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Relationship between Early Years' Activities of Daily Living and Alzheimer's Disease Onset

Linyi Fan
Walden University

Walden University

College of Health Sciences and Public Policy

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Linyi Fan

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Review Committee
Dr. Clarence Schumaker, Committee Chairperson, Public Health Faculty
Dr. Harold Griffin, Committee Member, Public Health Faculty
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Walden University
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Abstract

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MS, University of Florida, 2015

MS, Lawrence Technological University, 2002

Dissertation Submitted in Partial Fulfillment

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Abstract

A few promising studies have indicated that activities of daily life (ADL) may be a useful way of predicting Alzheimer's Disease (AD). However, the existing cross-sectional studies fail to show how ADL in early years predict AD, and how social factors influence health either in addition to or in interaction with individual risk factors. Using a social epidemiology framework, this study examined the relationship between early years' ADL and the development of AD in later years. This quantitative study included 4,526 participants derived from the Health and Retirement Study (HRS) dataset. The dependent variable was whether the participant has been diagnosed with AD. The independent variables were the ADL indices and changes in ADL indices. A four-step multilevel regression model approach was used to address the research questions. The results suggested that the only significant predictor of the onset of AD was changes in early years' ADL ($b = 20.253$, $z = 2.761$, $p < .05$). However, the result of the sensitivity analysis ($b = 7.562$, $z = 1.900$, $p = .058$), which included more control variables and increased the observation period of ADL, did not support this finding. The results suggested that the variances of random effects varied by Level-2 variables associated with random slopes were approximately zero; thus, early years' ADL variable was not influenced by sociodemographic factors. Findings indicated that an increase in changes in ADL leads to an increase in the probability of onset AD in the future. Implications for positive social change include identifying the predictors of AD that may help isolate causes and target screening to those at the highest risk.

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Table of Contents

List of Tables

List of Figures

Chapter 1: Introduction to the Study

Alzheimer's disease (AD) is an increasing problem for both public and personal health in the elderly. AD is a neurodegenerative disease characterized by loss of function over time; AD is responsible for nearly 70% of dementia in the elderly (Weller & Budson, 2018). Over time, patients with AD become increasingly impaired from both cognitive functions and the ability to complete daily tasks (Roehr et al., 2019). At present, there are over six million cases of AD in the United States; by 2050, the number is expected to exceed 14 million (Alzheimer's Association, 2021). Therefore, AD is a timely problem, and my goal for this study was to address it through understanding the risk and protective factors that are bound up in patient's activities of daily life (ADL). In Chapter 1, I provide a thorough discussion of the present study, including the background of the research topic, the identified the research problem, the purpose of the study, the research questions, and the theoretical framework in which the study is based from. The discussion also includes an overview of the nature of the study, definitions of key terminologies used in the study, the assumptions, the scope and delimitations, and the significance of the study.

Background

AD is a neurodegenerative disease, meaning that it causes the brain to deteriorate over time (Slot et al., 2019). In practical terms, this results in dementia and progressive loss of both cognitive functions and the ability to effectively carry out day-to-day tasks (Roehr et al., 2019). Although the underlying mechanism of AD is not known, increasing evidence shows that lifestyle factors have profound effects on the brain's neurochemistry,

which could potentially mitigate the development of AD (Lista & Sorrentino, 2010; Serrano-Pozo & Growdon, 2019). AD occurs primarily in the elderly, meaning that it has become an increasingly significant problem as advances in medicine have caused significant increases in average lifespan (Weller & Budson, 2018). AD is the third most common cause of death in the elderly as well (Alzheimer's Association, 2021; National Institute on Aging, 2021, July 08). AD represents a significant and increasingly central threat in today's world and to the extensive elderly populations in developed countries such as the United States (Alzheimer's Association, 2021).

At present, there is no cure for AD (Alzheimer's Association, 2021; Cummings, 2018). Most biomedical approaches to treating the disease have been unsuccessful, though research remains ongoing (Cummings, 2018). Treatments using lifestyle factors, such as exercise, have shown promise for both slowing the progression of AD and reducing its symptoms (Cass, 2017). In general, the causes of AD remain elusive, although a significant portion of the risk appears to result from genetic factors (Zhu et al., 2017). Outside of these, researchers have used factors such as the ADL as a measure of AD's progression (Kamiya et al., 2018; Kawaharada et al., 2019) or predictors thereof (Fuentes et al., 2020).

Given the potentially protective or therapeutic effects of lifestyle factors such as exercise (Cass, 2017), using ADL to predict the onset of AD shows promise (Roehr et al., 2019). At present, there is a gap in the research regarding such models. Researchers have called for additional studies using factors such as ADL to predict AD (Weintraub et al.,

2018). More specifically, the gap relates to the use of longitudinal data (Alberdi et al., 2018) and a combination of baseline data and data on changes over time (Li et al., 2017).

Problem Statement

AD is the most common cause of dementia in the world's growing elderly population (Weller & Budson, 2018), affecting over six million people in the United States and constituting the third leading cause of death in the elderly (Alzheimer's Association, 2021; National Institute on Aging, 2021, July 08). Biomedical efforts to treat AD have typically produced mixed to poor results (Cummings, 2018), while more lifestyle-focused treatments such as exercise may fare better than existing biomedical treatments (Cass, 2017). Despite this, most research on lifestyle factors such as the ADL in relation to AD have focused on how AD impairs ADL (Kamiya et al., 2018; Kawaharada et al., 2019), or on how ADL impairment affects the progression of AD (Fuentes et al., 2020). However, a few promising studies indicated that ADL may be a more broadly useful way of predicting AD (Roehr et al., 2019). This perspective aligns with the theory of social epidemiology (Krieger, 2001a). Therefore, the research problem was that it is not known how early years'ADL changes in early years' ADL may predict AD diagnosis at a later point in time. Further research problem was to what extent changing ADL can predict the development of AD (Weintraub et al., 2018), especially from a longitudinal perspective (Alberdi et al., 2018) using both baseline and change over time data (Li et al. 2017).

Purpose of the Study

The purpose of this study was to examine the relationship between early years' ADL that was defined in the definition section and the development of AD in later years while accounting for the influence of key sociodemographic factors. The population under study was U.S. adults 50-years old. This population were accessed through the HRS dataset, a representative national multilevel panel study by the RAND Corporation Center for Study of Aging. Data from the Health and Retirement Study (HRS) dataset are freely available for use in research. The independent variables were early years' ADL while the dependent variable was AD diagnosis onset in the later years. The control variables were sociodemographic factors (health, health services, labor force, economic status, family structure, and retirement expectations). Examining the relationships between these variables has the potential for positive social change through identifying risk and protective factors relating to AD onset and justifying resources for people at risk to practice such protective habits and fight AD.

Questions and Hypotheses

I developed the following research questions and corresponding hypotheses to fulfill the purpose of the study:

Research Question 1 (RQ1): What is the relationship-between different specific early years' ADLs and later onset of AD?

Null Hypothesis ($H_0$1): There is no relationship between early years' ADLs and the later onset of AD.

Alternative Hypothesis (H_a1): There is a significant relationship between early years' ADLs and the later onset of AD.

Research Question 2 (RQ2): What is the relationship between changes in early years' ADL and later onset of AD?

Null Hypothesis ($H_0 2$): There is no relationship between changes in early years' ADL and the later onset of AD.

Alternative Hypothesis (H_a1): There is a significant relationship between changes in early years' ADL and the later onset of AD.

Research Question 3 (RQ3): To what extent do sociodemographic factors moderate the relationship(s) between early years' ADL and later on set of AD?

Null Hypothesis ($H_0 3$): None of the sociodemographic factors moderate the relationships between early years' ADL and later on set of AD.

Alternative Hypothesis (H_a3): One or more of the sociodemographic factors moderate the relationships between early years' ADL and later onset of AD.

Theoretical Framework

The theoretical framework for this study was the social epidemiology. The theory of social epidemiology is used to study society and biology simultaneously, with a focus on how social conditions produce patterns of health and disease (Honjo, 2004; Krieger, 2001a). The notion of social epidemiology draws from a long tradition of thinking dating back to at least Villermé in the 1820s (Krieger, 2001a). Modern social epidemiology theory was codified by Yankauer in the 1950s, and since has grown into a significant theory of how society and disease interact (Yankauer, 1950). Yankauer's (1950) seminal

work on social epidemiology related to how residential racial segregation affected public health outcomes. Segregation, however, is but one of the many ways in which social factors can significantly influence health outcomes (Honjo, 2004; Krieger, 2001a). A key facet of some of these relationships is that they may be tacit, or not immediately apparent.

Social epidemiology was an appropriate framework for this study because I addressed the impact of both social factors and individual risk factors on the incidence of AD. One such factor was the diverse set of sociodemographic factors included under RQ3 including health services, labor force, economic status, family structure, and retirement expectations (Bugliari et al., 2016). Secondly, ADL is an individual risk factor, given that the daily activities of individuals differ from person to person. However, daily activities undertaken by persons from different social contexts may differ significantly. For example, a white-collar worker from an upper socioeconomic stratum, on average, engages in different daily activities than a blue-collar worker from a low socioeconomic stratum (Pieczyńska et al., 2019). This includes both physical and mental activities. Nonetheless, they are significantly influenced by social context and sociodemographic factors. Therefore, the theoretical framing of social epidemiology theory is an apt perspective from which to discuss the issues in this study. Further discussions of social epidemiology theory are included in Chapter 2.

Nature of the Study

The research methodology for this study was quantitative. Quantitative research is numerical and relational (Balnaves & Caputi, 2001). A quantitative study is used to examine variables that can be expressed in quantified forms and how these variables

relate to one another (Vogt, 2011). Quantitative inquiry is also empirical, able to achieve powerful results through high statistical power (Vogt, 2011). All of these attributes made a quantitative approach a good fit for this study. In this present study, I addressed issues that can be quantified as evinced by prior researchers such as Bugliari et al. (2016). The present study was also explicitly relational, as all of the research questions guiding the study pertained to the relationships between variables.

The research design was historical and correlational, and I used a dataset to conduct a multilevel hierarchical secondary data analysis. Correlational research is a nonexperimental design (Johnson, 2001). Nonexperimental research is appropriate when the variables under study cannot be manipulated (Curtis et al., 2016). I addressed such issues, including sociodemographic factors and the activities of daily living a person undertook in the past. A correlational approach is appropriate when seeking to find predictive relationships between key variables (Johnson, 2001; Martin et al., 2011). I was wholly concerned with such relationships. Moreover, I used a multilevel approach using generalized least squares, which represents a more advanced form of correlation modeling. Finally, a historical approach is appropriate when there are secondary data available (Curtis et al., 2016). Such data were available for this study. Further discussion of the research method and design are included in Chapter 3.

The population under this study was adults over age 50 in the United States. This is the only demographic inclusion or exclusion criterion for the study. The population was not sampled directly; instead, I used the RAND Health and Retirement Study (HRS) Fat files (RAND, 2021). HRS data are available for public researchers and are free to

download at the HRS Web site. This dataset is appropriate to this study as it contains data on HRS variables combined with household data at the respondent level (Bugliari et al., 2016). Hence, I retrieved the data from the publicly available files on the HRS website (RAND, 2021). Key study variables included the onset of AD, data regarding the participants' past ADL behaviors, data on changes in past ADL behaviors, and key sociodemographic factors of health, health services, labor force, economic status, family structure, and retirement expectations. I imported these data into R statistical software for use in multilevel hierarchical analyses to answer the research questions.

