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Examining Education Level Correlation with Cognitive Function Among People with Alzheimer's Disease

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Examining Education Level Correlation with Cognitive Function Among People with Alzheimer's Disease

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APPROVAL PAGE

EXAMINING EDUCATION LEVEL CORRELATION WITH COGNITIVE FUNCTION AMONG PEOPLE WITH ALZHEIMER'S DISEASE

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ABSTRACT

INTRODUCTION: Alzheimer's Disease (AD)is currently listed as the sixth leading cause of death among U.S. adults, killing more people than breast cancer and prostate cancer combined. While the number one risk factor for AD is increasing age, to date, little is known about preventive or protective factors of AD. Continued epidemiologic research that seeks to examine risk and protective factors, such as the role educational attainment plays in cognitive functioning among those with AD may offer important preventive insights.

AIM: The purpose of this study is to examine the correlation between education level and the cognition of persons with AD. An extensive data set was used that collects data from various locations, which will make for more reliable results. Ultimately, the hope is that interventions will be implemented to combat the detection bias due to later diagnosis of dementia (AD) in highly educated persons (Karp et al., 2002).

METHODS: The National Alzheimer's Coordinating Centers (NACC) dataset from (2005-2017) was used to examine associations of cognitive function / impairment with variables related to sample demographics, health history, neuropsychological testing, risk behaviors, and education. Tests of correlation, ordinary least square, and logic regression tests were conducted to examine the relationship between cognitive impairment and educational attainment, along with possible co-variates.

RESULTS: There was a small positive correlation between subjects with an education and MMSE score, ($r=0.2561$, $p < .05$). For a one unit increase in the years of education was associated with a 0.341 (SD, 0.011) increase in MMSE Score. For a change in the education group 13-16 years and education group >16 years there is a 2.056 (SD, 0.090) and a 2.658 (SD, 0.097) unit change in MMSE score respectively. As the continuous education variable increased the AD diagnosis decreased by 0.067 (SD, 0.005). As education group 13-16 and >16 years changed from one group to the other AD diagnosis decreased (-0.488, SD 0.040 and -0.629, SD 0.043).

DISCUSSION: Results from this study may be theoretically explained-that higher educational attainment may be associated with a fundamentally higher cognitive reserve among older adults who have cognitive disorders. The lower likelihood of AD pathology may be associated with higher functioning or potentially a lower diagnosis of AD. The role education plays among older adults with cognitive disorder diagnoses appears to be linked, yet this relationship, with AD pathology in particular, warrants further research attention.

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CHAPTER I

INTRODUCTION

Background

Alzheimer's Disease (AD) is increasingly becoming more of a burden for the United States (US). AD is currently listed as the sixth leading cause of death, killing more people than breast cancer and prostate cancer combined (CDC, 2016). AD is the most common type of dementia, causing memory loss and destroying vital cells. There are currently over 5 million people in the United States living with AD, and this number is projected to increase to 16 million by 2050 unless something changes this trajectory (Alzheimer's Association, 2017).

AD is a significant disability that interrupts the everyday life of the individuals who suffer from its life-altering outcome. A diagnosis of AD means symptoms will steadily intensify over time, which stresses the importance of prevention or early diagnosis. Like other chronic disease, individuals with AD and those providing them with care can learn strategies to cope with the illness to live as comfortable as possible. However, unlike a chronic disease such as diabetes, affected persons are eventually unable to live independently at the point AD becomes so debilitating that others must assist in carrying out basic activities of daily living. Caregivers must ensure safety of those suffering with AD due to memory loss and other tendencies that may arise from cognitive dysfunction such as wandering.

In addition to individual human suffering caused by the disease, AD poses an enormous strain on the health care system, support system members, and the federal budget. In 2017, treatment costs associated with AD and other forms of dementia were an estimated $259 billion, with 67% of

these costs covered by Medicare and/or Medicaid (Alzheimer's Association, 2017). This figure does not include hours dedicated to caregiving, which is estimated to be 18.2 billion work hours valued at $230 billion in compensation. (Alzheimer's Association, 2017)

AD pathology can be present long before the clinical diagnosis. The length of time between pathology and diagnosis differ among groups. Some studies have concluded that higher educated individuals can withstand greater AD pathology before exhibiting symptoms that lead to diagnosis. While the number one risk factor for AD is advancing age, there is no known prevention measures for AD at present. However, there are intervention opportunities to address early symptoms, behavior, and abnormal pathology of AD. Advancing knowledge about risk factors and potential moderating factors for AD, such as understanding the role education may play in buffering cognitive declines associated with AD, public health researchers may work to reveal be able to By knowing more about the cognitive reserve theory and the risk factors it is predicted by, such as education, action can be taken to decrease the prevalence of AD.

Purpose of the Study

Because of aging, many more individuals will be diagnosed with AD, with majority occurring in the elderly. The projected number of people 65 and older in 2050 is 88.5 million (Hebert et al, 2013). Since the aging process cannot be altered, there is critical need to evaluate modifiable factors that could play a role in improving cognition, to enhance the quality of life of this population. Because of the physical and financial burden, there is a dire need for interventions that can assist in improving quality of life through the modifiable factor for AD, such as education.

