 2 with effect modifiers	Gender	0.3681	(0.2526, 0.4837)
		Education	-0.0873	(-0.1285, -0.046)
		Education*Gender	0.1650	(0.0077, 0.0253)
		Education*Race: Black	-0.0051	(-0.0176, 0.0074)
		Education*Race: Other	-0.0228	(-0.0366, -0.0090)
		Education*Hispanic	-0.0626	(-0.0742, -0.0509)
		Education*Birth year	0.0105	(0.0087, 0.0123)
		Education*Birth year^2	-0.0001	(-0.0001, -0.00008)

Models 2 and 3 were adjusted for birth year, birth year^2, race, ethnicity, childhood SES, and childhood immigration status.

The Mediation Analyses

Table 4 shows the results from the mediation analyses. First, for immediate and delayed recall, the indirect effect estimates were negative for both unadjusted and adjusted models. The adjusted indirect effect estimated for immediate recall indicated that, on average, women recalled 0.04 (β= -0.04 (95% CI = (-0.05, -0.03)) fewer words than men, because they had fewer years of education on average than men. The unadjusted and adjusted direct and total effect estimates of gender on immediate recall were positive, indicating that on average, women had a higher immediate recall score, both before and after adjustment for years of education. The unadjusted direct effect was 0.45 (95% CI = (0.43, 0.48), the adjusted direct effect was 0.49 (95% CI = 0.47, 0.52), the unadjusted total effect was 0.38 (95% CI = 0.35, 0.41) and the adjusted total effect was

0.46 (95% CI = 0.43, 0.48). The indirect, total, and direct effect estimates were all statistically significant.

For delayed recall, the adjusted indirect effect estimate indicated that, on average, women recalled 0.04 (β= -0.04 (95% CI = (-0.05, -0.03)) fewer words than men, because they had fewer years of education than men. The unadjusted and adjusted direct and total effect estimates of gender on delayed recall were positive, indicating that on average, women had a higher delayed recall score, both before and after adjustment for years of education. The unadjusted direct effect was 0.51 (95% CI = (0.48, 0.54), the adjusted direct effect was 0.57 (95% CI = 0.54, 0.60), the unadjusted total effect was 0.43 (95% CI = 0.40, 0.47), and the adjusted total effect was 0.53 (95% CI = 0.50, 0.56). Similarly to immediate recall, the indirect, total, and direct effects were all statistically significant.

Table 4. Effect estimates from the mediation analyses in which years of education is assessed as a mediator of gender differences in episodic memory

Dependent variable	**Model**	**Effect**	**Estimate**	**95% Confidence interval‡**
Immediate recall	Model 1: unadjusted	Total effect	0.3829	(0.3519, 0.4138)
		Indirect effect	-0.0715	(-0.0896, -0.0535)
		Direct effect	0.4544	(0.4292, 0.4796)
	Model 2: adjusted for confounders	Total effect	0.4568	(0.4310, 0.4827)
		Indirect effect	-0.0370	(-0.0485, -0.0256)
		Direct effect	0.4939	(0.4706, 0.5171)
Delayed recall	Model 1: unadjusted	Total effect	0.4324	(0.3957, 0.4692)
		Indirect effect	-0.0778	(-0.0974, -0.0582)
		Direct effect	0.5101	(0.4790, 0.5413)
	Model 2: adjusted for confounders	Total effect	0.5331	(0.5022, 0.5642)
		Indirect effect	-0.0395	(-0.0517, -0.0274)
		Direct effect	0.5727	(0.5441, 0.6012)

Model 2 was adjusted for birth year, birth year^2, race, ethnicity, childhood SES, and childhood immigration status.
‡Monte Carlo confidence intervals are reported for indirect effect estimates, and normal-theory confidence intervals for total and direct effect estimates.

Moderated Mediation

Birth year, race, and ethnicity were all significant effect modifiers of the indirect effect of gender on both immediate and delayed recall through education. Moderation of the direct effect estimate was not assessed, so the size of this estimate was consistent across all analyses. Similar to the mediation analyses reported in Table 4, the total and direct effect estimates were consistently positive throughout the moderated mediation analyses, as seen in Table 5 and Table 6. The total effect estimates were consistently positive across all analyses, indicating that on average women recalled more words than men. The indirect effect estimates were consistently negative in individuals who identified as White or as a racial group other than White or Black. In White individuals and individuals who identified as racial groups other than White or Black, the indirect effect estimates were more negative for those who did not identify as Hispanic in comparison to those who did. The indirect effect estimates were most negative in other racial groups, specifically in those who identified as non-Hispanic. Thus, in other racial groups who did not identify as Hispanic, women recalled the fewest words in comparison to non-Hispanic men of other racial groups. Ethnicity was not an effect modifier of the association between gender and education, so this must be driven by differences in the size of the *b* path across Hispanic and non-Hispanic individuals. The indirect effect estimates for Black and African American populations were consistently positive, indicating women had higher words recalled in Black and African American populations, because women had more years of education.

Across all racial groups and ethnicities, indirect effect estimates had the largest magnitude (i.e., most positive, or most negative) for individuals born in 1940. For individuals born in 1940 who identified as White or other racial groups and either Hispanic or non-Hispanic, women had the fewest words recalled in comparison to men, because they had fewer years of education. In Black and African American populations, women born in 1940 had the most words recalled in comparison to men across both Hispanic and non-Hispanic subgroups. Birth year was not an effect modifier of the association between gender and education, so the larger effect in 1940 must be driven by a larger *b* path in 1940. These same trends were also observed for delayed recall.

Table 5. Mediation effect estimates for immediate recall conditional on levels of race, ethnicity, and birth year

Race	Ethnicity	Birth year	Effect	Estimate	95% Confidence interval‡
White	Non-Hispanic	1920	Total effect	0.4440	(0.4174, 0.4705)
			Indirect effect	-0.0538	(-0.0671, -0.0408)
			Direct effect	0.4978	(0.4746, 0.5209)
		1940	Total effect	0.4328	(0.4050, 0.4607)
			Indirect effect	-0.0649	(-0.0807, -0.0494)
			Direct effect	0.4978	(0.4746, 0.5209)
		1960	Total effect	0.4446	(0.4180, 0.4712)
			Indirect effect	-0.0532	(-0.0664, -0.0402)
			Direct effect	0.4978	(0.4746, 0.5209)
	Hispanic	1920	Total effect	0.4645	(0.4398, 0.4893)
			Indirect effect	-0.0332	(-0.0424, -0.0247)
			Direct effect	0.4978	(0.4746, 0.5209)
		1940	Total effect	0.4534	(0.4278, 0.4791)
			Indirect effect	-0.0443	(-0.0557, -0.0334)
			Direct effect	0.4978	(0.4746, 0.5209)
		1960	Total effect	0.4651	(0.4404, 0.4900)
			Indirect effect	-0.0326	(-0.0417, -0.0241)
			Direct effect	0.4978	(0.4746, 0.5209)
Black	Non-Hispanic	1920	Total effect	0.5683	(0.5284, 0.6082)
			Indirect effect	0.0703	(0.0380, 0.1031)
			Direct effect	0.4980	(0.4749, 0.5212)
		1940	Total effect	0.5828	(0.5375, 0.6281)
			Indirect effect	0.0847	(0.0458, 0.1239)
			Direct effect	0.4980	(0.4749, 0.5212)
		1960	Total effect	0.5664	(0.5272, 0.6055)
			Indirect effect	0.0683	(0.0369, 0.1002)
			Direct effect	0.4980	(0.4749, 0.5212)