Definitions

Activities of daily life (ADL)*:* ADL are the activities involved in day-to-day life, including personal hygiene, eating, doing tasks around the house, walking, and other such functions (Fuentes et al., 2020). The RAND HRS defines two activities of daily living indices (RwADLWA, RwADLA) and a variable indicates the change in the RwADLA (Bugliari et al., 2016).

Alzheimer's disease (AD): AD is a neurodegenerative disease characterized by loss of function over time, including dementia and a loss of ability to do daily tasks (Weller & Budson, 2018). The RAND HRS variable name for AD is RwALZHE, which represents the raw response to the questions regarding whether or not a doctor has told the respondent she/he had AD (Bugliari et al., 2016).

Early Years' Activities of daily life (eADL): Average ADL measures in a retrospective 10-years average ADL measure from 5 years prior to the baseline to 15 years prior to the baseline is defined as early years' activities. Changes of Early Years'

ADL is defined as average change of eADL in a retrospective 10 years change of ADL measures from 5 years prior to the baseline to 15 years prior to the baseline.

Protective factor: A protective factor represents a factor that has a negative correlation with the chance of a specific negative outcome (such as an AD diagnosis). These factors may not be causally protective, but are associated with better outcomes (Roehr et al., 2019).

Social factors: In the context of this study, social factors are those social conditions that may affect epidemiology, including socioeconomic status, living conditions, and other such factors (Bugliari et al., 2016). The social factor variables in RAND HRS include total household income (HxITOT), poverty threshold (HwINPOVR, HwPOVHHI), disability episode variables (RADNEPI, RADTYPE 1-10), health conditions (RwCONDE), and mental health (RwCESD).

Sociodemographic predictors: The sociodemographic predictors included in this study are social factors that may relate to AD, including health, health services, labor force, economic status, family structure, and retirement expectations (Bugliari et al., 2016).

Assumptions

Assumptions are foundational aspects of a study that cannot be proved or disproved (Balnaves & Caputi, 2001; Vogt, 2011). Firstly, I assumed that quantitative research can meaningfully assess the relationships between AD and ADL. Secondly, I assumed that the HRS dataset used in this study is accurate and appropriate as a means of

accessing the study population. Thirdly, I assumed that the participants of the HRS study responded accurately and completely to the survey items used in most or all cases. All are reasonable assumptions based on methodological tradition or prior research.

Scope and Delimitations

The scope of a study is the topic and other areas it covers (Balnaves & Caputi, 2001; Vogt, 2011). In keeping with this, delimitations represent deliberately set limitations on the scope and content of the research (Balnaves & Caputi, 2001; Vogt, 2011). The scope of the present study was that the research addressed the relationship between ADL and AD in US adults 50-years old years of age, with consideration of related sociodemographic factors. This scope was bounded by key delimitations. First, the study was delimited to the study of ADL and sociodemographic factors as predictors based on the existing literature. Though other factors may also predict AD, the chosen independent variables align with the research gap and most strongly aligned with the theoretical framework as well. The study was delimited to adults 50-years old as these adults are vastly more likely to experience AD, a disease that primarily affects the elderly; hence, the population under study was those at high risk for developing AD. The study was delimited to the entire US population geographically because of the availability of representative panel data regarding this population.

Limitations

In contrast to deliberately chosen delimitations, limitations are weaknesses of the study (Balnaves & Caputi, 2001; Vogt, 2011). There were also several key limitations in this study. Firstly, although the dataset that I used in the study included all of the desired

variables, the scope of what data could be used was limited by the data present in the HRS dataset. Secondly, the study was limited by the quantitative approach's focus on testing hypothesized relationships; I was not able to explore or uncover new relationships. I offset this limitation by the advantages of a quantitative approach, particularly the statistical power it afforded. This study is also limited in that I only considered a key subset of variables. However, these particular variables are supported in the literature (Fuentes et al., 2020; Kamiya et al., 2018; Kawaharada et al., 2019). Moreover, I used statistics such as the generalized least squares approach to determine the degree to which the variables included in the study can explain the variance in AD onset.

Significance

The present study may have significance academically, practically, and in terms of creating positive social change. The academic significance of the study derives from addressing the research gap. This gap was highlighted by three calls for research. Firstly, Weintraub et al. (2018) studied the ability of cognition and function to predict the development of AD. Though their results offered a promising model, they called for further research into the ability of functional-related issues such as ADL to predict AD. Along a similar line of research, Alberdi et al. (2018) studied the feasibility to use ADL to predict the onset of AD. Their model was good but imperfect, and they called for more research that includes longitudinal data. Finally, in a review of modeling approaches, Li et al. (2017) found that few prior researchers had used a combination of baseline and change over time factors. Therefore, they called for more research using such an

approach. In addition, Mauricio et al. (2019) reviewed and summarized the proceedings of the G8 dementia summit; the most significant conclusion of the summit was a need for more—and more innovative—research into dementia, of which AD is the primary cause. I fulfilled all these calls for research by examining the predictive power of ADL on AD longitudinally and with both baseline and change over time data.

The practical implications of this study derive from the importance of combatting AD. As noted above, the incidence of AD is quite high in older Americans today (Weller & Budson, 2018). Over six million Americans suffered from AD as of 2021 (Alzheimer's Association, 2021; National Institute on Aging, 2021, July 08). Therefore, there is an urgent need to identify which factors may be predictive of AD and which may protect against it. Identifying the predictors of AD may help isolate causes and also target screening at those at the highest risk. Identifying protective factors, on the other side of the issue, and especially those as straightforward as ADL factors may allow for people to practice such protective habits and fight AD.

The significance for positive social change inherent in the study is bound up in these practical implications. AD represents one of the most significant health threats to older Americans and causes great emotional harm to families who must cope with a relative still being technically alive yet not remembering them (Weller & Budson, 2018). This study contributes to the ongoing and essential battle against AD. Any results that meaningfully help reduce AD or offer incremental progress toward isolating causes and risk factors can lower AD prevalence and contribute to better targeting screening and early treatments. Therefore, this study has significantly to positive social change.

Summary

In Chapter 1, I provided an introduction to the study. The problem was that it is not known how early years' ADL and changes in early years' ADL may predict AD diagnosis at a later point in time. To address this problem, the purpose of the proposed quantitative historical correlational design was to examine the relationship between early year ADL and the development of AD in later years while accounting for the influence of key sociodemographic factors. The population under study was U.S. adults 50-years old, who were accessed through the HRS dataset, a representative national multilevel panel study by the RAND Center for Study of Aging. I used four research questions to guide the study: (a) What relationship exists between the earlier life sociodemographic predictors of health, health services, labor force, economic status, family structure, and retirement expectations and the later onset of AD? (b) What relationship exists between earlier life ADL and later onset of AD? (c) What relationship exists between earlier life changes in ADL and later onset of AD? and (d) To what extent do sociodemographic factors moderate the relationship(s) between ADL and AD? The study is significant because it addresses a research gap, a practical need, and contributes to positive social change. In Chapter 2, I will review key background literature in depth.

Chapter 2: Literature Review

Introduction

AD is an increasing epidemic in the United States (Alzheimer's Association, 2021). Although AD's underlying mechanism is not known, increasing evidence emerges that lifestyle factors have profound effects on the brain's neurochemistry, which could potentially mitigate the development of AD (Lista & Sorrentino, 2010; Serrano-Pozo & Growdon, 2019). Many previous epidemiological studies have demonstrated that dementia was associated with ADL difficulty (Pakstis et al., 2018). Although ADLs are studied as a risk factor epidemiologically or neurophysiological, the underlying mechanism and relationship between ADL and AD development are still unclear (Liu et al., 2019).

The purpose of this study was to evaluate the relationship between ADL in the early years and AD presence in the later years. Social epidemiology provides a strong theoretical basis to guide the multilevel interaction relationship. This study was grounded in social epidemiological frameworks and linked together the distribution of structural factors and individual risk factors that determine the incidence and prevalence of the disease and investigated the hierarchical relationships among the effect of the factors.

The current epidemiological and gerontological evidence suggests that mid-life healthy lifestyle choices are likely protective against AD (Serrano-Pozo & Growdon, 2019). The higher levels of everyday physical activity and mobility performance are associated with better executive function trajectories (Ogino et al., 2018; Thibeau et al., 2019). Neurophysiological research corroborated the risk of neurodegenerative disease is

associated with early developmental defects (Hou et al., 2019). Neuropsychiatric symptoms in AD are related to ADLs through various symptom interactions (Saari et al., 2020). Nonpharmacological interventions, including calorie restriction and physical activity, have a promising anti-inflammatory effect (Hou et al., 2019; Ogino et al., 2018). However, the clinic-pathological substrate of dementia in community-dwelling elderly people is unclear.

This chapter contains five major sections. The literature search strategy section includes the scope, the search strategy, and the resources of this thorough review. The theoretical foundation contains a thorough review of the study's theoretical foundation and provides the rationale for the theoretical framework's choice. The key variables and concepts section reviews and synthesizes the methodology, key independent, dependent variables to conduct the analysis. To emphasize the relationship between ADL and AD, I synthesize the current research from different disciplinary perspectives in research question section. The last section concisely summarizes major themes in the literature.

Literature Search Strategy

I conducted a systematic search of the literature with full text in the last 5 years. In order to identify the key article for original theory and statistical methodology, the literature search was extended and traced back to the earlier 70s. I conducted the literature search using the libraries at Walden University and the National Library of Medicine. Databases included ProQuest Central, Medline with full text, PubMed, and Google Scholar. The primary keywords and key phrases for this study included *Alzheimer's disease, dementia, cognitive impairments, cognitively impaired elderly,*

gerontology, activity of daily living or ADL, ADL instruction validity, independent living, social epidemiology, psychosocial assessment, social production of disease, social production of political economy, the political economy of health, ecosocial, and *multiple level models.*

Theoretical Foundation

The theoretical framework of this study was social epidemiology. Social epidemiology studies society and biology simultaneously and focuses on how social conditions produce health and disease (Honjo, 2004; Krieger, 2001a). Although contemporary social epidemiology was first named by Alfred Yankauer and developed in the 20th century, some social epidemiological insights have been identified in classic epidemiological studies in the 19th century (Krieger, 2001b). These studies revealed disparities in health care across all social classes and linked population health to early life deprivation (Krieger, 2001b). Based on these prior insights,-contemporary social epidemiology was established that emphasizes social determinants of population distributions of health, disease, and wellbeing (Krieger, 2001b).

Social epidemiology questions require exploration of social determinants in the present, past embodiment, and its manifestation and changing social inequalities in health (Krieger, 2001b). The major premise of social epidemiology is that each society forms its distribution of health and disease, reflecting the distribution of its characteristics in that society (Honjo, 2004). Social epidemiology emphasizes the population perspective that the risk of disease cannot be isolated from the population's disease risks (Honjo, 2004). Social epidemiology widely uses multilevel statistics approaches to build hypotheses and

interpret results, which allow epidemiologists to develop quantitative and structural analyses of social factors in health (Honjo, 2004; Pearce, 1996). Social epidemiologists select variables in statistical models base upon the conceptual framework that indicates hierarchical relationships among factors, rather than treating them as background to biomedical phenomena (Krieger, 2001b).

Three fundamental social epidemiology principles are psychosocial, social production of disease and/or the political economy of health, and ecosocial theory (Kreiger, 2001b). These are the theoretical frameworks of social epidemiology. The three frameworks elucidate the social equalization of health. In this study, I investigated the heterogeneity of social and biological aspects and social inequalities in population health in terms of disease distribution. These theoretical frameworks integrate social and biological explanations and recommendations for action (Kreiger, 2001b).