Studies that have examined potential impacts on buffering cognitive declines among adults with AD and other cognitive disorders have been inconsistent in their findings. In a systematic review that investigated studies focusing on education and survival time post-AD diagnosis failed to find that increased education predictive of decreased survival time (Paradise et al., 2009). In fact, other researchers have reported higher education was found to be correlated to faster cognitive decline among persons with AD (Roe et al., 2007). The purpose of this study is to use the NACC dataset from the National Institute of Aging (NIA), which includes a robust wealth of clinical, physical, psychoneurological data involving 19,820 individuals with a diagnosis of AD and other cognitive diseases. This data source represents data collected from various clinical sites (from 2005 to 2017) and providers of care to individuals meeting eligibility criteria which provides the ability to examine within person cognitive declines over a period of time.

Research Questions

Question #1: Does level of education positively correlate with cognitive function which lowers risk of AD diagnosis?

Null hypothesis: There is no difference in risk of developing AD based on level of educational attainment

Alternative hypothesis: There will be a lower risk of developing AD among persons with higher educational attainment

Question #2: What is the correlation between level of education and cognitive function among people with AD?

Null hypothesis: The correlation between education and cognitive function among people 65 and older with AD will be the same in different education level groups or

There is no correlation between education and cognitive function among people 65 and older with AD

Alternative hypothesis: There is correlation between education and cognitive function among people 65 and older with AD

Question #3: Is education attainment associated with the speed of cognitive decline among persons with an AD diagnosis?

Null Hypothesis: There is no difference in rate of cognitive decline in AD patients based on a gradient of education attainment

Alternative: Greater education is associated with faster cognitive decline in persons with an AD diagnosis

CHAPTER II

REVIEW OF LITERATURE

The following chapter is focused on presenting scientific literature that supports inclusion of the variables of interest to this study. The sections of this chapter are organized to synthesize scientific literature and how researchers have examined educational attainment and other risk factors in relation to cognitive functioning, rates of decline, and diagnosis of AD.

Background

The Alzheimer's Association defines Alzheimer's Disease (AD) as a progressive brain disorder that damages and eventually destroys brain cells, leading to loss of memory, thinking and other brain functions. Dementia is the generic term for the severe decline in mental ability that interferes with daily living, including AD. AD is the most common cause of dementia. AD was first discovered by Alois Alzheimer in 1906 after observing a patient under his care who exhibited strange behavior. Symptoms of AD commonly first appear in persons that are in their mid-60s (NIH, 2016). The knowledge about AD is relatively new as researchers only first knew of the chronic disease in the early 1900s when Alois Alzheimer described it.

The article entitled Use It or Lose It by the Swiss Medical Weekly discusses modifying the risk factor associated with dementia. They are seeking to create a program that will decrease cognitive decline through "motivational interviewing" called Brain Coaching (SWM, 2017). Alzheimer's disease etiology is not well understood. There appears to be a biologic/genetic predisposition for the disease as well as a host of recognized risk factors which include some that are unmodifiable (aging and sex) as well as modifiable such as education, occupation, and lifestyle behaviors. Therefore, with the increased social and economic burden, grossing 818

billion USD worldwide, looking at interventions and better understanding these modifiable risk factor is pertinent to maintaining brain health, delaying cognitive decline, and ultimately decreasing the prevalence of AD.

Biology

Dementia is the general term used to describe the decline in mental ability that interferes with daily life (Alzheimer's Association, 2018). AD is one type of dementia and the most common. Pathology of AD can persist in a person long before (sometimes a decade) the manifestation of clinical diagnosis (NIH, 2016). One may exhibit early signs of dementia that are missed in clinical encounters. Pathologic lesions of AD are thought to accumulate continuously for many years before sufficient brain pathologic alterations, presumably including synaptic and neuronal loss, which are precursors to clinical manifestations (SantaCruz et al., 2011). Clinical AD has specific characteristics that distinguish it from other types of dementia. The natural history of this disease is such that the neurodegenerative lesions (neuritic plaques) neurofibrillary tangles, and β-amyloid deposits develop slowly over time, eventually producing recognizable clinical symptoms (Beelen, 2009). Plaques and tangles play a significant role in symptoms such as memory loss and confusion, as they damage and kill nerve cells. These can be viewed through neuroimaging using magnetic resonance imaging (MRI).

Cognitive Reserve Theory (CRT)

Cognitive reserve theory (CRT) is the concept that a person can withstand brain trauma, such as lesions, caused by various diseases. Reserve is the moderator between the degree of brain damage or pathology and its clinical manifestations (Stern, 2009). Therefore, a person with more reserve should be able to withstand more brain damage before they begin to display any clinical

signs of disease. The concept of brain reserve (BR) is sometimes used interchangeably with CRT, while some researchers prefer to distinguish the two. Cognitive reserve is associated with better quality of life, even among people with AD (Lara et al. 2017).

CRT can be divided into two broad categories of measuring, both passive and active models. The passive model is one that is generalized to all people and has no specific differences from person to person. Meaning that there is nothing a person can do to increase or decrease the amount of reserve stored up. The passive CRT differences are due to brain size or neuronal count, while the active differences relate to neuronal changes, new synapse development, or increased efficiency of processing networks (Beelen, 2009). The passive model uses the theory of brain reserve, which is sometimes used interchangeably with cognitive reserve. It is also described using the threshold model which states that once a person reaches their threshold capacity for coping with brain lesion, then they begin to show clinical symptoms (Stern,2009). The cognitive reserve hypothesis suggests that these active changes develop in response to education and other cognitive stimuli throughout a person's lifetime. The active model, serves as the basis of this study, supports examination of individual cases in regards to modifiable contributing factors for disease. It describes that social, educational, and environmental factors that can influence the amount of cognitive reserve that a person has, which consequently, may impact diagnosis and progression of disease. Previous research has applied the CRT to examine the educational attainment relative to AD disease progression (Scarmeas et al., 2006).