Table 5 (continued)

	Hispanic	1920	Total effect	0.5382	(0.5080, 0.5684)
			Indirect effect	0.0402	(0.0213, 0.0604)
			Direct effect	0.4980	(0.4749, 0.5212)
		1940	Total effect	0.5527	(0.5182, 0.5872)
			Indirect effect	0.0546	(0.0293, 0.0808)
			Direct effect	0.4980	(0.4749, 0.5212)
		1960	Total effect	0.5363	(0.5068, 0.5657)
			Indirect effect	0.0382	(0.0203, 0.0573)
			Direct effect	0.4980	(0.4749, 0.5212)
Other	Non-Hispanic	1920	Total effect	0.3439	(0.3013, 0.3865)
			Indirect effect	-0.1530	(-0.1900, -0.1177)
			Direct effect	0.4970	(0.4738, 0.5201)
		1940	Total effect	0.3103	(0.2620, 0.3586)
			Indirect effect	-0.1867	(-0.2300, -0.1446)
			Direct effect	0.4970	(0.4738, 0.5201)
		1960	Total effect	0.3477	(0.3056, 0.3898)
			Indirect effect	-0.1493	(-0.1855, -0.1147)
			Direct effect	0.4970	(0.4738, 0.5201)
	Hispanic	1920	Total effect	0.4076	(0.3748, 0.4404)
			Indirect effect	-0.0894	(-0.1140, -0.0668)
			Direct effect	0.4969	(0.4738, 0.5201)
		1940	Total effect	0.3739	(0.3369, 0.4110)
			Indirect effect	-0.1230	(-0.1530, -0.0945)
			Direct effect	0.4969	(0.4738, 0.5201)
		1960	Total effect	0.4114	(0.3793, 0.4434)
			Indirect effect	-0.0856	(-0.1088, -0.0642)
			Direct effect	0.4969	(0.4738, 0.5201)

All models were adjusted for birth year, birth year^2, race, ethnicity, childhood SES, and childhood immigration status.
‡Monte Carlo confidence intervals are reported for indirect effect estimates, and normal-theory confidence intervals for total and direct effect estimates.

Table 6. Mediation effect estimates for delayed recall conditional on levels of race, ethnicity, and birth year

Race	Ethnicity	Birth year	Effect	Estimate	95% Confidence interval‡
White	Non-Hispanic	1920	Total effect	0.5251	(0.4941, 0.5562)
			Indirect effect	-0.0519	(-0.0649, -0.0392)
			Direct effect	0.5770	(0.5486, 0.6055)
		1940	Total effect	0.5045	(0.4712, 0.5377)
			Indirect effect	-0.0725	(-0.0902, -0.0551)
			Direct effect	0.5770	(0.5486, 0.6055)
		1960	Total effect	0.5149	(0.4827, 0.5472)

Table 6 (continued)

			Indirect effect	-0.0621	(-0.0777, -0.0469)
			Direct effect	0.5770	(0.5486, 0.6055)
	Hispanic	1920	Total effect	0.5488	(0.5193, 0.5784)
			Indirect effect	-0.0282	(-0.0369, -0.0203)
			Direct effect	0.5770	(0.5486, 0.6055)
		1940	Total effect	0.5282	(0.4972, 0.5591)
			Indirect effect	-0.0488	(-0.0616, -0.0367)
			Direct effect	0.5770	(0.5486, 0.6055)
		1960	Total effect	0.5386	(0.5081, 0.5689)
			Indirect effect	-0.0384	(-0.0492, -0.0283)
			Direct effect	0.5770	(0.5486, 0.6055)
Black	Non-Hispanic	1920	Total effect	0.6420	(0.6006, 0.6834)
			Indirect effect	0.0646	(0.0348, 0.0953)
			Direct effect	0.5774	(0.5489, 0.6058)
		1940	Total effect	0.6691	(0.6182, 0.7201)
			Indirect effect	0.0917	(0.0496, 0.1343)
			Direct effect	0.5774	(0.5489, 0.6058)
		1960	Total effect	0.6542	(0.6087, 0.6996)
			Indirect effect	0.0768	(0.0414, 0.1128)
			Direct effect	0.5774	(0.5489, 0.6058)
	Hispanic	1920	Total effect	0.6068	(0.5745, 0.6392)
			Indirect effect	0.0295	(0.0149, 0.0464)
			Direct effect	0.5774	(0.5489, 0.6058)
		1940	Total effect	0.6339	(0.5949, 0.6730)
			Indirect effect	0.0566	(0.0302, 0.0841)
			Direct effect	0.5774	0.5489, 0.6058)
		1960	Total effect	0.6190	(0.5842, 0.6538)
			Indirect effect	0.0416	(0.0219, 0.0629)
			Direct effect	0.5774	0.5489, 0.6058)
Other	Non-Hispanic	1920	Total effect	0.4313	(0.3863, 0.4765)
			Indirect effect	-0.1443	(-0.1812, -0.1098)
			Direct effect	0.5756	(0.5471, 0.6040)
		1940	Total effect	0.3687	(0.3135, 0.4239)
			Indirect effect	-0.2068	(-0.2555, -0.1600)
			Direct effect	0.5756	(0.5471, 0.6040)
		1960	Total effect	0.4036	(0.3538, 0.4533)
			Indirect effect	-0.1720	(-0.2142, -0.1319)
			Direct effect	0.5756	(0.5471, 0.6040)

Table 6 (continued)

Hispanic	1920	Total effect	0.5053	(0.4694, 0.5411)
		Indirect effect	-0.0703	(-0.0939, -0.0493)
		Direct effect	0.5756	(0.5471, 0.6040)
	1940	Total effect	0.4427	(0.4000, 0.4854)
		Indirect effect	-0.1328	(-0.1661, -0.1015)
		Direct effect	0.5756	(0.5471, 0.6040)
	1960	Total effect	0.4776	(0.4391, 0.5161)
		Indirect effect	-0.0980	(-0.1252, -0.0731)
		Direct effect	0.5756	(0.5471, 0.6040)

All models were adjusted for birth year, birth year^2, race, ethnicity, childhood SES, and childhood immigration status.

‡Monte Carlo confidence intervals are reported for indirect effect estimates, and normal-theory confidence intervals for total and direct effect estimates.

Chapter Five: Discussion

Main Findings

In this study, I aimed to investigate education as a mediator of gender differences in cognitive functioning using longitudinal data from the U.S. HRS. I found that women, on average, had lower years of educational attainment than men. In turn, higher years of education was protective on episodic memory, as approximately for every 8 additional years of educational attainment, respondents on average recalled one additional word in both immediate and delayed recall tests for both men and women. In my mediation analyses, education was shown to be a significant mediator of the association between gender and episodic memory (both for immediate and delayed recall models). This was consistent across unadjusted estimates and confounder-adjusted estimates. For both immediate and delayed recall models, the total and direct effects were positive, indicating that women, on average, performed better on both immediate and delayed recall tests than men.