The psychosocial framework contains three research areas, the interconnection between biology, psychology, and socio-environmental factors. The framework assumes that biology is determined in multilevel and interactive environments (Honjo, 2004). The psychosocial paradigm of social epidemiology assumes that diseases are the mutual interaction among social factors, individual factors, and biological factors. The individual factors are unique to each person and may vary according to their psychological and physiological health (Honjo, 2004). Conversely, biological factors are influenced genetically and by the environment (Honjo, 2004). The psychosocial frame posits that the social environment modifies host susceptibility by affecting neuroendocrine function (Cassel, 1976; Honjo, 2004; Kreiger, 2001b). In typical psychosocial studies, the

researchers investigate the pathogenic psychosocial stressors of disease and reveals how the social environment modifies the susceptibility (Cassels, 1976; Krieger, 2001b). Psychosocial studies focus on the endogenous biological responses to dynamic interaction, ongoing process, and circularity of cause-effect in terms of ‘host-agent-environment’ (Cassel, 1976, Kreiger, 2001b; Hollis, 1964). Cassel (1976) linked vulnerability to disease to physical and psychological stress using the 'host-agent-environment' model for psychosocial epidemiology. The psychosocial epidemiological question is to what extent do categories or classes of environmental factors change human resistance in important ways and make subsets of people more or less susceptible to these ubiquitous agents in our environment (Cassel, 1976). According to Krieger (2001b). The research questions of ecosocial theory is who and what drives current and changing patterns of social inequalities in health (p. 12). Unlike the psychosocial framework that establishes a triangle connecting host, agent, and environment, ecosocial theory establishes multi-level dynamic perspectives (Krieger, 2001b). The ecosocial theory framework emphasizes that to understand any aspect of biology, the researcher needs to understand individual and societal ways of living (Krieger, 2001b). The new multilevel dynamic perspectives regard current and shifting patterns of health, disease, and well-being distribution and study relation to each level of biological, ecological, and social organization, such as organization and family (Krieger, 2001a). One of the most important ecosocial constructs is to determine how to incorporate the biological material and social worldtogether (Krieger, 2001b). In terms of embodiment pathways, each aspect is distributed and structured at multiple and multiple domains (Krieger, 2001b).

The ecosocial theory contains a conceptual framework of relation to relevant ecological concepts and manifested in processes at multiple scales of time and space (Krieger, 2001b).

The relationship between personality and AD risks has been studied for-decades. Neurophysiological and epidemiological evidence showed that ADL seems to be related to AD development and progresses (Krieger, 2001a). However, the findings of previous studies are inconsistent, and the underlying mechanism is still unclear. The inconsistency could be caused by the heterogeneity of populations and methodology used in the analysis. Sohrabi et al. (2020) stated that there was a need for new research to look into the underlying mechanisms of AD, the potential relationship between personality risk factors and AD, and how they correspond to change in personality factors (Sohrabi et al., 2020). The need for additional research motivated the present study to investigate the relationship between AD and a specific personality factor: ADL. Grounded social epidemiology theory, I included the third research question "To what extent do sociodemographic factors moderate the relationship(s) between early years' ADL and later on set of AD" that intends to answer whether or what extent of categories or classes of environmental factors can influence subsets of people more or less susceptible to develop AD diagnosis in later years and the AD distribution in study population.

Guided by social epidemiology theory I constructed methodology selection in this study. Multilevel analysis has been applied in social and behavioral research. Multivariate analysis is useful as covariates are not solely treated as individual risk factors. Instead, the social epidemiologists select statistical models based upon the

conceptual framework that indicates hierarchical relationships among factors (Krieger, 2001b). Under the social epidemiology theory guidance, I selected the multilevel model as the statistical methodology and chose covariates for the model.

Literature Review Related to Key Variables

Multilevel analysis is an important statistical approach of social epidemiology that assumes that the biology is determined in multilevel and interactive environments and allows several analysis levels to be accounted for simultaneously (Honjo, 2004; Krieger, 2001b; Leeuw & Meijer, 2008). In epidemiological research grounded in social epidemiology theoretical frameworks, variable selection in the statistical model reflects the nature of hierarchical structure and multilevel relationships among factors, rather than treating them as background to biomedical phenomena (Krieger, 2001b). For example, the Alzheimer's Association suggested risk factors for individuals include age, genetic risk, family history, cardiovascular disease risk factors, head or brain trauma, education, and social and cognitive engagement (Beydour, 2014; Silva, 2019; Zeisel et al., 2020). In this study, the independent variables include both individual characteristics and social level characteristics. Therefore, I assess whether individual and social characteristics shape individuals' health in the analysis. Furthermore, the disease distribution could explain current and changing disease patterns across time and within and across social groups (Leeuw & Meijer, 2008; Mauricio et al., 2019). I evaluated ADL measurement in the early year and changing over time in this study.

Evolution of AD Research

To establish the current literature related to individual and social level characteristics for AD, it is first important to introduce the historical and contemporary literature. This section aims to synthesize current literature that discusses AD research's understanding and how this has influenced the literature gap in Chapter 1. Historically, the first diagnosis of AD was identified by Alois Alzheimer in 1901. The German psychiatrist diagnosed a 50-year-old female patient (Dubois et al., 2016). The work of Alois Alzheimer was followed by a series of 11 medical publications documenting the disease. Pathologically, AD's symptoms were described in medical detail by Kraepelin's work in 1910 (Dubois et al., 2016). At the 37th Southwester German convention, Kraepelin presented the diseases' features (Liu et al., 2019). However, despite the attention paid briefly in 1910, research regarding AD in pathology and psychology was absent until 1963 (Liu et al., 2019). The key clinical trials in 1963 are detailed in the coming sub-section after this brief history is provided.

During the 1900s, AD diagnosis was primarily associated with individuals aged 45 to 65 based on their display of dementia characteristics (Terry & Davies, 1980). However, in 1977 medical researchers corroborated that the term should be distinct but not separated from the manifestation of dementia. The historical work identifying AD also led to excluding age as a qualifying factor (Liu et al., 2019). In contemporary literature, AD is a neurodegenerative disease and worsens throughout a human's lifetime. Dementia is linked to AD in approximately 60% to 70% of cases documented (Liu et al., 2019; Terry & Davies, 1980).

The symptomology of AD is difficulty remembering events, increased risk of being disoriented and lost, poor motivation for daily tasks, extreme mood swings, and behavioral issues (Dubois et al., 2016). After the initial AD diagnosis, the individual has estimated a 3-to-9-year lasting lifespan (Liu et al., 2019). After identifying in the 1900s and expanding research in the 1990s, information on how AD manifests is predicted and treated emerged (Talboom et al., 2019). In the following subsection, I synthesize the pertinent historical clinical trials for AD to discuss AD's modern understanding from a clinical perspective.

Historical and Clinical Trials for AD

In this section, I summarize the relevant clinical trials that underpin AD research. Multiple hypotheses have been posed across the past two decades regarding how AD manifests and can be treated (Atri, 2019; Talboom et al., 2019). Therefore, it is not possible to cover the entire range of possible treatments for the scope of this literature review; however, the key studies that advance medical understandings of the diseases are covered in this section. In 1906 Alois Alzheimer presented the first case of AD, which was later expanded in 1910 by Kraepelin (Liu et al., 2019). In 1963, the first clinical trials would be performed to explore the disease medically. Terry and Kidd, in 1963, assessed neuropathological lesions through electron microscopic analysis. The results of their analysis indicated that neurofibrillary tangles (NFTs) are detected in biopsies of the two AD specimens. Although the sample size in the assessment was small, their work founded future pathological assessments. Overall, 2,173 clinical trials have been conducted since 1968.

Today, clinicians indicate two forms of the disease. The first is sporadic AD and familial AD (Aisen et al., 2017). Familial AD is found in 1% -5% of cases and was linked in 1990 to a genetic mutation in protein precursors (Aisen et al., 2017). Research regarding familial AD also indicated a sum of 20 genetic risk loci, such as the e4 allele (Moreno-Rodriguez et al., 2020; Penney et al., 2020). Detailed research regarding these risk factors are provided in future sections regarding individual and social level characteristics of AD risk. Sporadic AD is more common in patients and is recognized in 95% of cases (Liu et al., 2019). Sporadic AD refers to multiple possibilities for risk, such as linking the lymphatic system, the inflammatory hypotheses, obesity, sleep disorders, and hypertension (Liu et al., 2019).

Modern clinical treatment for AD is founded either through acetylcholinesterase inhibitors (AChEIs) (e.g., donepezil) or an antagonist for the N-methyl-D-aspartic receptor (e.g., memantine). (Liu et al., 2019). Clinical data for these treatment methods indicate that symptoms can be reduced but not delay the diseases' overall progression (Liu et al., 2019; Ochalek et al., 2017). As a result, researchers are considering alternative treatment and different risk factors, such as molecular mechanisms (Ochalek et al., 2017; Vogel et al., 2018). The following section is to provide a foundation for discussing the understanding of modern treatment options, risk factors, and hypotheses.

AD Hypotheses

In the research for AD, it is critical to understand the guiding hypotheses. I present the research regarding how these hypotheses relate to the current understanding of AD treatment and risk factors in the following sections (Liu et al., 2019). I briefly

discuss and synthesize each of these hypotheses in this section. I aim to frame the following sections regarding individual and social level characteristics. First, the cholinergic hypothesis is discussed in the next sub-section.

Cholinergic Hypothesis

The first AD proposal was the linkage between neurotransmitters. Researchers Terry and Davies (1980) noted that dopamine, noradrenaline, 5-hydroxytryptamine, acetylcholine, and y-Aminobutryic acid are found in 20 regions of the brain of individuals with AD. Clinical trials found that AD could ultimately be linked to a cholinergic system's failure. Subsequent clinical trials in the 1990s also found that AD patients' acetylcholine is inhibited, leading to treatment with AChEIs (Falcon et al., 2018). Some symptomology is reduced for patients treated with AChEIs (Drummond et al., 2017; Vogel et al., 2018). However, the drug treatment does not slow the progression of the disease. The cholinergic hypothesis is clinically noted to contribute to AD symptomology but is not linked to significantly effective treatment (Condello et al., 2018).

Amyloid Hypothesis

In 1991, Hardy and Allsop posited that pathogenic mutations found in specific chromosomes such as precursor proteins might be the etymology for AD. In clinical trials, AD patients were found to have pathological cascades that pointed to pathogenic mutations or an accumulation of Aβ (Makin, 2018). As a result, Glenner and Wong (1984) demonstrated isolated Aβ and found some preliminary evidence to link pathogenic mutations through Aβ pathways. Researchers indicate that Aβ protein can be neurotoxic

and lead to neuronal death, a key link in dementia or reduced cognition in AD patients (Fulop et al., 2018). As a result, treatment for Aβ production inhibition has been provided in some clinical trials. Despite advanced research on treatment for Aβ inhibition production, major trials were discontinued in 2018 due to failure to prevent the worsening of cognitive failure function (Liu et al., 2019; Makin, 2018). The FDA does approve the amyloid treatment; however, clinical trials indicate that symptomology is only addressed instead of treating cognitive failure (Mullane & Williams, 2018).

Tau Propagation Hypothesis

The Tau Propagation Hypothesis is underpinned by the pathological features of NFTs, which include tau proteins (Liu et al., 2019). Tau proteins stabilize microtubules and transport dendrites and axons critical for neuronal function (Guan et al., 2019). Tau cDNA, discovered in 1988, indicated that the distribution of the tau gene could spread across the brain and may misfold into prions that create a cognitive reduction (Guan et al., 2019). Clinical trials in mice indicated that some augmentation of tau could be present through hyperphosphorylation and increased AD patients (Sepulcre et al., 2018). The Tau Propagation Hypothesis led to clinical trials for treatments to inhibit tau aggregation, which showed promising results in some patients (e.g., improved cognitive functions; Sepulcre et al., 2018). However, clinical trials remain underway, and it is unclear if the pharmaceutical options are ultimately effective for AD patients (Liu et al., 2019).