The CRT is applicable to health beyond AD. It has also been studied in Human Immunodeficiency Virus, (HIV) and stroke victims. The reason I have decided to look at it in Alzheimer’s patients is that it allows for better generalization since AD pathology is more likely to affect people similar anatomic sites (Stern, 2002). Whereas in stroke there is more variability

in the outcome of affected anatomy. Another reason being the aging population which was discussed before this section.

The CRT was initially posited as a moderator between brain change and clinical outcome, but there are recent suggestions that life experience may also act to prevent or minimize pathology (Stern,2012). Some of these life experiences include the type of job you had, the highest level of education completed, or the kind of lifestyle you lived. Since there is not a direct method to measure cognitive reserve a proxy must be used, in this case, that will be education level. Education has often been used as a proxy measure for cognitive reserve (Stern, 2012). The relationship between education and the progression of AD has been predicted by the cognitive reserve hypothesis (Scarmeas et al., 2006).

Cognitive Decline (Dependent Variable of Interest)

Cognitive decline can happen at different rates for different people. Most tests used to measure cognition were developed for persons with several years of education (Demier et al., 2014). Therefore, these tests may not be the best choice for detecting dementia for person with little to no formal education. Researchers recommended that increasing the cutoff point on the Mini-Mental State Examination (MMSE) for highly educated populations from a score of 24 to 27 as a more sensitive threshold of detecting cognitive impairment (O'Bryant et. al, 2009). The MMSE is a simplified version of the Cognitive Mental State Examination (Folstein et. al, 1975). This tool is used to systematically detect cognitive impairment. The examination includes eleven questions/ activities related to the person orientation, registration, attention and calculation, recall, and language ad praxis. Each category has a specific number of points allowed for it, with detailed instructions on how to go about the scoring. The maximum number of points that can be earned is

30. Cutoff scores are determined prior to testing to avoid any bias. The MMSE has been used since 1975, when it was created, in both research and clinical settings (Folstein et. al, 1975). The MMSE is appropriate for serial use and is valid in showing changes in clinical state over time.

Risk Factors (Independent Variables of Interest)

Scientific understanding of patterns of risk relative to AD is continually advancing. Risk factors for AD include non-modifiable and modifiable characteristics. A summary of research on select risk factors examined within the context of this study are presented in the section that follows.

Aging

Although AD is not a part of normal aging, increasing age is the most significant risk factor for the disease (Alzheimer's Association, 2013). Forty-seven million or 15 percent of the US population is 65 years and older (CDC, 2017). Aging is medically defined as the explanation of dying cells and the decrease rate of new cells. As people grow older, aging begins to occur in their brain, such as fewer synapses and decreasing cell regeneration. The likelihood of an AD diagnosis doubles every five years after the age of 65 (Alzheimer's Association, 2017). Aging is a predictor of AD regardless of education level (Bowler et al., 1998).

Education

Education influences a person's life in many ways. This factor also affects how and when they will present with AD, their clinical course, and how we can best diagnose this disorder (Beelen, 2009). Education is used to as a modifier of the link between brain pathology and cognitive function (Boots et al., 2015). Education can introduce you to opportunities that determine a person's lifestyle, socioeconomic status, and your cognition (Pampel et al., 2010). Research has

indicated that higher levels of education have been associated with reduced risk of AD in old age (Wilson et al., 2004).

However, research that has examined education level within the context of AD has been inconsistent. A study by Stern and colleagues (1999) reported that individuals with AD had faster cognitive declines after diagnosis than those with less education (Stern et al., 1999). Conversely, a later study found slower rates of decline among AD patients with higher levels of education (Scarmeas et al., 2006). Paradise and colleagues concluded that higher education did not lead to shorter survival after diagnosis (Paradise et al., 2009). Another paper stated that people with higher education have a higher cognitive function with AD (O'Bryant et al., 2004).

Lifestyle

Lifestyle behaviors and exposures that may impact a diagnosis of AD and its progression may include diet, drinking or smoking behaviors, and relationship status. Marital status was examined as a measure for lifestyle.

Summary

According to the Centers for Disease Control, AD is the sixth leading cause of death. Higher education is linked to higher socioeconomic status which may translate into greater accessibility of health care resources; however, whether or not it is a protective factors from AD is not understood (Bruandet et al., 2007). This study is designed to examine education and a number of personal risk factors (representative of the theoretical construct cognitive reserves) to determine their association with AD diagnosis and rate of cognitive decline among a sample of adults with disordered cognition.

CHAPTER III
METHODOLOGY

This section describes the methods used to research questions of this study. This study examines longitudinal data collected among adults with a diagnosed cognitive disorder regarding health status and functioning. used a longitudinal design to assess the correlation between education and cognitive function in persons with cognitive impairment.