As noted in previous sections, women have a higher risk of dementia compared to men (CDC, 2019; GBD 2019 Dementia Forecasting Collaborators, 2022). However, in my analyses, I found that women scored better on episodic memory tests. Additionally, my mediation analyses indicated that if women would have had the same educational attainment as men, then their recall scores would have been even higher. It is possible that the women in this dataset may have higher cognitive ability than seen within the general U.S. population. It's also important to note that dementia is not just measured by episodic memory, and many other factors contribute to dementia risk. Mediators studied in previous research include health related conditions (i.e., heart disease, depression, high cholesterol, and hypertension), lifestyle-related factors (i.e., diet, smoking, and alcohol-use), and biomarkers (i.e., creatinine in urine, apolipoprotein A in the blood, and blood lymphocyte percentage) (Shang et al., 2023). I have shown that education partly explains the gender differences seen within dementia. However, these factors may also explain these differences.

I assessed potential effect modification by race, ethnicity, childhood SES, and birth year by the addition of interaction terms to the regression models. These analyses showed that the level of protective effect of education on episodic memory varied between levels of race, ethnicity, and birth year. On average, women had a higher immediate and delayed recall score across all racial and ethnic groups for all listed birth years, both before and after adjustment for education. For White and other racial groups, the indirect effect estimates were consistently negative across both models with immediate recall and delayed recall, indicating that women recalled fewer words in comparison to men, due to having fewer years of education. In Black and African American populations, the indirect effect estimates were consistently positive, indicating that women recalled more words in comparison to men, due to having more years of education. Those who identified as other race and non-Hispanic had the most negative indirect effect. Across the listed birth years (1920, 1940, 1960), the indirect effect estimates were largest in magnitude (i.e., more negative for White individuals and individuals identifying as other racial groups than White or Black and more positive for Black individuals) for people born in 1940.

Comparison and Contrasts with Previous Studies

Prior studies have investigated the role of education as a mediator between gender and cognitive performance or dementia (Ford & Leist., 2021; Hasselgren et al., 2020). One study showed that education was a mediator between these gender differences (Ford & Leist, 2021) and one study did not (Hasselgren et al., 2020). In my analyses, education was found to be a statistically significant mediator of the association between gender on episodic memory. Similar to Ford & Leist (2021), education was found to be a significant mediator and an increase in education was associated with an increase in cognitive ability, and these associations were more pronounced for larger education values. However, Ford & Leist measured cognitive ability by using the Korean version of the Mini-Mental State Examination (MMSE), which was developed as a global assessment of cognitive status (Gluhm et al., 2014). In their study, women had lower MMSE scores compared to men, whereas I found women to score higher on recall tests. The MMSE is a general indicator of dementia, but it may consider other components aside from memory performance. Lastly, I found statistically significant interactions with birth year, race, and ethnicity for both immediate and delayed recall models, which neither prior study investigated.

Findings with respect to the association between gender and education indicated that race was the only significant effect modifier of the association between gender and years of education. Diaz-Venegas et al., showed that, for White and Hispanic racial groups, men had more years of education than women; in Black and African American racial groups, this was reversed (2016). My findings were similar for those of White and Black and African American populations. However, the association between gender and years of education in other reported racial groups was not significant in my analyses. Birth year, ethnicity, and childhood SES were not significant effect modifiers of the association between gender and years of education even though past research has shown differently (Amao & Gbadamosi, 2015; Cha et al,m 2021; Diaz-Venegas et al., 2016; Esteve et al., 2012; Zeng et al., 2014).

For the *b* and *c'* path, I did find statistically significant interactions with birth year, race, and ethnicity as effect modifiers for both immediate and delayed recall models. This was consistent with past research that concluded that these variables were effect modifiers (Diaz-Venegas et al., 2016; Eagan & Etowa, 2009; Peterson & Shakeel, 2022).

A difference between my study and past research is the use of childhood SES as an effect modifier. Past research has shown that gender differences on education are more prominent in those of low childhood SES (Amao & Gbadamosi, 2015) and that the effect of education on episodic memory is larger for certain subgroups of childhood SES (Cha et al., 2021; Greenfield et al., 2021; McHutchison et al., 2017). However, I did not find significant interactions between gender and childhood SES nor between education and childhood SES and concluded it was not a significant effect modifier within any of my analyses. This could be explained by the fact that I assessed other effect modifiers that are strongly associated with childhood SES, including race and ethnicity (Crimmins et al., 2004).

Study Strengths and Limitations

This study has several strengths. First, I had a very large sample, and this resulted in high statistical power for detecting associations. The increased statistical power was important because I was able to investigate many potential effect modifiers, and I needed this for my analyses into effect modification. Even when subsetting the sample for effect modification, I still had a large sample, which resulted in high statistical power in my tests for significance. Second, HRS included numerous variables that I could use in analyses. Thus, I was able to adjust for a wide array of factors that could have contributed to confounding bias and had access to potential effect modifiers. Finally, considering HRS is a nationally representative study, the inclusion of individuals aged ≥51 years across various sociodemographic backgrounds leads to increased generalizability for the U.S. population (Weiss et al., 2020).

This study has several limitations. Although a non-linear effect of education on episodic memory was found (Appendix A), I did not address this in the analyses. The effect estimates in my current analyses are over- and under-estimated based on the omission of higher order terms. To see these trends, I compared gender curves based on the coefficients from the linear-mixed effects models for both immediate and delayed recall, as seen in Appendix A. 0 years of education had, on average, higher estimates of episodic memory than early years of education (i.e., 1-4 years of educational attainment). However, as years of education increased (i.e., 8+ years of educational attainment), the positive effect of education on episodic memory became increasingly pronounced. In addition, I found interactions with age in the unadjusted model (Appendix A). These interactions terms with age were not significant in the confounder-adjusted models and were therefore not included in the models presented in my thesis. Additionally, I did not apply any missing data techniques within my linear models. Therefore, my descriptive statistics encompassed slightly more respondent observations than within my linear models. In addition, considering people with worse cognition tend to drop-out (i.e., selective dropout) of these kinds of cohort studies, this may have affected my results. I also found significant interactions with education and type of cognitive test (i.e., web-based, or oral presentation), but I did not include these interactions in the analyses due to the small subset of observations that completed web-based cognition tests.

As seen in the theoretical model section of this thesis, there were several variables that were included in the original DAG (Figure 1) that were not included in the final DAG (Figure 2). I do believe, however, that I may have indirectly controlled for several of these variables with the use of other confounders, including childhood SES. For example, variables including childhood adversity have been closely correlated with childhood SES (Suglia et al., 2022). If I had been able to adjust for all variables within my theoretical model, it is hypothesized that I would have seen a slightly less strong effect after adjustment.