Mitochondrial Cascade Hypothesis

The Mitochondrial Cascade Hypothesis dictated that mitochondrial function may impact Aβ accumulation in AD patients (Swerdlow, 2018). An individual's mitochondrial cascade is impacted by genetics and environmental factors that drive AD patients' phenotypes and epigenetics (Aka et al., 2019; Cassel, 1976; Honjo, 2004; Kreiger, 2001b; Marioni et al., 2018). Clinical trials demonstrated that Aβ pathology is present before clinical symptoms of AD, lined with mitochondrial change by the onset of symptomology (Albensi, 2019). Researchers studying the mitochondrial effect indicated that variables such as epigenetic dysregulation and environmental modifications might be linked to AD diagnosis (Albensi, 2019). The mitochondrial Cascade Hypothesis remains at the forefront of AD research due to the linkage with possible environmental risk factors, underpinning future discussions in this chapter regarding risk factors (Aka et al., 2019).

Calcium Homeostasis

In 1992, the Calcium Homeostatic Hypothesis was proposed, which indicated that Aβ is positively linked with intracellular calcium levels that impact the response to neurons from the environment (Popugaeva et al., 2017). Calcium levels are known to mitigate signaling in the human body (Kastanenka et al., 2017). As a result, medication and signaling may impact cognitive function (Syrjanen et al., 2020). Pharmaceutical treatments such as NMDA Glutamate have been marketed in the United States and Europe. However, researchers indicate that the effect is minimal on cognitive repair (Popugaeva et al., 2017; Sryjanen et al., 2020).

Neurovascular Hypothesis

The Neurovascular Hypothesis relies on the ideology that the brain's microenvironment and metabolism must effectively regulate waste in the blood, vascular cells, and neurons (Liu et al., 2019). Dysregulation of the vascular system is clinically found to decrease cerebrovascular function and is also linked to an increased level of Aβ in the cerebral regions (Chawla & Parikh, 2020). The effect of hypertension, obesity, high cholesterol, and inflammation is associated with neurovascular dysregulation and AD patient symptomology (Kapadia et al., 2020; Solis et al., 2020). Patients with diabetes are also at a higher risk for AD due to the neurovascular system's disruption (Katsumoto et al., 2018; Madmoli et al., 2019). Researchers indicate that the neurovascular hypothesis is best used in conjunction with other hypotheses for ideal treatment methods.

Inflammatory Hypothesis

The inflammatory hypothesis indicates that microglia and astrocytes in the central nervous system are linked with the macrophages found in AD patients (Kinney et al., 2018; Newcombe et al., 2018). In addition, researchers found that AD patients hold a higher level of inflammatory microglia and astrocytes through controlled trial assessments (Ozben & Ozben, 2019). As a result, inflammatory treatment methods are considered a means of treatment (Katsumoto et al., 2018). However, Liu et al. (2019) noted a lack of evidence for the efficacy of inflammatory treatment models.

Lymphatic System Hypothesis

The lymphatic System hypothesis contains the idea that the lymphatic and blood vascular systems are key to fluid balance—imbalances in fluid increase meningeal waste, proteins, and metabolites that can impact neural behavior (Tsonada, 2017). As an individual age, the lymphatic system's failure can increase Aβ in the brain and be linked with AD (Pappolla et al., 2018). Some clinical research is evident for addressing lymphatic vessel balance, but further clinical trials are required to produce efficacy (Da Mesquita et al., 2018; Sweeney & Zlokovic, 2018).

Individual Characteristics and AD Risk

AD is a degenerative disorder associated with individual and social risks (C. Liu et al., 2019). Research findings reported increasing trends in AD incidence over time, while other studies have shown no change or even a decrease in high-income countries (Alzheimer's Association, 2021; C. Liu et al., 2019). The hypotheses and evolution of clinical trials that demonstrated AD's pathological path were presented in the previous section. In the following two sections, research that considers individual characteristics and social risks are discussed in alignment with this study's aim. First, the individual characteristics of AD are discussed as presented in previous literature.

In the United States, AD is the 6th leading cause of death and is associated with extreme cognitive decline, memory loss, and inability to function independently (Alzheimer’s Association, 2021). The key risks for AD are based on age, gender, and race, and ethnicity (C. Liu et al., 2019; Matthews et al., 2019; Mielke, 2018). Research by Matthews et al. (2019) indicated that individual risk estimations for these subgroups are

absent but recommended for future researchers. However, it is important to discuss how individual characteristics such as gender, age, race, and ethnicity may play a role in AD's burden to address treatment options and address high-risk patients (Matthews et al., 2019).

Race and Ethnicity

The subpopulation of race and ethnicity is one risk factor for AD. According to a meta-analysis of Medicaid data by Matthews et al. (2019), non-Hispanic whites, African Americans, Asian and pacific islanders, Hispanic and American Indians, and Alaska Native populations are all at risk for AD. However, African American and Hispanic populations over 75 are at the greatest risk for AD. Hispanic groups are predicted to carry the disease's burden based on calculations of the sub-group risk rate.

The reasoning for race and ethnicity disparities for AD currently lacks research. According to Matthews et al. (2019), the reasoning for increasing the burden for minority groups may be disproportionate care and socioeconomic disparities in the United States. Barthold et al. (2018) similarly noted that the racial and ethnic disparities might be linked to increased hypertension and diabetes among Hispanic and African American groups. The authors performed a retrospective assessment of Medicare from 2007 to 2013 and found that patients over the age of 65 who were Hispanic and African American females were at the highest risk. The current literature indicates that individual risk factors related to race and ethnicity require further exploration to treat AD's burden among these groups (Barthold et al., 2018).

Age

Age is a key risk for AD. Individuals over the age of 75 are at the highest risk of diagnosis. According to Frigerio et al. (2019), the risk factor of age can be largely linked to exposure to the microglia response that develops faster in females and increases over time. Similarly, Abate et al. (2017) noted the microglia link, which is in part correlated with food and nutrition that decreases over an individual's lifetime. For example, elderly populations are often at lower income levels and intake foods that fail to meet cognitive function's neurological needs. Thus, diet plays a complex role in preventative measures and effective brain processes based on an individual's age (Abate et al., 2017).

A retrospective cohort study by Choi et al. (2020) showed that participants with age-related macular degeneration in the early year had a higher risk for AD (Choi et al., 2020). Another neurophysiological evidence by Taylor et al., 2018, observed the association between hippocampal atrophy and age (Taylor et al., 2018). The results showed that part of the perirhinal cortex is a specific hippocampal region exhibiting atrophy in prodromal AD. The study also showed the greater hippocampal atrophy effects of age in late-life depression (Taylor et al., 2018). One recent neurological research studied the classification parameters of functional connectivity strength in age subgroups. The study successfully distinguished the discrepant pattern of bran functions in different age populations. The author found that an aging process can affect functional connectivity and is associated with cognitive function in the elderly concluded that aging is the primary risk factor of AD and most other neurodegenerative diseases (Zhang et al., 2020). Research on Age-related brain function shows that gender and genetic factors are

confounded with other risk factors (Thibeau et al., 2019). This longitudinal study investigated whether the association between nondemented executive function trajectories and physical activity is moderated by sex and AD genetic risk factors. The results showed that everyday physical activity had a significant effect on executive function in females and a significant effect on mobility in both females and males, and a significant effect on the interaction of gender and APOE factors (Thibeau et al., 2019). A systemic review by Rahman et al. (2019) synthesized genetic, medical, societal, and lifestyle risk, focusing on the role of hormonal changes. The authors noted that the female sex is the major risk factor for late-onset AD (Rahman et al., 2019).

Gender

In terms of gender, African American women and Hispanic women are at the greatest risk for developing AD (Matthews et al., 2019). (Matthews et al., 2019). Nebel et al. (2018) argued gender is a predictive factor based on pathological factors and the social burden. However, Nebel et al. (2018) noted that evidence varies based on geographic location and the population. In the United States, females hold the highest burden of risk for AD (Matthews et al., 2019). Women are also more likely to be at risk for heart diseases linked genetically to a risk of AD diagnosis. Andrew et al. (2018) also noted that framing AD individual risk for gender requires both a pathogenic perspective and a consideration of socio-ecological factors that impact disparities in access for women to healthcare, education, and opportunities post-retirement. Overall, gender is linked as a risk factor for AD but requires further exploration from a clinical standpoint

to encourage preventative efforts and treatment for these sub-groups (Matthews et al., 2019; Nebel et al., 2018).

Age, Genotype, and Sex

Zhao et al. (2020) conducted a neurophysiological study that investigated the interaction among the three major risk factors for AD: age, apolipoprotein E (APOE) genotype, and sex. The study identified interactive molecular pathways underlying AD risk factors. The authors observed a significant interaction between age, APOE, and sex on unfolded protein response pathway and emphasized that the AD gene expression drove a distinct blood metabolome profile (Zhao et al., 2020). Evidence suggests interaction among the three major risk factors for AD: age, APOE genotype, and sex. Zhao et al. (2020) conducted a quantitative study that studied the interactive molecular pathways underlying AD risk factors. The authors observed a significant interaction between age, APOE genotype, and sex on unfolded protein response pathway (Zhao et al., 2020). Previous studies on AD also indicated that gender, age, and lower-income, and education status was associated with the risk of AD, and management of lifestyle and behavioral change reduced the risk of dementia and AD (Akyol et al., 2020; Lista & Sorrentino, 2010; Pakstis et al., 2018; Zeisel et al., 2020). Nationwide research on the change of incidence and prevalence of dementia and AD in Taiwan demonstrated that both incidence and prevalence increased with age and were higher in women than in men (C. Liu et al., 2019). The results illustrate the same trends as the Alzheimer's Association report in 2019. However, the incidence rates reported in this study are much lower than Alzheimer's Association's report (Alzheimer's Association, 2021; C. Liu et al., 2019).

The study by Zhao et al. (2020) identified interactive molecular pathways underlying AD risk factors. The neurological studies corroborated the relationship between aging and AD (Hou et al., 2019; Choi et al., 2019). A systematic review by Hou et al. (2019) determined aging as a risk factor for neurodegenerative disease (Hou et al., 2019). The authors highlighted that aging's biological hallmarks correlate with susceptibility to neurodegenerative disease and that aging is a central risk factor for AD and other neurodegenerative diseases (Hou et al., 2019). Hou et al. (2019) summarized the associations between nine biological hallmarks of aging and the risk of increasing AD (Hou et al., 2019). The authors suggested that aging is associated with physical deterioration, leading to an increased risk of AD (Hou et al., 2019). Cellular senescence and inflammation response to the primary damage of brain function (Hou et al., 2019). The molecular evidence identifies that abnormal deposits of aggregated proteins are commonly found in older individuals (Hou et al., 2019). These brain structural changes might occur much earlier than cognitive impairment presence. The revealing of central biological mechanisms of aging leads to potential targets of novel therapies for neurodegenerative diseases, including inhibition of cellular senescence and targeting of protein aggregation, metabolism, or inflammation (Hou et al., 2019).

Health Risk and Protective Factors

In addition to subgroups of age, gender, race, and ethnicity, personal risk factors play a role in AD. According to Galvin (2017), risk factors include family history, holding the e4 allele, obesity, diabetes, metabolic syndrome, hypertension, depression, physiological and psychological stress, smoking, alcohol abuse, a traumatic brain

disorder. Conversely, the modifiable protective factors are mental activity, educational attainment and lifeline learning, cognitive leisure activities, social engagement, diet, omega-3 intake, and optimism in life (Galvin, 2017).