Data Source and Study Population

Secondary data utilized in this study was obtained upon request from the National Alzheimer's Coordinating Centers (NACC) Uniform Data Set (UDS). The National Institute of Aging (NIA) appointed the clinical task force to standardize the data collection process. The NACC database is one of the largest and most comprehensive databases of its kind, maintaining records over 36,500 enrolled subjects (NACC, 2018). Data is collected from 29 Alzheimer's Disease Centers (ADCs) across the US (Beekly et al., 2007). These centers conduct clinical and laboratory research on the cause and clinical course of AD (Koepsell, et al. 2008). The NACC maintains three distinct data and surveillance efforts-the Minimum Data Set (MDS), Neuropathology Data Set (NDS), and the Uniform Data Set. Data for this study stems from the UDS which was established September 2005. The UDS provides researchers a standard set of assessment procedures collected longitudinally from initial to final visit (Beekly et al., 2007). This data set provides the characteristics of ADC patients who may present mild AD and cognitive impairment but it also includes control cases (individuals without a dementia diagnosis).

Data were collected prospectively by clinicians, neuropsychologists, and other ADC researchers, using standardized forms for each visit. Once the initial visit was completed,

subjects were followed-up on an annual basis or at a major clinical milestone event, such as AD diagnosis or death. Incident cases of AD were diagnosed by a clinician based on National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association (NINCDS/ADRDA) criteria and National Institute on Aging and Alzheimer's Association NIA-AA criteria.

Eligibility Criteria/Sample Selection

Subjects were enrolled into the research study based on the ADCs own protocol, which differs between centers. Subjects where recruited either by physician referral, self-referral by patient or family, active community recruitment, or volunteers. Written informed consent was obtained for each subject. The dataset utilized in this study included 91,211 observations pertaining to 19,802 unique IDs. Subjects were excluded if they did not complete six or more visits or AD was not the primary disease diagnosis following the initial visit. To be included in the analysis, designation of the minimum baseline age as 65 years old or older was set because this is the recognized age cut-point associated with the greatest risk for AD diagnosis.

Study Measures

Study measures included in the UDS pertain to demographics, health history, physical, neuropsychological batteries, clinical diagnosis, and genetic information. The analytic plan for the primary research questions of this study focus on AD, cognition, and education. Other co-variates for ad-hoc analyses include stroke, hypertension, diabetes, smoking, drinking, marital status, and APOE genotype.

Outcome: Cognitive Function/Decline

Cognitive status was reported at the initial visit and each follow up visit. The data was transposed from long format to wide format so that cognitive function could be observed longitudinally for each subject. Cognitive decline was measured using both a continuous variable (Raw Score from the MMSE) and a categorical variable (3-point decline MMSE). The MMSE had an allowable score of 0-30, with a cutoff point of 27 or greater for persons with no cognitive impairment. A cognitive decline over time was defined as a decrease of 3 points on the MMSE between the first and second visits. The cognitive status was reported at each visit.

Predictor: Education

Education was reported as a whole number ranging from 0-36 for possible answers at the initial visit. This only includes years of completed education. Education was analyzed both continuously and categorically. For the categorical analysis education was separated into three categories which were, less than high school diploma, high school diploma, college graduate/professional degree. When analyzed continuously, thresholds were established to align with levels of education, specifically: 12=high school, 18=master's degree, and 20=doctorate.

Age

Age was reported as a whole number in years at the initial and follow-up visits (derived from self-reported month and date of birth on initial visit form). Subjects that did not meet the age minimum of 65 years old at baseline were excluded from study analyses.

AD

Two variables captured Alzheimer's Disease etiologic diagnosis. The first variable (NACCALZD) is a presumptive diagnosis of the cognitive disorder, that says whether the subject has normal cognition, cognitive impairment without AD, or cognitive impairment and AD. Criteria for diagnosis varies between the versions of the form used at the time the assessment was completed. Versions 1.2 and 2 used NINCDC/ADRDA and version 3 used the NIA-AA criteria, which only have subtle differences. The second variable (NACCALZP) determines whether AD is the primary, contributing, or non-contributing cause of the observed cognitive impairment. Eligibility criteria for the purpose of this research was limited to subjects with AD as the primary cause of cognitive impairment. Diagnosis was made by a single or team of physicians which varies according to each ADC's protocol.

Co-variates

Numerous covariates were included in the study analysis that aligned with elements described by the CRT. These covariates include age, race, hypertension, diabetes, stroke, alcoholism, smoking tobacco, marital status, and APOE genotype.

Statistical Analysis

The truncating and organization of the data for this paper was completed using SAS software, Version 9.4 of the SAS system for Windows. Copyright © SAS Institute Inc. Data from SAS were converted and study analysis was completed in Stata (StataCorp 2013).

Descriptive frequencies were performed for demographic information including, sex, age, and race, education, as well as vascular disease, drinking, and smoking variables. For continuous variables means and standard deviation values were calculated. Correlation coefficients were calculated to examine the relationship of education with MMSE scores and cognitive decline,

respectively. Ordinary least squares (OLS) regressions were performed to examine education continuously and categorically-with the continuous outcome MMSE score, as well as to determine possible covariates interactions. Logistic (Logit) regression was performed to examine education (continuously and categorically) with the categorical outcome of AD diagnosis. OLS and Logit regressions were done to observe patterns of continuous decline or a categorical 3-point/4-point decline, respectively. For all the analysis performed a p-value of 0.05 and confidence level of 95% was used to determine statistical significance.

CHAPTER IV

RESULTS

This section is dedicated to answering the research questions based on the analysis that was performed.