Recommendations for Future Research

Recommendations for future research include studying the non-linearity of the effect of education on cognition. To adjust for selective dropout, future studies could use inverse probability of censoring weighting. Future research can also further investigate the impact of web-based versus oral presentation of cognitive tests. Web-based tests were offered beginning in 2018, so this would be important for future studies investigating episodic memory using HRS. Further, by not using missing data measures within the regression analyses, those that were not included in the model would not have been included in the descriptive statistics or the confounder-adjusted effect estimates. Thus, future studies could utilize missing data measures (e.g., multiple imputation) to minimize information loss and to mitigate bias. In addition, I observed an exposure-mediator interaction in analyses. This means that the direct effect varies across values of education and education is an effect modifier of the association between gender and episodic memory. Therefore, future papers should investigate this by estimating the pure natural direct effect (PNDE), total natural direct effect (TNDE), pure natural indirect effect (PNIE), and the total natural indirect effect (TNIE). Next, considering universities often accepted more male applicants during the early-mid 1900s (Parker, 2015), it may be beneficial to consider using policy as an instrument to examine the association between education and late life memory in future research. Finally, to address the dependence of the repeated measurements of episodic memory, I used a linear mixed-effects model. However, there is a possibility that memory performance will be correlated within the same household. Thus, considering I clustered these observations, it would be beneficial to further investigate this topic in future research.

Clinical Relevance

With the significant burden of dementia globally, it is important to further our knowledge into this devastating illness. By being aware of the risk factors and sociodemographic variables that increase the risk of dementia onset, we can better aim to reduce the disparities and prevalence. To my knowledge, this is the first study to investigate education as a mediator of the gender differences in episodic memory, while encompassing childhood SES, race, ethnicity, and birth year as effect modifiers of these associations. In this study, I have shown that increased years of education are protective of dementia, and race, ethnicity, and birth year all impact the association between education and episodic memory. Further, I have shown education is a significant mediator of the association between gender and episodic memory, and that women would have had an even higher recall score than men (on average) if they would have had the same average years of education. By educating individuals on risk factors associated with dementia onset, we can aim to help others in reducing their risk.

Conclusion

In conclusion, I aimed to investigate education as a mediator of gender differences in cognitive functioning using longitudinal data from the U.S. HRS. In my analyses, I found education to be a significant mediator of the association between gender and episodic memory. I also found race to be a significant effect modifier of the association between gender and years of education, as well as race, ethnicity, and birth year to be significant effect modifiers in the relationship between education and episodic memory. All direct and total effects were positive across the mediation analyses, indicating that women had a higher immediate and delayed recall score across all racial and ethnic groups for all listed birth years, both before and after adjustment for education. The indirect effects were negative in those who identified as White and other race, indicating that women recalled fewer words in comparison to men, because they had fewer years of education. Finally, the indirect effects were positive in those who identified as Black and African American, indicating that women recalled more words in comparison to men, because they had more years of education. With this information and investigation into the gender differences in dementia and the mediating role of education, we now have additional information into the risk factors associated with dementia, can strive to learn more, and aim to reduce the disparities associated with this devastating illness.

References

Aggio, D., Smith, L., & Hamer, M. (2018, Jan). Early life cognitive function and health behaviours in late childhood: testing the neuroselection hypothesis. *J Epidemiol Community Health, 72*(1), 41-46. https://doi.org/10.1136/jech-2017-208896

Amao, S.R., & Gbadamosi, J. (2015). Gender disparities and socio-economic factors on learning achievements in agricultural science in rural and urban secondary schools of Ogbomoso north local government area Oyo State, Nigeria. Journal of Education and Practice, 6(25).

Aro, T., Eklund, K., Eloranta, A. K., Närhi, V., Korhonen, E., & Ahonen, T. (2019). Associations Between Childhood Learning Disabilities and Adult-Age Mental Health Problems, Lack of Education, and Unemployment. *Journal of learning disabilities*, *52*(1), 71–83. https://doi.org/10.1177/0022219418775118

Azad, N. A., Al Bugami, M., & Loy-English, I. (2007). Gender differences in dementia risk factors. *Gender medicine*, *4*(2), 120–129. https://doi.org/10.1016/s1550-8579(07)80026-x

Beagan, B. L., & Etowa, J. (2009). The Impact of Everyday Racism on the Occupations of African Canadian Women. *Canadian Journal of Occupational Therapy, 76*(4), 285-293. https://doi.org/10.1177/000841740907600407

Bellis, M. A., Hughes, K., Ford, K., Hardcastle, K. A., Sharp, C. A., Wood, S., Homolova, L., & Davies, A. (2018, Jun 26). Adverse childhood experiences and sources of childhood resilience: a retrospective study of their combined relationships with child health and educational attendance. *BMC Public Health, 18*(1), 792. https://doi.org/10.1186/s12889-018-5699-8

Bennett, E. E., Kwan, A., Gianattasio, K. Z., Engelman, B., Dowling, N. M., & Power, M. C. (2021). Estimation of dementia prevalence at the local level in the United States. *Alzheimers Dement (N Y), 7*(1), e12237. https://doi.org/10.1002/trc2.12237

Beydoun, M. A., Weiss, J., Beydoun, H. A., Fanelli-Kuczmarski, M. T., Hossain, S., El-Hajj, Z. W., Evans, M. K., & Zonderman, A. B. (2022). Pathways explaining racial/ethnic disparities in incident all-cause and Alzheimer's disease dementia among older US men and women. *Alzheimers Dement (N Y), 8*(1), e12275. https://doi.org/10.1002/trc2.12275.

Boraxbekk, C. J., Lundquist, A., Nordin, A., Nyberg, L., Nilsson, L. G., & Adolfsson, R. (2015, May-Aug). Free Recall Episodic Memory Performance Predicts Dementia Ten Years prior to Clinical Diagnosis: Findings from the Betula Longitudinal Study. *Dement Geriatr Cogn Dis Extra, 5*(2), 191-202. https://doi.org/10.1159/000381535

Boydroyzlova, Y., Kim, A., Michaud, X., Andre, C., Belanger, E., & Moullec, G. (2022, June 9). Social class and the risk of dementia: A systematic review and meta-analysis of the prospective longitudinal studies. *Scandinavian Journal of Public Health, 1*(51)1-14. https://doi.org/10.1177/14034948221110019

Bugliari, D., Carroll, J., Hayden, O., Haynes, J., Hurd, M., Karabatakis, A., Main, R., Mccullough, C., Meijer, E., Moldoff, M., Pantoja, P., Rohwedder, S., & Clair, P. (2022). RAND HRS Longitudinal File 2018 (V2) Documentation. *RAND Corporation.*

Burgin, D., Boonmann, C., Schmid, M., Tripp, P., & O'Donovan, A. (2020). Fact or artefact? Childhood adversity and adulthood trauma in the U.S. population-based Health and Retirement Study. Eur J Psychotraumatol, 11(1), 1721146. https://doi.org/10.1080/20008198.2020.1721146

Centers for Disease Control and Prevention (2019). Minorities and Women Are at Greater Risk for Alzheimer's Disease. Retrieved from https://www.cdc.gov/aging/publications/features/Alz-Greater-Risk.html

Cha, H., Farina, M. P., & Hayward, M. D. (2021, Sep). Socioeconomic status across the life course and dementia-status life expectancy among older Americans. *SSM Popul Health, 15*, 100921. https://doi.org/10.1016/j.ssmph.2021.100921

Chang, C. D. (2019, Jan). Social Determinants of Health and Health Disparities Among Immigrants and their Children. *Curr Probl Pediatr Adolesc Health Care, 49*(1), 23-30. https://doi.org/10.1016/j.cppeds.2018.11.009

Clouston, S. A. P., Smith, D. M., Mukherjee, S., Zhang, Y., Hou, W., Link, B. G., & Richards, M. (2020, Aug 13). Education and Cognitive Decline: An Integrative Analysis of Global Longitudinal Studies of Cognitive Aging. *J Gerontol B Psychol Sci Soc Sci, 75*(7), e151-e160. https://doi.org/10.1093/geronb/gbz053

Corley, J., Gow, A. J., Starr, J. M., & Deary, I. J. (2012, Aug). Smoking, childhood IQ, and cognitive function in old age. *J Psychosom Res, 73*(2), 132-138. https://doi.org/10.1016/j.jpsychores.2012.03.006

Crimmins, E. M., Kim, J. K., Langa, K. M., & Weir, D. R. (2011). Assessment of cognition using surveys and neuropsychological assessment: the Health and Retirement Study and the Aging, Demographics, and Memory Study. *Journals of Gerontology Series B: Psychological Sciences and Social Sciences, 66*(suppl_1), i162-i171. https://doi.org/10.1093/geronb/gbr048.