One of the key health and protective risk factors is vascular disease and chronic high blood pressure. There is epidemiological evidence that chronic high blood pressure increases AD's risk (de Heus et al., 2019; Prince et al., 1996). Other emerging evidence indicated that several medical, environmental, and lifestyle risk factors that lead to AD development are modifiable (Beydoun et al., 2014; Rahman et al., 2019). A review by Silva et al. (2019) summarized the contribution of risk factors to AD development. The author stated that rather than genetic risk factors, acquired factors increase AD development risk. The acquired factors investigated in this study included cerebrovascular diseases, diabetes, hypertension, obesity, and dyslipidemia increase the risk of AD development (Silva et al., 2019). In a longitudinal study in 1996, Skoog et al. (1997) indicated that hypertension has negatively affected cognitive performance and increased the risk of developing AD at late ages (Skoog et al., 1997; Steassen et al., 2007). A longitudinal cohort study by Luchsinger et al. (2005) investigated the association of four major vascular risk factors and AD incidence. The study followed 1,138 individuals without dementia at baseline. The results showed that diabetes and current smoking were associated with AD. Hypertension and heart disease were associated with AD when diabetes and/or current smoking presence. The results also showed that the number of risk factors was highly associated with AD. The adjusted hazard ratio of probable AD for the presence of 3 or more risk factors was 3.4 (95% CI:

1.8, 6.3; p <0.0001) reduced compared to no risk factors (Luchsinger et al., 2005). A European phase III randomized trial studied the associations between blood pressure variability (BPV) and AD. The results showed significant associations between day-to-day BPV and deterioration on Alzheimer's Disease Assessment Scale cognitive subscale (Systolic: p =0.036) and Disability Assessment for Dementia (Systolic: p =0.020; Diastolic: p =0.007) after one year, but not after 1.5 years (de Heus et al., 2019).

Köbe et al. (2020) investigated the association of individual vascular risk and a combined vascular risk score (measured using the Framingham Coronary Risk profile) with global β-amyloid peptide (Aβ) entorhinal tau burden. The results showed that higher Aβ deposition was significantly associated with higher total cholesterol level (β = −0.002 [SE, 0.001]; p = .02), low-density lipoprotein cholesterol level (β = −0.002 [SE, 0.001]; P = .006), systolic blood pressure (β = −0.006 [SE, 0.002]; P = .02), pulse pressure (β = −0.007 [SE, 0.002]; P = .004), and Framingham Coronary Risk Profile score (β = −0.038 [SE, 0.011]; P = .001) among participants not using vascular medications. The study corroborated findings that the vascular risk factors were associated with AD pathogenesis (Köbe et al., 2020). Furthermore, some neurological studies suggested promise for treating AD with anti-hypertensive medications, but it is unclear which anti-hypertensive class is most beneficial for symptomatic versus prophylactic treatment (Lithell et al., 2003; Khachaturian et al., 2006). The health risk factors are considered both individual as well as social variables.

Vascular risks serve as an epidemiological risk for AD patients. Researchers have also indicated that dysregulation of vascular processes increases amyloid-b, linked to AD

(Elias et al., 2018). According to Alby et al. (2018), AD can be linked to a history of obstructive sleeping disorders and vascular diseases. Patients with AD are more likely to have vascular issues and also sleep obstruction as a result. Elias et al. (2018) argued the importance of exploring vascular risk in AD patients as a preventative and intervention measure. According to Clark et al. (2017), a secondary reason for the increase of vascular diseases can be hyper capillary fusion, which increases the flow to cerebral arteries linked to AD (Clark et al., 2017). Overall, vascular-related issues increase the risk of AD (Clark et al., 2017; Elias et al., 2018).

Tau and amyloid b are associated with the risk of AD, which is also linked to vascular diseases. Rabin et al. (2019) explored vascular risks of patients in 152 control samples. The authors explore Tau and amyloid b among these same patients. Rabin et al. (2019) found that amyloid-b, as a result of vascular disease, increased tau deposition, which can also increase the risk of AD later in life. Gottesman et al. (2017) similarly found in a prospective cohort sample of 345 patients with vascular disease that the risk of amyloid -b deposits was higher, increasing their risk of AD and dementia. The role of vascular disease is also linked to lifestyle choices such as diet and exercise (Liu et al., 2019), which are discussed at length in the proceeding sections of this chapter. As such, the following section moves to explore social factors and their relationship with AD risk.

Social Level Characteristics and AD Risk

The second category for AD risk characteristics is broadly categorized as behavioral and social risk characteristics that may increase AD's risk. Social risk factors can be defined as engaging in cognitive stimulation, exercise, diet, and leisure-time

activities. In this section, each of these variables is discussed in relationship with previous literature. The available literature indicates that social factors may serve as preventative factors and a mild treatment method for AD symptomology. First, the social level characteristic of cognitive stimulation is discussed.

Cognitive Stimulation

Cognitive stimulation refers to the process of using education, puzzles, watching informational media programs, and engaging in social groups to increase brain activity (Kim et al., 2017). Cognitive stimulation is considered a top non-pharmaceutical approach to dementia and AD (Kim et al., 2017). Kim et al. (2017) provided a meta-analysis of approaches and found a moderate benefit for cognitive stimulation. However, limitations to the approach included small-sample sizes and a possible risk of bias in some studies. Clinical trial data, however, indicate positive outcomes for cognitive stimulation. Lara et al. (2020) performed a trial analysis of 40 patients with AD during COVID-19 lockdown in Spain. The patients were provided a cognitive stimulation program and evaluation after the program. Lara et al. (2020) found observant differences in agitation reduction, an increase of apathy, reduction of anxiety, and neuropsychiatric symptoms. However, the authors noted that limitations include worsening behavior and social outbursts from AD increased due to the pandemic's isolated status.

Researchers studied non-cognitive and cognitive benefits in their studies. For example, Capotosto et al. (216) assessed cognitive stimulation therapy on 39 AD patients over seven weeks. A control group was also included that performed only exercise therapy. Capotosto et al. (2016) found positive outcomes in quality of life, language tests,

functional activities, and behavior for patients that underwent cognitive stimulation therapy. Poubadie et al. (2018) also reported that cognitive stimulation might affect microphage in AD patients by targeting amyloid-beta accumulation. In samples of mice and rats, the accumulation of amyloid-beta (associated with AD) was reduced, and cognitive outcomes were increased. However, there was a call for replicating human AD samples (Poubadie et al., 2018).

Technological approaches are also key in cognitive stimulation programs. Astell et al. (2018) explored the outcomes on computer uses in dementia and AD groups through three-month pre-and post-tests. According to Astell et al. (2018), patients that underwent the computer training programs experienced a significant improvement in their quality of life and cognition. However, the findings were not replicated in terms of slowing the progression of AD. Cognitive stimulation therapy in a Brazilian sample also found positive results (Marinho et al., 2020). Marinho et al. (2020) assessed the use of cognitive stimulation therapy on a sample of 49 dementia and AD patients and found an increase in quality of life and cognitive behavior. The patient's mood was also improved, as well as a reduction in caregiver burden. Marinho et al. and Astell et al. both suggested the continued use of cognitive stimulation to prevent and manage dementia and AD.

Exercise

Exercise is one approach that can be considered effective for reducing AD diagnosis likelihood (Cass, 2017). Cass's (2017) systematic literature review indicated that exercise could reduce morbidity and mortality rates and reduce AD's burden. The impact of exercise is seen in terms of hippocampal volume, blood flow to the brain, and

the brain's neurogenesis. Further, clinical trials illustrated the importance of exercising for elderly populations (Cass, 2017). Similarly, Valenzuela et al.'s (2020) systematic review of exercise and AD indicated that it could prevent cardiovascular issues and diabetes associated with AD risk. Exercise is also associated with promoting myokines that produce muscle and metabolic proteins ant that critical for brain activity and reduce inflammation. However, Cass (2017) and Valenzuela et al. (2020) called for large-scale studies to explore AD patients' impact.

In terms of empirical evidence, some clinical trials demonstrate the impact of exercise on AD. Morris et al. (2017) performed a randomized controlled pilot study on a sample of 76 participants over the age of 70. The patients exercised for six months, and the pre-and post-tests for memory, executive function, ability, and depression were compared statistically. Morris et al. (2017) found that aerobic exercise increased functional ability, increased associated cardiovascular fitness, and improved memory performance. The authors did find that hippocampal atrophy was reduced, which could be key for AD patients. Conversely, a clinical trial by van der Kleij et al. (2018) explored the impact of aerobics on 22 elderly AD patients. The patients were provided training for exercise over 16 weeks. Van der Kleij et al. (2018) reported that the regional cerebral blood flow outcomes were not significant and could not address the reduction of patients with mild AD symptoms. However, both van der Kleij et al. and Morris et al. warned that exercise might be best for low symptomology at the onset of diagnosis.

Researchers evaluated the exercise in terms of impact on the microbiome. Abraham et al. (2019) explored the impact of exercise and probiotics on a sample of

transgenic AD mice. The authors performed subjected exercise training and probiotic supplementation in control and treatment samples. Abraham et al. found that probiotic treatment and exercise decrease AD's progress by altering the mice's microbiome. However, the same assessment has yet to be applied to human samples since the 2019 publication. However, Cui et al. (2018) argued that pharmacotherapy might be a possible treatment that can address cognitive decline through exercise and p[possibly nonpharmacological treatments such as probiotics. The findings of Cui et al. and Abraham et al. indicate the need for future research in human trials.

Diet

Diet plays a key role in regulating risk factors for cardiovascular burden, obesity, and diabetes, linked with AD (Taylor et al., 2018). Various dietary approaches are recommended and explored for AD patients, including the ketogenic diet tested by Taylor et al. (2018). According to Taylor et al. (2018), a ketogenic diet can mildly impact AD patients in a clinical sample of 11 participants. Dietary outcomes were based on the impact of cognitive improvement after one month of adherence to the diet. Broom et al. (2019) similarly suggested a ketogenic diet through reviewing related ketogenic research in AD patients. According to Broom et al., glucose metabolism and amyloid-beta is reduced through ketone increase. The ketogenic diet is also encouraged based on the premise that ketones' increase addresses amyloid plaques' neurotoxicity in AD patients.

Dietary changes are also associated with a change in inflammation, which is linked to AD. According to McGrattan et al. (2019), dietary changes reduce inflammation and improve cognitive aging by addressing inflammatory pathways through anti-

inflammation dietary supplementation. Pinto et al. (2018) also noted that inflammatory issues could be addressed through the acetogenic diet that addresses neurons that reduce inflammation, which is key for protecting individuals against AD's risk or slowing the diseases' progression. A limitation of understanding dietary changes for AD is the lack of empirical assessments such as controlled or randomized studies. Hill et al. (2019) advocated for dietary changes but found that only a small effect was found for addressing AD biomarkers in randomized trials. The meta-analysis performed by Hill et al. (2019) only identified 13 studies that demonstrated a significant positive result on AD patients. Hill et al. argued that while diet may be an important nonpharmacological approach, extensive clinical assessments are required for demonstrated efficacy.