Sample Characteristics

The total sample of the NACC study participants that met the eligibility criteria was 19,802. The analysis did not limit cases to those with a primary cognitive disorder diagnosis of AD, which would limit the ability to observe incident cases of AD. The overall study sample in terms of distribution of age, race, sex, education and select clinical characteristics as measured at baseline are presented in Table 1.

More females were included in the dataset, representing 56% of the study sample compared to 43% males. About 50% of the sample was between the ages of 65 and 75. Eighty-two percent of the participants identified themselves as Whites, while Blacks, Asian, and Others together represented about 15% of the sample population. Nearly half of the sample reported having a college education (40.1%). A small percentage of subjects reported having diabetes or stroke, 13.25% and 5.39% respectively. Over half reported having hypertension, whether recent/active or remote/inactive (55.23%). The average MMSE score at baseline was 25.87 (SD, 5.16)

Table 1. Baseline Study Sample Profile

Baseline Characteristics	No. Subjects	Percentages
Sex		
Male	8,664	43.25
Female	11,138	56.25
Age		
65-75	9,950	50.25
76-85	7,883	39.81
>85	1,969	9.94
Race	missing=53	
White	16,235	81.99
Black or African American	2,669	13.63
Asian	421	2.13
Other	384	2
Education (Years)	missing=86	
Continuous (Mean)		15.11 (3.48)
<=12	5,275	26.64
13-16	7,937	40.08
>16	6,504	32.85
MMSE Score at Baseline (mean, SD)	25.87 (5.16)	
APOE e4 Carriers	6,512	32.88
Hypertension	10,937	55.23
Diabetes	2,624	13.25
Stroke	10,204	5.39
Alcoholism	942	4.76
Smoking	9, 191	46.41

Correlation

A Pearson's correlation was run to assess the relationship between education and cognitive function/decline, AD diagnosis, number of days from initial to follow up, and number of visits. These variables are listed below in Table 2. Of highest importance is the relationship between education and cognitive function, which was predicted by the MMSE scores. There was a small positive correlation between subjects with an education and MMSE score, ($r=0.2561$, $p < .05$).

Table 2. Correlation Matrix of Education with Cognitive Function, Decline and AD Diagnosis

Parameters	MMSE Score	MMSE Decline	Days from Initial to Final	Number of Visits	Education Cont.
MMSE Score	1				
MMSE Decline	-0.1564	1			
Dyas from Initial to Final	0.2679	-0.1718	1		
Number of Visits	0.2693	-0.1757	0.9553	1	
Education Cont.	0.2561	-0.0336	0.0726	0.0815	1

*P-value <0.05

Association of Education and Cognitive Function/Decline

Linear Regression

Tables 3, 4, and 5 displays the results of the association between education (continuously and categorically) and MMSE score, education and MMSE decline, and education and days/visits completed, controlling for age, sex, race, marital status, hypertension, diabetes, alcoholism, smoking, APOE genotype, and stroke. Results were found statistically significant at a *p*-value <0.05.

All educational groups were found to be statistically significant for its association with MMSE score (Table 3). For a one unit increase in the years of education was associated with a 0.341 (SD, 0.011) increase in MMSE Score. For a one unit increase in the education group 13-16 years and education group >16 years there is a 2.056 (SD, 0.090) and a 2.658 (SD, 0.097) unit change in MMSE score respectively. Among the variables being controlled for they were all statistically significant for an association with MMSE for the models with continuous education in years and

grouped education in years except one. All races (Blacks, Asian, and Others) had a negative association with MMSE score, -0.338 (SD, 0.110) -0.396 (SD, 0.110), -0.082 (0.268), and -3.052 (SD ,0.263) (grouped education in years only), respectively for continuous and categorical education. Positive indications of stroke, APOE genotype, smoking, and alcoholism had lower MMSE scores. Hypertension however had a positive association for recent/active subjects and a negative association for remote/inactive subjects. For a one unit change in recent/active hypertension there was a 0.411 (SD, 0.075) unit change in MMSE score in the continuous education model, and a 0.038 (SD, 0.076) for the categorical education model. The difference between the coefficients between the two models was very small or almost the same. There was no statistical association found between Diabetes and MMSE score.

Table 4 had a statistically significant negative association for education in years (both models) and MMSE decline. For a one unit increase in the years of education was associated with a 0.029 (SD, 0.007) decrease in MMSE decline. For a one unit increase in the education group 13-16 years and education group >16 years there was a 0.242 (SD, 0.054) and a 0.304 (SD, 0.058) unit decrease in MMSE decline respectively. Diabetes, alcoholism, and smoking and associated MMSE declines were not found to be statistically significant. Blacks or African American were the only race that had a statistically significant association with MMSE decline (-0.146, SD 0.066). Hypertension however had a negative association for recent/active subjects and a positive association for remote/inactive subjects. For a one unit change in recent/active hypertension there was a -0.102 (SD, 0.045) unit change in MMSE decline in the continuous education model, and a 0.104 (SD, 0.045) for the categorical education model.