Crimmins, E., Hayward, M., & Seeman, T. (2004). *Critical Perspectives on Racial and Ethnic Differences in Health in Late Life*. Washington D.C.: The National Academics Press. https://doi.org/10.17226/11086

Diaz-Venegas, C., Downer, B., Langa, K. M., & Wong, R. (2016, Sep). Racial and ethnic differences in cognitive function among older adults in the USA. *Int J Geriatr Psychiatry, 31*(9), 1004-1012. https://doi.org/10.1002/gps.4410

Ding, X., Barban, N., Tropf, F. C., & Mills, M. C. (2019, Oct). The relationship between cognitive decline and a genetic predictor of educational attainment. *Soc Sci Med, 239*, 112549. https://doi.org/10.1016/j.socscimed.2019.112549

Duong, S., Patel, T., & Chang, F. (2017, Mar-Apr). Dementia: What pharmacists need to know. *Can Pharm J (Ott), 150*(2), 118-129. https://doi.org/10.1177/1715163517690745

Esteve, A., García-Román, J., & Permanyer, I. (2012). The Gender-Gap Reversal in Education and Its Effect on Union Formation: The End of Hypergamy? *Population and Development Review, 38*(3), 535-546. https://doi.org/10.1111/j.1728-4457.2012.00515.x

Fletcher, J., Topping, M., Zheng, F., & Lu, Q. (2021, Jul). The effects of education on cognition in older age: Evidence from genotyped Siblings. *Soc Sci Med, 280*, 114044. https://doi.org/10.1016/j.socscimed.2021.114044

Ford, K. J., Kobayashi, L. C., & Leist, A. K. (2022, Aug 11). Childhood Socioeconomic Disadvantage and Pathways to Memory Performance in Mid to Late Adulthood: What Matters Most? *J Gerontol B Psychol Sci Soc Sci, 77*(8), 1478-1489. https://doi.org/10.1093/geronb/gbac075

Ford K.J. &, Leist, A.K. (2021). Returns to Educational and Occupational Attainment in Cognitive Performance for Middle-Aged South Korean Men and Women. *Gerontology and Geriatric Medicine*. 7, 1-12. https://doi.org/10.1177/23337214211004366

GBD 2019 Dementia Forecasting Collaborators. (2022, Feb). Estimation of the global prevalence of dementia in 2019 and forecasted prevalence in 2050: an analysis for the Global Burden of Disease Study 2019. *Lancet Public Health, 7*(2), e105-e125. https://doi.org/10.1016/S2468-2667(21)00249-8

Gluhm, S., Goldstein, J., Loc, K., Colt, A., Liew, C. V., & Corey-Bloom, J. (2013). Cognitive performance on the mini-mental state examination and the Montreal cognitive assessment across the healthy adult lifespan. *Cognitive and behavioral neurology: official journal of the Society for Behavioral and Cognitive Neurology*, *26*(1), 1–5. https://doi.org/10.1097/WNN.0b013e31828b7d26

Greenfield, E. A., Moorman, S., & Rieger, A. (2021, Jun 14). Life Course Pathways From Childhood Socioeconomic Status to Later-Life Cognition: Evidence From the Wisconsin Longitudinal Study. *J Gerontol B Psychol Sci Soc Sci, 76*(6), 1206-1217. https://doi.org/10.1093/geronb/gbaa062

Gross, A. L., Mungas, D. M., Crane, P. K., Gibbons, L. E., MacKay-Brandt, A., Manly, J. J., Mukherjee, S., Romero, H., Sachs, B., Thomas, M., Potter, G. G., & Jones, R. N. (2015, Dec). Effects of education and race on cognitive decline: An integrative study of generalizability versus study-specific results. *Psychol Aging, 30*(4), 863-880. https://doi.org/10.1037/pag0000032.

Hale, J. M., Bijlsma, M. J., & Lorenti, A. (2021, Sep). Does postponing retirement affect cognitive function? A counterfactual experiment to disentangle life course risk factors. *SSM Popul Health, 15*, 100855. https://doi.org/10.1016/j.ssmph.2021.100855

Hale, J. M., Schneider, D. C., Mehta, N. K., & Myrskyla, M. (2020, Aug). Cognitive impairment in the U.S.: Lifetime risk, age at onset, and years impaired. *SSM Popul Health, 11*, 100577. https://doi.org/10.1016/j.ssmph.2020.100577

Hasselgren, C., Ekbrand, H., Hallerod, B., Mellqvist Fassberg, M., Zettergren, A., Johansson, L., Skoog, I., & Dellve, L. (2020, Sep 4). Sex differences in dementia: on the potentially mediating effects of educational attainment and experiences of psychological distress. *BMC Psychiatry, 20*(1), 434. https://doi.org/10.1186/s12888-020-02820-9

Health and Retirement Study Staff (2021). Proxy Selection in the Health and Retirement Study. https://hrs.isr.umich.edu/sites/default/files/biblio/Proxy%20selection%20in%20HRS_0.pdf

Health and Retirement Study Staff (2017). Sample Sizes and Response Rates. Health and Retirement Study. https://hrs.isr.umich.edu/sites/default/files/biblio/sampleresponse.pdf

Hillman, A., & Latimer, J. (2017, Mar). Cultural representations of dementia. *PLoS Med, 14*(3), e1002274. https://doi.org/10.1371/journal.pmed.1002274

Hunt, T. K. A., Slack, K. S., & Berger, L. M. (2017, May). Adverse childhood experiences and behavioral problems in middle childhood. *Child Abuse Negl, 67*, 391-402. https://doi.org/10.1016/j.chiabu.2016.11.005

James, B. D., & Bennett, D. A. (2019, Apr 1). Causes and Patterns of Dementia: An Update in the Era of Redefining Alzheimer's Disease. *Annu Rev Public Health, 40*, 65-84. https://doi.org/10.1146/annurev-publhealth-040218-043758

Kim, R., & Chung, W. (2022, Jun 8). Effect of Aging on Educational Differences in the Risk of Cognitive Impairment: A Gender-Specific Analysis Using Korean Longitudinal Study of Aging (2006-2016). *Healthcare (Basel), 10(*6). https://doi.org/10.3390/healthcare10061062

Langa, K. M., Ryan, L. H., McCammon, R. J., Jones, R. N., Manly, J. J., Levine, D. A., Sonnega, A., Farron, M., & Weir, D. R. (2020). The Health and Retirement Study Harmonized Cognitive Assessment Protocol Project: Study Design and Methods. *Neuroepidemiology, 54*(1), 64-74. https://doi.org/10.1159/000503004

Health and Retirement Study, (RAND HRS Longitudinal File 2018 (V2)) public use dataset. Produced and distributed by the University of Michigan with funding from the National Institute on Aging (grant number NIA U01AG009740). Ann Arbor, MI, (July 2022).