Leisure Time Activities

Leisure time activities are a sub-variable of cognitive stimulation, considered as a risk factor and possibly a preventative factor for AD (Ogina et al., 2019). Ogina et al. (2019) assessed AD patients' metabolic energy expenditure before diagnosis to assess the impact and the possible correlation as a risk and protective factor. According to Ogina et al. (2019), a sample of 1345 individuals revealed that past leisure time activities were associated with reduced AD risk and a hazard ratio. Individuals who performed leisure time before diagnosis were at a decreased risk and experienced some symptomology reduction. Similarly, Palta et al. (2019) assessed if leisure time activities reduced cognitive decline and dementia in a sample of 10705 patients. The statistical analysis indicated that leisure time activities were associated with a lower risk of dementia and a reduced cognitive decline risk. Palta et al. and Ogina et al. (2019) indicated that leisure

time activities are a modifiable factor that can impact AD and serve as a model for reducing symptomology (e.g., use of cognitive stimulation and exercise in AD patients.

Leisure time activities may prevent the risk of AD (Khoury et al., 2019; Zotcheva et al., 2018). However, Khoury et al. (2019) noted that leisure time activities might also be key for delaying AD in some patients. Leisure time activities are associated with reducing issues such as cardiovascular disease, diabetes, and obesity. Patients that completed leisure time activities are also less likely to smoke and be at risk of comorbidities. Khoury et al. (2019) performed an analysis based on a meta-analysis, randomized controlled trials, controlled study, quasi-experimental study, and a review of expert committee reports and options. The authors concluded that key recommendations for preventing and delaying AD should be engaging in social activity and adjusting diet and exercise. Overall, lifestyle changes were recommended as a predictive and preventative factor for AD patients (Khoury et al., 2019).

Leisure time activities are also associated-with a reduced risk of mortality for AD patients. Zotcheva et al. (2018) explored a sample of 36,945 Norwegian patients ranging from 50-74 years of age. These patients were surveyed regarding psychological distress and dementia-related mortality related to inactivity or engagement in leisure time activities. Zotcheva et al. (2018) found that leisure time activities, compared to inactivity, were associated with lowered dementia-related mortality risk. Psychological distress was also reduced for patients that performed leisure time activities. Similarly, findings were reported by Patel et al. (2018) in a U.S. sample that explored leisure time activities and nutrition and cause-specific diseases. Leisure time activities were associated with a

reduction of mortality for cause-specific diseases, such as AD. Overall, the evidence presented in empirical literature presents positive outcomes for leisure time activities and the importance of considering inactivity as a risk factor (Khoury et al., 2019; Patel et al., 2018; Zotcheva et a., 2018).

Previous and Ongoing Educational Opportunities

In the previous section discussing individual risk factors, in terms of cognitive function, I emphasized the importance of education and ongoing learning. Educational background and the ongoing learning of an individual are considered preventative risk factors for AD patients. According to Anderson et al. (2020), a sample of 1,700 AD cases compared with 37,154 control samples revealed that intelligence and learning could increase AD's risk. The patient's genetic results were compared using a multivariable randomization effect, and a bidirectional relationship was found with intelligence and educational attainment. Individuals with higher levels of education and intelligence were at a reduced risk of AD. In these cases, risk-based education is largely associated with the ability to continually challenge brain function and maintain cognitive stimulation across a lifetime.

In terms of life-long learning, researchers indicated that patients must engage in learning and cognitive stimulation activities to engage brain activity (Velazquez et al., 2019). According to Velazquez et al. (2019), life-long learning can increase cognitive function when combined with nutritional supplementation such as Choline. Quinn and Blandon (2017) similarly argued that life-long learning could be essential not only for cognitive growth but for humanizing patients with AD. According to Quinn and Blandon

(2017), patients with AD are placed in positions that limit their independence and feel dehumanizing; however, life-long learning opportunities increase brain engagement and autonomy.

Empirical evidence for life-long learning is reduced compared to topics such as nutrition and social alterations (Liu et al., 2019). However, Rosenberg and Nygård (2015) presented a phenomenological approach that emphasized the importance of continuing to provide opportunities for engagement and learning for AD patients. A sample of seven dementia patients revealed themes regarding the need to rely on learning as a means of remaining updated with the external environment. The qualitative perspectives of Rosenberg and Nygård (2015) and considerations of Quinn and Blandon (2017) emphasize the importance of also considering what is best for the patient from a social perspective.

Educational opportunity and life-long learning are also linked in terms of gender differences. Female groups are often denied the same educational opportunities and life-long learning spaces as male groups (Laws et al., 2018; Soldan et al., 2017). As a result, disparities are present in terms of the gender of females for AD. However, researchers noted that such gender disparities vary greatly on geographic location and age sample (Liesinger et al., 2018). For example, current AD assessments included participants more likely to participate in traditional gender roles that reduced female education and learning opportunities (Nebel et al., 2018). As a result, bias exists in these samples and requires a continual examination to assess if changes in socio-cultural gender divides have reduced

the burden of risk in terms of women lacking educational and life-long learning opportunities (Nebel et al., 2018).

Synthesized Studies Related to the Research Questions

This study's primary research question was the extent to which the level exists between the earlier life sociodemographic predictors of health, health services, labor force, economic status, family structure, retirement expectations, and the later onset of AD. Theoretically grounded in the socio-ecological framework, there are hierarchical relationships among the factors. Through a systematic search of the literature, there is no similar conducted study. This section summarizes some recent epidemiological and neuropsychological research regarding the relationship between the mid-lifestyle risk factor and AD development.

Epidemiological and gerontological research suggested that mid-life healthy lifestyle choices are considered protective against AD (Serrano-Pozo & Growdon, 2019). The results showed that mid-life (age <65 years) vascular risk factors increase the risk of late-onset (age ≥ 65 years) AD and dementia. Healthy lifestyle factors, such as leisure activities, physical exercise, and Mediterranean diet, are protective against AD development (Serrano-Pozo & Growdon, 2019). Previous neurological research suggests that frontal pathology could underlie these relationships. However, clinical-pathological studies have shown that the most common pathological substrate of dementia in community-dwelling elderly people is mixed. Saari et al. (2020) conducted a longitudinal study that followed 236 patients with mild AD for 5 years. The study provided direct evidence that neuropsychiatric symptoms in AD are related to ADLs (Saari et al., 2020).

The results showed that as AD progresses, common (apathy) and uncommon neuropsychiatric symptoms (NPSs; aberrant motor behavior, appetite disturbances, delusions) seem to be related to ADLs through various symptom interactions (Saari et al., 2020). Gerontological research was studied in a small population from a primary care clinic (Akyol et al., 2020). The study suggested that lifestyle and behavioral change management reduced the risk of dementia and AD (Akyol et al., 2020). Another gerontological study showed that higher levels of everyday physical activity and mobility performance (EPA) are associated with better executive function (EF) trajectories (Thibeau et al., 2019). This longitudinal study investigated whether this association is moderated by sex and AD genetic risk factors. The results showed that the EPA had a significant effect on EF in females and a significant effect on both sexes' mobility. The authors pointed that there were significant sex x APOE interaction effects. The study's findings lead to a precision health approach to research of effects of physical activity and mobility on EF (Thibeau et al., 2019).

A review conducted by Roberts et al. (2017) investigated the effects of physical activities in older adults over age 60. The research studied the association between physical activity and different ADL types (Roberts et al., 2017). Different types of ADLs were investigated, including levels of mental (e.g., memory, attention), physical (e.g., coordination, balance), and social (e.g., social interaction) demands (Roberts et al., 2017). Neurophysiological rationale and potential intervention were studied in previous studies. A comprehensive review by Hou et al. (2019) synthesized the association between nine biological hallmarks of aging and increasing AD risk. The authors noted that the risk of

neurodegenerative disease is associated with early developmental defects. Non-pharmacological interventions, including calorie restriction and physical activity, have a promising effect of an anti-inflammatory (Hou et al., 2019). Spielman et al. (2016) corroborated that physical activity as non-pharmacological interventions have anti-inflammatory effects. The study showed that a physically active lifestyle reduces the risk of developing brain diseases (Spielman et al., 2016). A neuropsychological study by Sutin et al. (2019) evaluated the association between cognitive functions and personality traits that could partially be explained by physical activity level. The linear regression model was used to examine the association between personality and cognitive functions controlled for age, sex, race, ethnicity, education, and hospital care assurance program (HCAP) administration language (Sutin et al., 2019). The results demonstrated that personality traits have differential associations with five cognitive function domains and suggest that personality is associated with intermediate markers of cognitive health (Sutin et al., 2019).

The effect modification and inconsistent relationship between risk factors and AD have been explored in previous studies (Reitz et al., 2011; Shih et al., 2018). The results showed interactions between ADL and other risk factors (Reitz et al., 2011; Shih et al., 2018). A large prospective cohort study conducted in a community-dwelling Mexican-American population showed that low levels of physical activity and diabetes increase the overall risk of dementia/cognitive impairment without dementia (CIND) (Shih et al., 2018). The overall hazard ratio for physically active and diabetes were 0.70 and 2.20, which indicated a risk of AD. However, the subgroup analysis showed that the effect of

ADL was modified by diabetes. The risk of CIND increased by the low level of physical activity (Shih et al., 2018). The increases were 0.55 and 0.72 in the diabetes group and no-diabetes, respectively (Shih et al., 2018). Reitz et al. conducted a systematic review of epidemiological studies before 2010 (Reitz et al., 2011). The authors noted that the high risk of blood pressure (BP) on AD was modified by age (Reitz et al., 2011). High blood pressure increases the overall risk of AD (Reitz et al., 2011). However, as age increases, the risk of BP for AD decreases or is even inverted (Reitz et al., 2011). The lifestyle-based interventions could maximize public engagement in dementia risk reduction. A cross-sectional study indicates that males, older adults, and lower-educated and income are priority groups that should be guided for lifestyle and behavioral changes regarding dementia risk reduction (Akyol et al., 2020). Better understanding the effect modification over time can promote earlier detections, preventing AD in an earlier stage (Reitz et al., 2011). In this study, I hypothesized that the effect of ADL on AD is modified by other health conditions, including high blood pressure, diabetes, cancer, lung disease, heart disease, stroke, psychiatric problems, and arthritis. The interactions between ASL and these risk factors were examined in this study.

Summary and Conclusions

This study's primary research question was the extent to which the level exists between the earlier life sociodemographic predictors of health, health services, labor force, economic status, family structure, retirement expectations predict the later onset of AD. Grounded in the social epidemiology frameworks, this study incorporated the distribution of structural factors and individual risk factors that determine the incidence

and prevalence of the disease and investigate the hierarchical relationships among the effect of the factors. The current epidemiological and neuropsychological research has studied the relationship between ADL and AD development throughout this literature research. However, the research only investigates ADL as an independent risk factor. Furthermore, although many researchers conducted their statistical models adjusting on the risk factors, such as age, gender, medical history, and social characteristics, there is no study investigating the relationship in a hierarchical structure (Krieger, 2001a; Lista & Sorrentino, 2010; Serrano-Pozo & Growdon, 2019; Rahman et al., 2019).

The epidemiological and neuropsychological evidence demonstrates that ADL is associated with AD development (Saari et al., 2020). Previous epidemiological research suggested the healthy lifestyle choices in mid-life are protective against AD. The findings also show that these lifestyle factors confound with the other risk factors (Rahman et al., 2019). Epidemiological research showed that mid-life vascular risk factors increase the risk of late-onset AD. In contrast, healthy physical exercise is protective against AD development (Serrano-Pozo & Growdon, 2019).