Table 3. Linear Regression Results for Education and MMSE Score Association

Predictors	MMSE Score (1)	MMSE Score (2)
Education (Continuous) (1)	0.341*** (0.011)	
Education 13-16 (2)		2.056*** (0.090)
Education >16 (2)		2.658*** (0.097)
Age >65	-0.095*** (0.005)	-0.096*** (0.005)
Male	-0.780***(0.076)	-0.659*** (0.076)
Black or AA	-0.338***(0.110)	-0.396*** (0.110)
Asian	-0.206 (0.267)	-0.082 (0.268)
Other	-2.392 (0.265)	-3.052*** (0.263)
Married	0.187*** (0.029)	0.182*** (0.029)
Hypertension (Recent/Active)	0.411*** (0.075)	0.388*** (0.076)
Hypertension (Remote/Inactive)	-1.364*** (0.213)	-1.335*** (0.214)
Diabetes (Recent/Active)	-0.087 (0.111)	-0.146 (0.111)
Diabetes (Remote/Inactive)	-0.004 (0.488)	-0.013 (0.490)
Alcoholism (Recent/Active)	-.940** (0.390)	-0.929** (0.392)
Alcoholism (Remote/Inactive)	-1.186*** (0.184)	-1.225*** (0.185)
Smoking	0.520*** (0.072)	0.486*** (0.073)
APOE (e3,e4)	-1.584*** (0.088)	-1.571*** (0.088)
APOE (e4,e4)	-3.445*** (0.166)	-3.426*** (0.166)
APOE (e4,e2)	-0.756*** (0.241)	-0.695*** (0.242)
Stroke (Recent/Active)	-0.994*** (0.328)	-1.077*** (0.329)
Stroke (Remote/Inactive)	-1.055*** (0.182)	-1.092*** (0.183)
R-Squares	0.146	0.139

Standard Errors reported in parentheses

*=p<0.1, **<0.05, ***p<0.01 , AA=African American N=17,619

Table 4. Linear Regression Results for Education and Decline in MMSE Association

Predictors	Decline in MMSE (1)	Decline in MMSE (2)
Education (Continuous) (1)	-0.029*** (0.007)	
Education 13-16 (2)		-0.242*** (0.054)
Education >16 (2)		-0.304*** (0.058)
Age >65	0.014*** (0.003)	0.013*** (0.003)
Male	0.143*** (0.046)	0.142*** (0.046)
Black or AA	-0.146** (0.066)	-0.152** (0.066
Asian	-0.233 (0.160)	-0.235 (0.160)
Other	-0.261 (0.164)	-0.234 (0.161)
Married	-0.100*** (0.018)	-0.099*** (0.018)
Hypertension (Recent/Active)	-0.102** (0.045)	-0.104** (0.045)
Hypertension (Remote/Inactive)	0.256* (0.132)	0.246* (0.132)
Diabetes (Recent/Active)	0.091 (0.067)	0.090 (0.067)
Diabetes (Remote/Inactive)	0.390 (0.298)	0.384 (0.298)
Alcoholism (Recent/Active)	-0.065 (0.236)	-0.073 (0.236)
Alcoholism (Remote/Inactive)	0.167 (0.112)	0.162 (0.112)
Smoking	-0.063 (0.044)	-0.060 (0.044)
APOE (e3,e4)	0.511*** (0.053)	0.508*** (0.053)
APOE (e4,e4)	1.244*** (0.101)	1.241*** (0.101)
APOE (e4,e2)	0.272* (0.145)	0.270* (0.145)
Stroke (Recent/Active)	0.009 (0.196)	0.015 (0.196)
Stroke (Remote/Inactive)	0.236*** (0.110)	0.232*** (0.110)
R-Squares	0.027	0.028

Standard Errors reported in parentheses

*=p<0.1, **<0.05, ***p<0.01 , AA=African American N=16,074

Table 5. Linear Regression Results for Education and Days Visited Association

Predictors	Days from Baseline to Final	Days from Baseline to Final	Number of Visits	Number of Visits
Education (Continuous) (1)	17.408*** (2.264)		0.046*** (0.006)	
Education 13-16 (2)		133.190** (18.650)		0.354*** (0.046)
Education >16 (2)		188.743** (19.921)		0.482*** (0.0490
Age >65	-7.136*** (1.072)	-6.873*** (1.071)	-0.015*** (0.003)	-0.014*** (0.003)
Male	-118.823*** (15.731)	-119.173*** (15.677)	-0237*** (0.039)	-0.235*** (0.039)
Black or AA	84.449*** (22.686)	88.326*** (22.654)	0.140** (0.056)	0.149*** (0.056)
Asian	-57.915 (51.069)	-56.704 (51.010)	-0.150 (0.126)	-0.145 (0.126)
Other	-36.252 (54.210)	-52.669 (53.562)	-0.154 (0.134)	-0.201 (0.132)
Married	10.361*(5.994)	9.209 (5.997)	0.011 (0.015)	0.008 (0.015)
Hypertension (Recent/Active)	-16.545 (15.524)	-15.476 (15.507)	-0.040 (0.038)	-0.038 (0.038)
Hypertension (Remote/Inactive)	-96.728** (44.207)	-91.018** (44.180)	-0.323*** (0.109)	-0.309*** (0.109)
Diabetes (Recent/Active)	-119.621*** (22.908)	-118.444*** (22.875)	-0.288*** (0.056)	-0.286*** (0.056)
Diabetes (Remote/Inactive)	-204.619** (98.044)	-200.292** (97.969)	-0.506** (0.242)	-0.496*** (0.242)
Alcoholism (Recent/Active)	-39.624 (82.830)	-35.527 (82.764)	-0.173 (0.204)	-0.162 (0.204)
Alcoholism (Remote/Inactive)	-167.832*** (38.409)	-165.050*** (38.376)	-0.359*** (0.095)	-0.353*** (0.095)
Smoking	-5.939 (14.913)	-6.321 (14.918)	0.000 (0.037)	-0.002 (0.037)
APOE (e3,e4)	-120.582*** (18.341)	-118.685*** (18.329)	-0.319*** (0.045)	-0.313*** (0.045)
APOE (e4,e4)	-262.193*** (34.631)	-260.256*** (34.604)	-0.627*** (0.085)	-0.622*** (0.085)
APOE (e4,e2)	-74.578 (50.005)	-71.645 (49.960)	-0.191 (0.123)	-0.183 (0.123)
Stroke (Recent/Active)	-253.971*** (68.829)	-257.472*** (68.761)	-0.630*** (0.170)	-0.641*** (0.170)
Stroke (Remote/Inactive)	-116.012*** (38.184)	-114.409*** (38.140)	-0.314*** (0.094)	-0.311*** (0.094)
R-Squares	0.051	0.053	0.053	0.054