LaRue, A., Hermann, B., Wright, N., Dowling, M., & Sager, M. A. (2008). P4-084: Interactive effects of family history of Alzheimer's disease and childhood learning problems on midlife memory performance. *Alzheimer's & Dementia, 4*(4S_Part_21). https://doi.org/10.1016/j.jalz.2008.05.2149

Lindberg, L., Persson, M., Danielsson, P., Hagman, E., & Marcus, C. (2021, Mar 11). Obesity in childhood, socioeconomic status, and completion of 12 or more school years: a prospective cohort study. *BMJ Open, 11*(3), e040432. https://doi.org/10.1136/bmjopen-2020-040432

Liu, H., Zhang, Z., & Zhang, Y. (2021, Aug). A national longitudinal study of marital quality and cognitive decline among older men and women. *Soc Sci Med, 282*, 114151. https://doi.org/10.1016/j.socscimed.2021.114151

Ma, J., Yang, Y., Wan, Y., Shen, C., & Qiu, P. (2021). The influence of childhood adversities on mid to late cognitive function: From the perspective of life course. *PLoS One, 16*(8), e0256297. https://doi.org/10.1371/journal.pone.0256297

Maccora, J., Peters, R., & Anstey, K. J. (2020). What does (low) education mean in terms of dementia risk? A systematic review and meta-analysis highlighting inconsistency in measuring and operationalising education. *SSM-Population Health*, *12*, 100654.

Marden, J. R., Tchetgen Tchetgen, E. J., Kawachi, I., & Glymour, M. M. (2017, Oct 1). Contribution of Socioeconomic Status at 3 Life-Course Periods to Late-Life Memory Function and Decline: Early and Late Predictors of Dementia Risk. *Am J Epidemiol, 186*(7), 805-814. https://doi.org/10.1093/aje/kwx155

McCammon, R., Fisher, G., Hassan, H., Faul, J., Rodgers, W. & Weir, D. (2019, October 11). Health and Retirement Study: Imputation of Cognitive Functioning Measures: 1992-2016. *University of Michigan.* https://hrsdata.isr.umich.edu/sites/default/files/documentation/data-descriptions/1651088507/COGIMP9218_dd.pdf..

McHutchison, C. A., Backhouse, E. V., Cvoro, V., Shenkin, S. D., & Wardlaw, J. M. (2017, Jul). Education, Socioeconomic Status, and Intelligence in Childhood and Stroke Risk in Later Life: A Meta-analysis. *Epidemiology, 28*(4), 608-618. https://doi.org/10.1097/EDE.0000000000000675

Mielke, M. M., Vemuri, P., & Rocca, W. A. (2014). Clinical epidemiology of Alzheimer's disease: assessing sex and gender differences. *Clin Epidemiol, 6*, 37-48. https://doi.org/10.2147/CLEP.S37929

Parker, P. (2015). The Historical Role of Women in Higher Education. *Administrative Issues Journal Education Practice and Research, 5*(1). https://doi.org/10.5929/2015.5.1.1

Peterson, P., & Shakeel, M. A half century of student progress nationwide. *Education Next, 22*(4). https://eric.ed.gov/?id=EJ1359326

Power, M. C., Bennett, E., Ciarleglio, A., Glymour, M. M., Turner, R., Dowling, M., & Gianattasio, K. Z. (2020). Little progress in reducing relative racial disparities in the incidence and prevalence of dementia in the United States, 2000-2016. *Alzheimer's & Dementia, 16*(S10). https://doi.org/10.1002/alz.039905

Psaki, S., Haberland, N., Mensch, B., Woyczynski, L., & Chuang, E. (2022, Mar). Policies and interventions to remove gender-related barriers to girls' school participation and learning in low- and middle-income countries: A systematic review of the evidence. *Campbell Syst Rev, 18*(1), e1207. https://doi.org/10.1002/cl2.1207

Puolakka, E., Pahkala, K., Laitinen, T. T., Magnussen, C. G., Hutri-Kahonen, N., Mannisto, S., Palve, K. S., Tammelin, T., Tossavainen, P., Jokinen, E., Smith, K. J., Laitinen, T., Elovainio, M., Pulkki-Raback, L., Viikari, J. S. A., Raitakari, O. T., & Juonala, M. (2018, May 1). Childhood socioeconomic status and lifetime health behaviors: The Young Finns Study. *Int J Cardiol, 258*, 289-294. https://doi.org/10.1016/j.ijcard.2018.01.088

Rapp, M. A., Schnaider-Beeri, M., Wysocki, M., Guerrero-Berroa, E., Grossman, H. T., Heinz, A., & Haroutunian, V. (2011, Apr). Cognitive decline in patients with dementia as a function of depression. *Am J Geriatr Psychiatry, 19*(4), 357-363. https://doi.org/10.1097/JGP.0b013e3181e898d0

RAND HRS Longitudinal File 2020 (V1). Produced by the RAND Center for the Study of Aging, with funding from the National Institute on Aging and the Social Security Administration. Santa Monica, CA (March 2023).

Reynolds, A., Rolnick, A., & Temple, J. (Eds.). (2015). Health and Education in Early Childhood: Predictors, Interventions, and Policies. *Cambridge: Cambridge University Press.* doi:10.1017/CBO9781139814805

Robinson, K. A., Perez, T., White-Levatich, A., & Linnenbrink-Garcia, L. (2022). Gender Differences and Roles of Two Science Self-Efficacy Beliefs in Predicting Post-College Outcomes. *J Exp Educ, 90*(2), 344-363. https://doi.org/10.1080/00220973.2020.1808944

Rocca, W. A., Mielke, M. M., Vemuri, P., & Miller, V. M. (2014, Oct). Sex and gender differences in the causes of dementia: a narrative review. *Maturitas, 79*(2), 196-201. https://doi.org/10.1016/j.maturitas.2014.05.008

Rockers, P. C., Zuilkowski, S. S., & Fink, G. (2023). Childhood adversity and educational attainment: Evidence from Zambia on the role of personality. *Front Psychol, 14*, 995343. https://doi.org/10.3389/fpsyg.2023.995343

Rouanet, A., Avila-Rieger, J., Dugravot, A., Lespinasse, J., Stuckwisch, R., Merrick, R., Anderson, E., Long, L., Helmer, C., Jacqmin-Gadda, H., Dufouil, C., Judd, S., Manly, J., Sabia, S., Gross, A., & Proust-Lima, C. (2022, Feb 19). How Selection Over Time Contributes to the Inconsistency of the Association Between Sex/Gender and Cognitive Decline Across Cognitive Aging Cohorts. *Am J Epidemiol, 191*(3), 441-452. https://doi.org/10.1093/aje/kwab227

Shang, Roccati, E., Zhu, Z., Kiburg, K., Wang, W., Huang, Y., Zhang, X., Zhang, X., Liu, J., Tang, S., Hu, Y., Ge, Z., Yu, H., & He, M. (2023). Leading mediators of sex differences in the incidence of dementia in community-dwelling adults in the UK Biobank: a retrospective cohort study. *Alzheimer's Research & Therapy*, *15*(1), 7–7. https://doi.org/10.1186/s13195-022-01140-2

Sharp, E. S., & Gatz, M. (2011). Relationship between education and dementia: an updated systematic review. *Alzheimer disease and associated disorders*, *25*(4), 289–304. https://doi.org/10.1097/WAD.0b013e318211c83c.