Researchers observed the inconsistent effects on self-reported ADL measures. Roberts et al. (2017) showed that moderate physical activity levels with high mental, physical, and social demands might produce the greatest benefits on ADL physical performance (Roberts et al., 2017). Linear regression was used to examine the association between the five different personality traits and each cognitive task and a composite score while controlling for age, sex, race, ethnicity, and education (Sutin et al., 2020). Sutin et al. (2020) also assessed whether these sociodemographic factors or mental status

moderated the associations. The results showed that some shared mechanisms are likely to contribute to the associations between personality and cognition. Still, specific mechanisms are more relevant for some traits than others (Sutin et al., 2019). A longitudinal study showed that everyday physical activity had a significant effect on executive function in females and a significant effect on mobility in both females and males, and a significant effect on the interaction of gender and APOE factors (Thibeau et al., 2019).

Although the previous studies have expounded that personality factors are associated with AD and dementia, they have not been examined against markers of brain functioning, such as regional brain glucose metabolism (Sohrabi et al. 2020). A previous neurological study found that physical activity as a non-pharmacological intervention has anti-inflammatory effects. In addition, the study showed that a physically active lifestyle reduces the risk of developing brain diseases (Spielman et al., 2016). Clinic-pathological studies have shown that the most common pathological substrate of dementia in community-dwelling elderly people is mixed (Serrano-Pozo & Growdon, 2019). From a neuropsychiatric perspective, AD progress is related to ADLs through various symptom interactions (Saari et al., 2020). Sohrabi et al. (2020) found significant relationships between personality factors and glucose metabolism in neural regions more susceptible to AD neuropathology in older adults.

The personality traits study by Sutin et al. (2019) concluded no robust evidence to support that the association between personality and cognition was moderated by sociodemographic characteristics or global cognitive function (Sutin et al., 2020). These

findings support the need for longitudinal research into the potential mechanisms underlying the relationship between personality and dementia risk, including measurement of change in other AD biomarkers (amyloid and tau imaging) and how they correspond to personality factors. Men and people with more lifestyle risk factors for common chronic diseases (e.g., smoking, obesity, and excess alcohol consumption) are less willing to adhere to current low-risk alcohol guidelines to reduce dementia risk (Oliveira D et al., 2019). Alzheimer's Research UK developed a strategic action plan that provides long-term dementia and AD research guidance and develops life-changing treatments (Mauricio et al., 2019). The plan tackled the research gaps and articulated the unmet research needs in how the effect of ADL influence the incidence and prevalence of AD (Mauricio et al., 2019). The plan called for innovative approaches in conducting clinical trials to detect disease 10-15 years earlier than we currently do today (Mauricio et al., 2019).

In Chapter 2, I summarized the search strategy and databases used for the literature, synthesized the theoretical foundation, and described the theoretical frameworks to guide this study's analysis. The key variables and concepts section reviewed the literature regarding this study's key independent, dependent variables. To emphasize the relationship between ADL and AD, I also synthesized the current studies related to the research. Chapter 3 discusses the methodology, the research design and approach, setting and sample, instruments and materials, data, data analysis, methodological limitations, and the ethical safeguards to my research.

Chapter 3: Research Method

Introduction

As of 2021, there were over six million cases of AD in the United States (Alzheimer's Association, 2021). As the size of the U.S. population age 65 and older continues to increase, the number of Americans with AD will grow to make it a persisting national problem that requires immediate attention (Kamiya et al., 2018; Kawaharada et al., 2019). Both the number and proportion will escalate rapidly in coming years, thus AD risk factors including age, genetic risk and family history, cardiovascular risk factors, and brain trauma must be assessed and minimized as soon as possible (Serrano-Pozo & Growdon, 2019). On the other hand, engaging in healthy lifestyle choices such as leisure activities and physical exercise can be protective against AD (Serrano-Pozo & Growdon, 2019). Given the potentially protective effects of lifestyle factors (Cass, 2017), using ADL to predict the onset of AD shows promise (Roehr et al., 2019). However, modifiable factors, such as social characteristics, moderate the protective effect and relationship between protective factors and AD development (Beydoun et al., 2014; Shih et al., 2018; Sutin et al., 2019). At present, there is a gap in the research regarding how early years' ADL and changes in early years' ADL may predict AD diagnosis at a later point in time.

The purpose of this study was to examine the relationship between early year ADL and the development of AD in later years while accounting for the influence of key sociodemographic factors. The population of interest was adults 50 years old in the United States. The independent variables were the sociodemographic factors (health, health services, labor force, economic status, family structure, and retirement

expectations), past ADL, and past change in ADL. The dependent variable was the onset of AD diagnosis. Grounded in social epidemiology theoretical frameworks, this study examines the hierarchical relationships between these variables.

In this chapter, I provide an overview of the methodology of the study. The discussion includes the rationale of the chosen research design, description of the target population, sampling strategies, and procedures followed. Furthermore, I provide a discussion about the operational definitions of the study variables, data analysis plan, threats to validity, and ethical procedures adhered to. A summary of the key details on the methodology concludes the chapter.

Research Design and Rationale

The research questions of the study pertain to the relationships between early year ADL and the development of AD in later years while accounting for the influence of key sociodemographic factors. The independent variables were the sociodemographic factors (health, health services, labor force, economic status, family structure, and retirement expectations), past ADL, and past change in ADL. The dependent variable was the onset ofAD diagnosis. The research methodology for the present study was quantitative.I address the question about whether the quantitative method with a correlational research design is appropriate to this study in the following discussions and connects the quantitative analysis to the research questions.

Quantitative research involves statistical methodology to provide objective measurements and inferences about a group of people and generalize it to a larger population (Camm, 2012; Hancock & Mueller, 2010; Wisniewski, 2016). Thus,

quantitative research is numerical and relational (Balnaves & Caputi, 2001). A quantitative study is used to examine variables that can be expressed in quantified forms and how these variables relate to one another (Vogt, 2011). A quantitative inquiry is also empirical, able to achieve powerful results through high statistical power (Vogt, 2011). Quantitative methodology is used with studies that have research questions that require the collection of numerical data, implementation of statistical analysis, and reporting of objective measurements (Leedy & Ormrod, 2016). All of these attributes make a quantitative approach a good fit for this study. In present study, I intend to address issues that can be quantified as evinced by prior researchers such as Bugliari et al. (2016).

Research regarding neurodegenerative disease studies age-dependent patterns within or between individual changes in traits during a lifetime. Because of the lack of longitudinal and adequate data on neurodegenerative diseases, existing studies are mostly cross-sectional. Researchers identified the gap and suggested the use of longitudinal data (Alberdi et al., 2018) and a combination of baseline data, and data on changes over time (Li et al., 2017). The associations reported between variables based on cross-sectional comparisons may be confounded with progressive changes and phenotypic population characteristics (van de Pol & Verhulst, 2006). Unbiased estimation of patterns of age-dependent requires disentanglement of individual change and intraclass change (van de Pol & Verhulst, 2006). Moerbeek et al. (2008) stated that the research questions in a relational study pertain to the relationships between variables (Moerbeek et al., 2008).Therefore, the proposed study was explicitly relational study.

The research design was historical and correlational. In present study, I used a secondary dataset and conducted a multilevel hierarchical analysis. Correlational research is a nonexperimental design (Johnson, 2001). Nonexperimental research is appropriate when the variables under study cannot be manipulated (Curtis et al., 2016). I addressed such issues in this study by including sociodemographic factors and the activities of daily living a person undertook in the past. Researchers investigate relationships between numerically measured variables without manipulating any of the variables in a correlational research design(Curtis et al., 2016; Goodwin & Goodwin, 2016). Using correlational research design I have an opportunity to observe two or more variables in order to establish a statistically conforming relationship between or among them (Leedy & Ormrod, 2016; Whitley et al., 2013). I considered such relationships in present study. Finally, a historical approach is appropriate when there are secondary data available (Curtis et al., 2016).

The secondary data source contains rich individual and family variables. The core content areas include health, health services, labor force, economic status, family structure, and retirement expectations (Bugliari et al., 2016). Key study variables include the onset of AD, the participants' early years' ADL indices, and sociodemographic factors. The independent variables were sociodemographic factors (health, health services, labor force, economic status, family structure, and retirement expectations), past ADL, and past change in ADL, whereas onset of AD diagnosis is the dependent variable. I imported these data into R software, and used multilevel hierarchical analyses to address the research questions and test the study hypotheses.

The statistical methodology for the present study was a practical and robust approach that was introduced by Aguinis et al. (2013). This four-step approach estimates cross-level interaction effects using multilevel modeling tests different hypotheses and evaluates the hierarchical structure relationships (Aguinis et al., 2013). Moreover, the present multilevel approach uses a generalized linear model. Through an iterative generalized least squares process, the approximate standard errors of the parameter are estimated, the relationships between ADL and AD can be investigated. I will discuss hypothesis, formulas, and detailed analysis procedures in the analysis plan section.

Methodology

Population

The Health and Retirement Study (HRS) is a representative national multilevel panel study by the RAND Corporation Center for Study of Aging (RAND, 2021). HRS population is grouped into six cohorts by year of birth and year of the first interview (Bugliari et al., 2016). The questions about AD and dementia are first asked in Wave 10 (Bugliari et al., 2016). Based on the RAND manual, 15,329 participants answered the questions regarding whether or not a doctor has told the respondent he/she has AD or dementia in Wave 10 (Bugliari et al., 2016).

I extracted the RAND HRS Fat files through the HRS website. The target population of this study was adults 50 years old years old in the United States who participated in the HRS study and completed the survey questionnaire about AD and dementia. Furthermore, those who do not have any ADL indices recorded were excluded from this study. The RAND HRS Fat data are available for public research and free to

download at the HRS website. There is no need to secure permission to use the data from HRS administrators.

Sampling and Sampling Procedures

The population was not sampled directly; instead, I used the RAND Health and Retirement Study (HRS) Fat files (RAND, 2021). Two inclusion/exclusion criteria applied to RAND HRS fat files. Only participants who participated in the HRS study and completed the survey questionnaire about AD and dementia and completed details on ADL indices were included in the data for analysis. The data were screened for missing values and extreme outliers. All patients with more than 50% missing data on the sociodemographic variables were excluded from the analysis. Mean imputation was used to replace missing values for the remainder of the participants. Following this procedure, a total of 4,526 patients were selected for the analysis.

Power Analysis

The sample size for this study was based on the number of participants who met the inclusion and exclusion criteria. However, to have sufficient sample size and power to reject the primary null hypothesis, I conducted a power analysis to suggest minimum sample sizes across a range of parameters. In a multilevel model, the power calculation is not a monotonic function (Maas & Hox, 2005; Paccagnella, 2011; Scherbaum, 2009). Mathieu et al. (2012) introduced a simulation approach to estimate the statistical power for multilevel models (Mathieu et al., 2012). I used the "SIMER" R package to

determine the recommended sample size (Green & MacLeod, 2016). The results of the power analysis are presented in the Appendix.

Procedures for Recruitment, Participation, and Data Collection

Walden University Institutional Review Board (IRB) approved this study before data were extracted from the HRS website. After securing IRB approval, I extracted the data following the prespecified extraction plan. The population was not sampled directly; instead, I used the secondary data from HRS . HRS data are available for public researchers and are free to download at the HRS website. Thus, there is no need to secure permission to use data from HRS administrators. All patients who satisfied the inclusion and exclusion criteria were considered as the target population and the sampling procedures mentioned above were followed to select the participants for the study. I only extracted relevant variables from the HRS data and used for the study analysis.

I accessed the HRS website and located the dataset relevant to the study. Patients met inclusion criteria of the study were adults 50 years old years in the United States who participated in the HRS study and completed the survey questionnaire about AD and dementia. Only patients who completed details on ADL indices were included in the data for analysis. Data contain all sociodemographic factors (health, health services, labor force, economic status, family structure, and retirement expectations). I imported data into a .CSV file and processed in Microsoft Excel.