Standard Errors reported in parentheses

*=p<0.1, **<0.05, ***p<0.01 , AA=African American N=16,074

Logistic Regression

Table 6 and 7 displays the results of the logistic regression analyses conducted to examine the association between each predictor variable education and the categorical outcome variables AD diagnosis and a 3-point decline in MMSE score, controlling for age, sex, race, marital status, hypertension, diabetes, alcoholism, smoking, APOE genotype, and stroke. Results were found statistically significant at a *p*-value <0.05.

Education was statistically significant for its association with AD diagnosis, which can be found in Table 6. There is a model for education continuously and categorically. As the continuous education variable increased AD diagnosis decreased by 0.067 (SD, 0.005). As education group 13-16 and >16 years changed from one group to the other AD diagnosis decreased (-0.488, SD 0.040 and -0.629, SD 0.043). Asian Race, Diabetes, Remote/Inactive Hypertension, and Recent/Active Stroke were not statistically significant. Subjects who were married had a decrease in having an AD diagnosis (-0.120 (SD, 0.014), -0.116 (SD, 0.014).

Table 7 presents results of a logistic regression test examining the association between education and having a 3-point decline in MMSE. In order to account for the difference in time between visits the 'windsor' test condition was selected within the statistical program menu. Having a 3-point decline decrease with increased education. In the education group >16 years has the highest decrease (-0.543 (SD, 0.055)) in 3-point decline. Having two APOE e4 alleles decreases your likelihood of AD diagnosis (-1.88, SD 0.076).

Table 6. Logistic Regression Results for Education and AD Diagnosis Association

Predictors	AD Diagnosis (1)	AD Diagnosis (2)
Education (Continuous) (1)	-0.067*** (0.005)	
Education 13-16 (2)		-0.488*** (0.040)
Education >16 (2)		-0.629*** (0.043)
Age >65	0.048*** (0.002)	0.048*** (0.002)
Male	0.255*** (0.034)	0.245*** (0.034)
Black or AA	-0.186*** (0.050)	-0.194*** (0.050)
Asian	0.175 (0.110)	0.164 (0.110)
Other	0.642*** (0.114)	0.725*** (0.113)
Married	-0.120*** (0.014)	-0.116*** (0.014)
Hypertension (Recent/Active)	-0.087** (0.034)	-0.087*** (0.034)
Hypertension (Remote/Inactive)	0.131 (0.094)	0.116 (0.094)
Diabetes (Recent/Active)	0.065 (0.050)	0.070 (0.050)
Diabetes (Remote/Inactive)	0.054 (0.206)	0.046 (0.206)
Alcoholism (Recent/Active)	0.800*** (0.173)	0.791*** (0.174)
Alcoholism (Remote/Inactive)	0.377*** (0.082)	0.375*** (0.082)
Smoking	-0.142*** (0.033)	-0.138*** (0.033)
APOE (e3,e4)	0.939*** (0.039)	0.936*** (0.039)
APOE (e4,e4)	1.888*** (0.076)	1.890*** (0.076)
APOE (e4,e2)	0.637*** (0.104)	0.626*** (0.105)
Stroke (Recent/Active)	-0.194 (0.152)	-0.170 (0.152)
Stroke (Remote/Inactive)	0.162** (0.080)	0.165** (0.081)
Pseudo R-Squares	0.083	0.085

Standard Errors reported in parentheses

*=p<0.1, **<0.05, ***p<0.01, AA=African American N=17,619

Table 7. Logistic Regression Results for Education and 3-Point Decline in MMSE Association