Smits, L. L., van Harten, A. C., Pijnenburg, Y. A., Koedam, E. L., Bouwman, F. H., Sistermans, N., Reuling, I. E., Prins, N. D., Lemstra, A. W., Scheltens, P., & van der Flier, W. M. (2015, Apr). Trajectories of cognitive decline in different types of dementia. *Psychol Med, 45*(5), 1051-1059. https://doi.org/10.1017/S0033291714002153

Sonnega, A., Faul, J. D., Ofstedal, M. B., Langa, K. M., Phillips, J. W., & Weir, D. R. (2014, Apr). Cohort Profile: the Health and Retirement Study (HRS). *Int J Epidemiol, 43*(2), 576-585. https://doi.org/10.1093/ije/dyu067

Stern, Y., Arenaza-Urquijo, E. M., Bartres-Faz, D., Belleville, S., Cantilon, M., Chetelat, G., Ewers, M., Franzmeier, N., Kempermann, G., Kremen, W. S., Okonkwo, O., Scarmeas, N., Soldan, A., Udeh-Momoh, C., Valenzuela, M., Vemuri, P., Vuoksimaa, E., the Reserve, R., Protective Factors, P. I. A. E. D., & Conceptual Frameworks, W. (2020, Sep). Whitepaper: Defining and investigating cognitive reserve, brain reserve, and brain maintenance. *Alzheimers Dement, 16*(9), 1305-1311. https://doi.org/10.1016/j.jalz.2018.07.219

Suglia, S. F., Saelee, R., Guzman, I. A., Elsenburg, L. K., Clark, C. J., Link, B. G., & Koenen, K. C. (2022, Jun). Child socioeconomic status, childhood adversity and adult socioeconomic status in a nationally representative sample of young adults. *SSM Popul Health, 18*, 101094. https://doi.org/10.1016/j.ssmph.2022.101094

Tingley, D., Yamamoto, T., Hirose, K., Keele, L., & Imai, K. (2014, Aug). Mediation: R Package for Causal Mediation Analysis. *Journal of Statistical Software, 59*(5). doi:10.18637/jss.v059.i05

Walsemann, K. M., & Ailshire, J. A. (2020, May 5). Early Educational Experiences and Trajectories of Cognitive Functioning Among US Adults in Midlife and Later. *Am J Epidemiol, 189*(5), 403-411. https://doi.org/10.1093/aje/kwz276

Wan, Rolls, E. T., Feng, J., & Cheng, W. (2022). Brain functional connectivities that mediate the association between childhood traumatic events, and adult mental health and cognition. *EBioMedicine, 79*, 104002–104002. https://doi.org/10.1016/j.ebiom.2022.104002

Wang, Zhang, H., Rizzo, J. A., & Fang, H. (2018). The Effect of Childhood Health Status on Adult Health in China. *International Journal of Environmental Research and Public Health, 15*(2), 212. https://doi.org/10.3390/ijerph15020212

Williams, A., Lyeo, J.S., Geffros, S. *et al.* The integration of sex and gender considerations in health policymaking: a scoping review. *Int J Equity Health* **20**, 69 (2021). https://doi.org/10.1186/s12939-021-01411-8.

Zarulli, V., Barthold Jones, J. A., Oksuzyan, A., Lindahl-Jacobsen, R., Christensen, K., & Vaupel, J. W. (2018, Jan 23). Women live longer than men even during severe famines and epidemics. *Proc Natl Acad Sci U S A, 115*(4), E832-E840. https://doi.org/10.1073/pnas.1701535115

Zeng, J., Pang, X., Zhang, L., Medina, A., & Rozelle, S. (2014). Gender Inequality in Education in China: A Meta-Regression Analysis. *Contemporary Economic Policy, 32*(2), 474-491. https://doi.org/10.1111/coep.12006

Appendix A: Supplemental Tables and Figures from Analyses

Table A1: Associations between gender, years of education, and the non-linear effect of education on episodic memory in participants of the Health and Retirement Study, 1998-2018

Dependent variable	Model	Independent variable	*β*	95% Confidence interval
Immediate recall	Model 2: adjusted for confounders	Gender	0.5042	(0.4810, 0.5274)
		Education	0.0385	(0.0228, 0.0541)
		Education*Education	0.0043	(0.0036, 0.0050)
Delayed recall	Model 2: adjusted for confounders	Gender	0.0587	(0.5580, 0.6150)
		Education	0.0144	(-0.0047, 0.0336)
		Education*Education	0.0058	(0.0050, 0.0066)

Model 2 was adjusted for birth year, birth year^2, race, ethnicity, childhood SES, and childhood immigration status.

Table A2: Associations between gender, years of education, the non-linear effect of education, and age on episodic memory in participants of the Health and Retirement Study, 1998-2018

Dependent variable	Model	Independent variable	*β*	95% Confidence interval
Immediate recall	Model 1: unadjusted	Gender	0.4785	(0.4552, 0.5019)
		Education	0.0463	(0.0243, 0.0682)
		Education*Education	0.0049	(0.0031, 0.0059)
		Education*Age	0.0012	(0.0002, 0.0022)
		Education*Education*Age	-0.00003	(-0.00008, 0.00001)
Delayed recall	Model 1: unadjusted	Gender	0.5409	(0.5120, 0.5698)
		Education	0.0069	(-0.020, 0.0338)
		Education*Education	0.0072	(0.0060, 0.0084)
		Education*Age	0.0018	(0.0006, 0.0030)
		Education*Education*Age	-0.00006	(-0.00011, -0.000002)

Table A2 (continued)

Immediate recall	Model 2: adjusted for confounders	Gender	0.5055	(0.4820, 0.5289)
		Education	0.0192	(-0.0046, 0.0429)
		Education*Education	0.0051	(0.0040, 0.0061)
		Education*Age	0.0008	(-0.0003, 0.0018)
		Education*Education*Age	-0.00002	(-0.00006, 0.00003)
Delayed recall	Model 2: adjusted for confounders	Gender	0.5873	(0.0559, 0.6160)
		Education	-0.0023	(-0.0310, 0.0265)
		Education*Education	0.0067	(0.0055, 0.0080)
		Education*Age	0.0007	(-0.0005, 0.0020)
		Education*Education*Age	-0.00003	(-0.00009, 0.00003)

Model 2 was adjusted for birth year, birth year^2, race, ethnicity, childhood SES, and childhood immigration status.

Table A3: Associations between gender, years of education, and the cognitive test indicator in participants of the Health and Retirement Study, 1998-2018

Dependent variable	**Model**	**Independent variable**	***β***	**95% Confidence interval**
Immediate recall	Model 2: adjusted for confounders	Gender	0.4835	(0.4401, 0.5269)
		Education	0.1531	(0.1256, 0.1805)
		Education*Cognitive Test Indicator	-0.0279	(-0.0525, -0.0033)

Table A3 (continued)

Delayed recall	Model 2: adjusted for confounders	Gender	0.5721	(0.5193, 0.6248)
		Education	0.1758	(0.1438, 0.2078)
		Education*Cognitive Test Indicator	-0.0302	(-0.0588, -0.0017)

Model 2 was adjusted for birth year, birth year^2, race, ethnicity, childhood SES, and childhood immigration status.

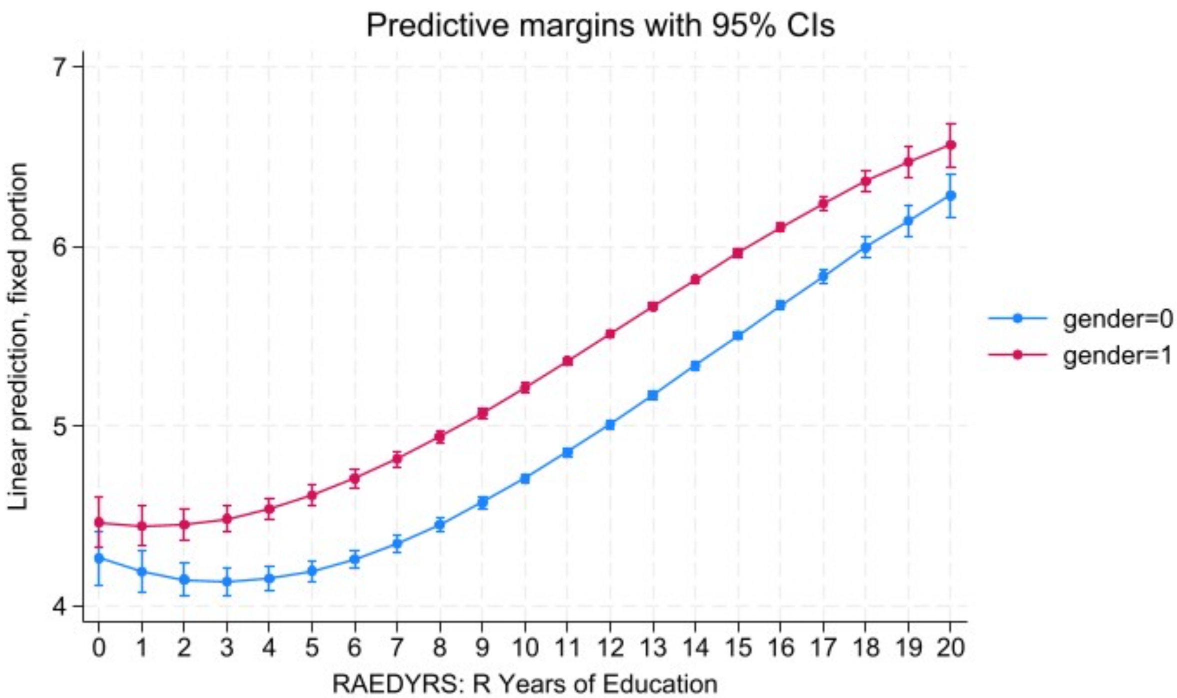

Figure A1: Output from linear mixed-effects model showcasing the coefficients of the association between education and immediate recall

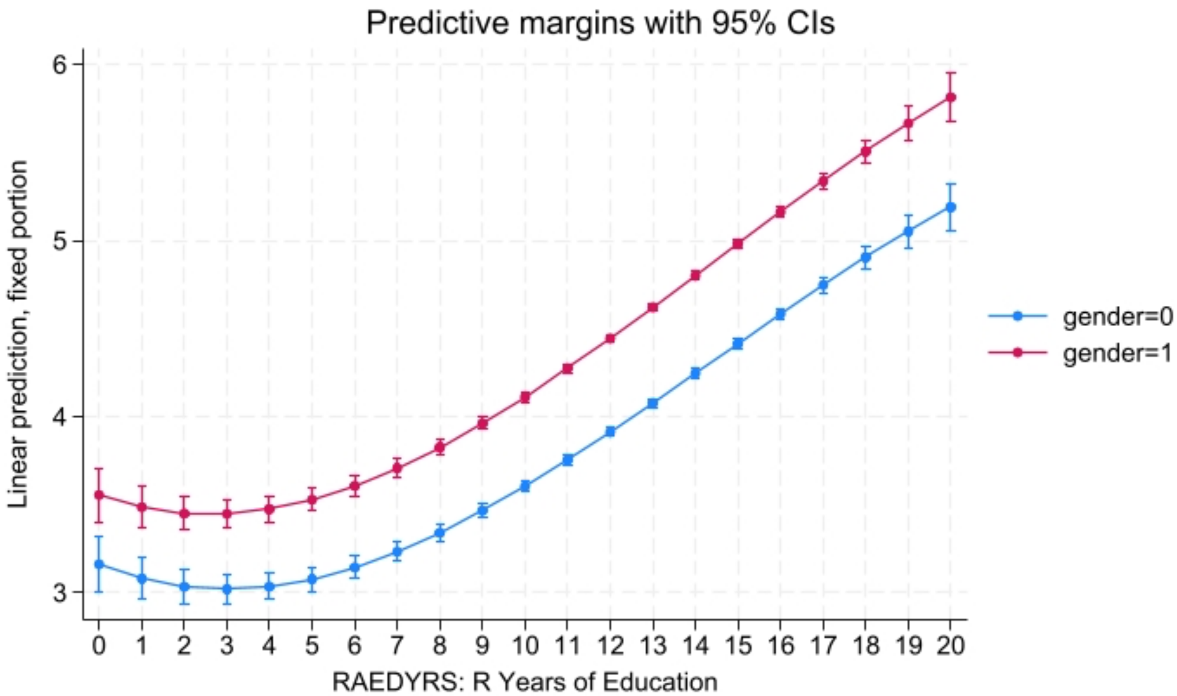

Figure A2: Output from linear mixed-effects model showcasing the coefficients of the association between education and delayed recall

Appendix B: IRB Exemption

UNIVERSITY of SOUTH FLORIDA

NOT HUMAN SUBJECTS RESEARCH DETERMINATION

February 9, 2023

Dear Ms. Sara Robinson:

On 2/9/2023, the IRB reviewed the following protocol:

IRB ID:	STUDY005308
Title:	Education as a Mediator of the Association Between Gender and Cognitive Function

The IRB determined that the proposed activity does not constitute research involving human subjects as defined by DHHS and FDA regulations.

IRB review and approval is not required. This determination applies only to the activities described in the IRB submission. If changes are made and there are questions about whether these activities constitute human subjects research, please submit a new application to the IRB for a determination.

While not requiring IRB approval and oversight, your project activities should be conducted in a manner that is consistent with the ethical principles of your profession. If this project is program evaluation or quality improvement, do not refer to the project as research and do not include the assigned IRB ID or IRB contact information in the consent document or any resulting publications or presentations.

Sincerely,

Myah Luna
IRB Research Compliance Administrator

Institutional Review Boards / Research Integrity & Compliance
FWA No. 00001669
University of South Florida / 3702 Spectrum Blvd., Suite 165 / Tampa, FL 33612 / 813-974-5638