Standard Errors reported in parentheses

Predictors	MMSE 3-Point Decline (1)	MMSE 3-Point Decline (2)
Education (Continuous) (1)	-0.061*** (0.006)	
Education 13-16 (2)		-0.338*** (0.049)
Education >16 (2)		-0.543*** (0.055)
Age >65	0.022*** (0.003)	0.022*** (0.003)
Male	0.310*** (0.043)	0.303*** (0.043)
Black or AA	-0.060 (0.062)	-0.053 (0.062)
Asian	-0.166 (0.160)	-0.180 (0.160)
Other	-0.043 (0.143)	0.091 (0.140)
Married	-0.102*** (0.019)	-0.098*** (0.019)
Hypertension (Recent/Active)	-0.047 (0.043)	-0.046 (0.043)
Hypertension (Remote/Inactive)	0.141 (0.117)	0.130 (0.117)
Diabetes (Recent/Active)	0.165*** (0.061)	0.172*** (0.061)
Diabetes (Remote/Inactive)	0.430* (0.246)	0.417* (0.246)
Alcoholism (Recent/Active)	0.114 (0.211)	0.110 (0.211)
Alcoholism (Remote/Inactive)	0.181* (0.099)	0.181* (0.099)
Smoking	-0.114*** (0.041)	-0.114*** (0.041)
APOE (e3,e4)	0.558*** (0.050)	0.554*** (0.050)
APOE (e4,e4)	1.198*** (0.082)	1.194*** (0.082)
APOE (e4,e2)	0.384*** (0.135)	0.373*** (0.135)
Stroke (Recent/Active)	0.159 (0.175)	0.175 (0.174)
Stroke (Remote/Inactive)	0.191** (0.096)	0.193** (0.096)
Pseudo R-Squares	0.040	0.040

*=p<0.1, **<0.05, ***p<0.01, AA=African American N=16,074

CHAPTER V

DISCUSSION AND CONCLUSION

Discussion of Research Questions

The objective of this study was to further research the correlation between years of education and cognitive function in AD patients to understand the importance of proper intervention and earlier diagnosis. The NACC data set is unique in that it provides follow-up visits, so it makes for stronger implications than cohort studies. Utilization of this longitudinal dataset adds a unique perspective to the body of AD research because previous research has typically been limited in terms of research designs and clinical scores and assessments within the UDS captures rich integrated insights to explore incident AD cases and functional declines over time.

The main research question was to determine education attainment relationship with the risk/odds of AD diagnosis. The results from this study revealed that an increase in the years of education was protective against a diagnosis of AD (lowers the likelihood). The most significant association was observed among the group having greater than or equal to 16 years of education (which is indicative of graduate level education), in support of my hypothesis. These results align with tenets of the CRT, which may be explained that individuals with graduate level education have a greater cognitive reserve which may relate with less manifestation of AD pathology and therefore, less likely to be diagnosed with AD.

There is a lot of contradiction among studies on education and cognitive function. Many studies have used many methods to determine decline that may not be the best choice. Many have used the MMSE, that has shown to be biased in that higher educated persons test better (O'Bryant et

al, 2009). Higher cutoff points have been suggested to reduce this bias and increase early detection. Others have been retrospective in design, which make it difficult to know the stage of a person's AD (Scarmeas et al., 2005).

There was a moderate correlation between education and AD diagnosis, which supports the hypothesis for research question two. There was a small positive correlation between education and MMSE score, which represents the subject having a more cognitive function. I was expecting to see a stronger correlation between the education and AD diagnosis. From the analysis we found that there is a slower decline among person with higher education attainment, failing to reject the null hypothesis. It is possible that we may have seen a difference if we looked over a longer period of time. This is contradictory to some of the literature out there concerning this matter. This will add to the literature that results agree to what I found with my research.

Study Strengths and Limitations

The strength of this study is the large number of subjects in the data source used for the analyses, which allows for more reliable results. Another strength would be that this study examined the variable education both continuously and categorically and looked at both linear and non-linear associations. There aren't any studies that I researched that included that in their studies. It provided access to clinical measures, such as the MMSE, and longitudinal data capture which enabled analysis of declines overtime and determination of incident cases.

Limitations would be the way the subjects were selected, which makes the study less generalizable since the general population was not sampled. Some came as volunteers, while

other were recommended to the study which may have created some bias. Because the ADC were the point of enrollment-volunteers were recruited from centers whereby a cognitive disease concern has brought an individual to seek care-which tells me these individuals may be very distinct from the general US adult aging population. Therefore, interpreting the results beyond this population requires additional care and caution. Another limitation would be the lack of diversity in races, majority of the subjects were White/Caucasian. The population is highly educated which may skew the results, which I did try to control for it by increasing the cut-off for cognitive impairment on the MMSE.

Future Recommendations

Continued research on AD related to patterns of risk, diagnosis among minority subgroups, and cognitive functioning/declines between males and females is warranted. Additional studies to further examine education impacts on AD would shed important light on the cumulative value of educational in the context of brain health in late stages of life. Investigating the severity of AD of prevalent cases could be important for future research to better understand the association.

Conclusion

This study is important because AD is the sixth leading cause of death in the US and the rate of AD is estimated to triple by 2050. AD imposes a burden on the US economy as well as the patients, patient's family/caregivers, and the health care system. The results of this study build upon research that has examined educational attainment impacts related to AD. This research is important so that public health professionals can learn of potential intervention opportunities that may afford individuals efficient screening, treatment, and prevention resources. If the positive

finding that greater levels of education are predictive of stable cognitive functioning and have a negative association with AD diagnoses, educational investments early in life may be justified as a solution to improve AD. Further, understanding how comorbid conditions (such as hypertension and stroke) and lifestyle choices (such as smoking and drinking) affect one's likelihood of a diagnosis of AD may be of tremendous benefit for young generations. Increased attention on early manifestations of cognitive impairment may allow public health professionals and others to stave off a crisis. This is especially important in our more highly educated patients, as obvious symptoms appear later and may herald more rapid decline than in patients with lower education (Beelen, 2009). This information is important for early detection and early intervention-so AD will no longer be a leading cause of death in the US.

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