Instrumentation and Operationalization of Constructs

According to Bugliari et al. (2016), the HRS study surveys a sample of approximately 20,000 people in the United States. The questions about AD and dementia

were first asked in Wave 10 and based on the preliminary analysis conducted, 15,329 participants answered the questions regarding whether or not a doctor has told the respondent they have AD or dementia in Wave 10 (Bugliari et al., 2016). Data on sociodemographic factors (health, health services, labor force, economic status, family structure, and retirement expectations), past ADL, past change in ADL, and current AD diagnosis were retrieved from the HRS data set. I will include discussion of operationalization for each variable in next section.

In HRS, the core content areas include health, health services, labor force, economic status, family structure, and expectations (Bugliari et al., 2016). The level of economic status and family structure reflect the social structure level characteristics of the target population. The social structure level variables explain the between-group variability. The demographics and health status are personal level characteristics. The scale of all covariates were standardized with Mean 0 and Variance 1. The personal economic status and number of family members also served as the personal level variables. The values were centered by denoting the mean value of the social structure group. The centered scale represents the relative score for individuals in each social structure group.

Dependent Variable

AD diagnosis was the dependent variable in this study and was a binary variable derived from the original RAND HRS questionnaire. The original variable, RwALZHE, represents the raw response to the questions regarding whether or not a doctor has told the respondent they had AD (Bugliari et al., 2016). If the interviewed participant

responded “same as in the prior interview,” a preload value was entered. Only those who have either values “1. Yes”, “0. No”, “3. Disp prev record and had cond”, and “4. Disp prev record and no cond” were included in this study. Those who have missing values or refused to respond were not included.

Independent Variables

In the first model, the independent variable was 10 years average of ADL indices. The range of years are from 5 years to 15 years prior to the year of AD diagnosis. In the secondary model, the independent variable was 10 years average of ADL index change in the same time ranges. In the calculation above, I used the original ADL indices. The original ADL indices in HRS are enhanced format of Wallace and Herzog’s ADL indices (Bugliari et al., 2016; Wallace & Herzog, 1995). In order to increase the generalizability, I included sensitivity analysis to increase generalizability of the study. The independent variables in sensitivity analysis were 5 years average of ADL indices with a range from 10 years to 15 years prior to the AD diagnosis. In order to establish a meaningful interpretation across the models, the ADL measurements were re-scaled into [0,1].

Data Analysis Plan

I used the R software Version 4.1.1 for all data analysis in this study. R provides a comprehensive range of statistical tests (Lafaye de Micheaux et al., 2013). All data were preprocessed using Microsoft Excel. Preprocessing aims to ensure a clean data set by excluding missing data and extreme outliers. I conducted a visual screening of the data set to identify any missing data. A listwise deletion is useful tool to identify the extensive missing data(Hawthorne & Elliott, 2005). I applied a listwise deletion on those

participants who have extensive missing data on sociodemographic factors (more than 50% missing data). That is, I excluded these participants from the analysis. On the other hand, I used the box and whisker plots to determine any extreme outliers in the data. I also included accuracy of the responses checks in the study. Transformation methods such as different *log* transformations were conducted to help mitigate these problems. Once a complete, the data set was ready to use, then, I exported it to R software for data analysis.

The following were the research questions and corresponding hypotheses that were addressed and tested, respectively:

RQ1: What is the relationship-between different specific early years' ADLs and later onset of AD?

$H_0$1: There is no relationship between early years' ADLs and the later onset of AD.

H_a1: There is a significant relationship between early years' ADLs and the later onset of AD.

RQ2: What is the relationship between changes in early years' ADL and later onset of AD?

$H_0$2: There is no relationship between changes in early years' ADL and the later onset of AD.

H_a2: There is a significant relationship between changes in early years' ADL and the later onset of AD.

RQ3: To what extent do sociodemographic factors moderate the relationship(s) between early years' ADL and AD?

$H_0$3: None of the sociodemographic factors moderate the relationships between early years' ADL or ADL changes and AD.

H_a3: One or more of the sociodemographic factors moderate the relationships between early years' ADL and/or ADL changes and AD.

Due to the nature of hierarchical structure data, both the intercept and slope of the model varied across groups. In this study, I employed a multilevel model through a four-step approach to handling these statistical challenges.

Grounded in Raudenbush and Bryk's (2002) and Snijders and Bosker's (2012) research studies, Aguinis et al. (2013) proposed a four-step approach to implement a multilevel model. Aguinis' approach test three types of hypotheses to evaluate the relationships or effects in hierarchical structure data (Aguinis et al., 2013). These effects are low-level direct effects, cross-level direct effects, and cross-level interaction effects (Aguinis et al., 2013). For this study, I extended the Aguinis et al.'s example in his paper by replacing the Linear Regression Model (LML) with the Generalized Linear Model (GLM).

The generalized linear model allows the new approach to accepting a binary variable as a dependent variable. Specifically, the estimates of parameter standard errors and the relationship between ADL and AD was determined from the iterative generalized least squares process. I express the basic formula in Equations 1, 2, and 3. Substituting Equations 1, 2, and 3, I express the final cross-level interaction model in equation 4.

$$\text{Ln}\left(\frac{p}{1-p}\right) = \beta_{oj} + \beta_{1j}(X_{ij} - \bar{X}_j) + \gamma_{ij} \quad (1)$$

$$\beta_{oj} = \gamma_{oo} + \gamma_{01}(W_j - \bar{W}) + \mu_{oj} \quad (2)$$

$$\beta_{1j} = \gamma_{1o} + \gamma_{11}(W_j - \bar{W}) + \mu_{1j} \quad (3)$$

$$\text{Ln}\left(\frac{p}{1-p}\right) = \gamma_{oo} + \gamma_{01}(W_j - \bar{W}) + \gamma_{10}(X_{ij} - \bar{X}_j) + \gamma_{11}(X_{ij} - \bar{X}_j)(W_j - \bar{W}) + \mu_{oj} + \mu_{1j}(X_{ij} - \bar{X}_j) + \gamma_{ij} \quad (4)$$

Where p is the probability of the AD presence. γ_{oo} , the fixed portion of the intercept in Equation 2, indicates how a level 2 variable intercepts deviate from the grand mean intercept. γ_{01}, the random portion of the intercept is interpreted as the possibility of AD presence of a cross-level direct effect associated with a one-unit increase in ADL measurement. Slope γ_{10} indicates the slope of AD presence on ADL measurement. The residual μ_{1j} in Equation 3 indicates how groups' slopes differ from the pooled slope across the groups. The μ_{1j} and its variance τ_{1j} depict how the slope varies across groups. If the lower bound does not include zero, then we can conclude that the slope is significantly different across groups. The γ_{ij}, the level 1 residual, indicates how the AD presence varies in the individual level around the predicted value.

I tested the components in Equation 4 through the sequence steps. Through an iterative generalized least squares procedure, a set of parameters were estimated. The Maximum Likelihood Estimate (MLE) method maximizes the likelihood of estimates in the study population. The hypothesis and the formula express the relationship, and procedures that are used to account for statistical tests are described in each step.

Step 1

Because of the nature of hierarchical structure data, the intercept and slope of the model vary across the groups. It is likely that the average means are different across groups. The hypothesis tested in this step, therefore, was that there is no difference in intercepts γ_{oo} across groups. The purpose of this step was to establish a function that parameterizes the grand mean, across-group mean's difference, and within-group difference. Aguinis et al. (2013) named this model as NULL model. I express the combined formula in Equation 5.

$$\text{Ln}\left(\frac{p}{1-p}\right) = \gamma_{oo} + \mu_{oj} + \gamma_{ij} \quad (5)$$

In this equation, γ_{oo} and μ_{oj} are fixed components of intercept that inherit from Equation 4. γ_{oo} and μ_{oj} represent the deviation in intercept, and are estimated in this null model. In this step, the predictors were omitted. An alternative interpretation of this model is that the variance of μ_{oj} explains the degree of heterogeneity in intercepts across the level 2 groups, and the variance of γ_{ij} explains the within-group difference. The intraclass correlation (ICC) was also calculated in this step.

Step 2

The test interest in this step was the significance of the regression coefficient and the random component of the intercept. The null hypothesis for testing the regression coefficient is that the beta (coefficient) is zero, and the alternative hypothesis is that the beta is not zero. In multilevel analysis, the standard normal sampling distribution is assumed under the null hypothesis. The statistic testing the estimated regression coefficient over its standard error indicate the significance. The null hypothesis for

testing the variance of intercept is different from zero across groups, and the alternative hypothesis is that the variance of intercept across groups is zero. Testing the statistical significance of variance is to use the likelihood ratio that is matches deviance in the model fitting.

In this step, I added the random portion of the intercept γ_{01} and predictors to the model. Aguinis et al. (2013) named this model as a random intercept and fixed slope model (RIFSM). The likelihood ratio was then calculated by comparing the deviance of RIFSM and NULL model. I express the RIFSM model in Equation 6.

$$\text{Ln}\left(\frac{p}{1-p}\right) = \gamma_{\text{oo}} + \gamma_{01}(\text{W}_\text{j} - \bar{W}) + \gamma_{10}(\text{X}_\text{ij} - \bar{X}_\text{j}) + \mu_{\text{oj}} + \gamma_{\text{ij}} \quad (6)$$

Where, γ_{01} represents the random proportion of the intercept in Equation 4. This cross-level direct effect can be explained as the average change of the logit of AD presence in level 2 groups associated with a 1-unit increase of ADL measure. The coefficient γ_{10} represents the slope in equation 4. In this step, the γ_{10} is assumed to be constant across all groups. The cross-level direct effect and predictor is rescaled by the group mean. The centered scale represents the relative score in that level 2 group.

Step 3

The purpose of step 3 was to understand whether the random slope $\mu_{1\text{j}}$ vary across groups. The hypothesis for testing the random coefficient is that the variance of coefficient across groups is different from zero. In this step, I added the random portion of the slope $\mu_{1\text{j}}$ to the model. Aguinis et al. (2013) named this model the random intercept and fixed slope model (RIRSM). The likelihood ratio is calculated by

comparing the deviance of RIRSM and RIFSM model. I express the RIRSM model in Equation 7.

$$\mathrm{Ln}\left(\frac{p}{1-p}\right) = \gamma_{oo} + \gamma_{01}(\mathrm{W_j} - \bar{W}) + \gamma_{10}(\mathrm{X_{ij}} - \bar{X}_j) + \mu_{oj} + \mu_{1j}(\mathrm{X_{ij}} - \bar{X}_j) + \gamma_{ij} \quad (7)$$

Where, μ_{1j} is the residual in equation 3, which contributed to the random proportion of the slopes. The μ_{1j} and its variance τ_{1j} explain how the slope varies across groups.

Step 4

I built a more general model in this step. The previous models can be viewed as a simplification formula of this model by removing one or more random or fixed components. The hypothesis for testing the cross-level interaction is that the level 2 predictor moderate the relationship between AD presence and ADL measures. By comparing the difference of likelihood ratio, the significance of cross-level interaction are tested. In this step, I added the cross-level interaction γ_{11} to the model. The final finding illustrates whether cross-level interaction explains variance τ_{1j}. I express the full model in Equation 8.

$$\mathrm{Ln}\left(\frac{p}{1-p}\right) = \gamma_{oo} + \gamma_{01}(\mathrm{W_j} - \bar{W}) + \gamma_{10}(\mathrm{X_{ij}} - \bar{X}_j) + \gamma_{11}(\mathrm{X_{ij}} - \bar{X}_j)(\mathrm{W_j} - \bar{W}) + \mu_{oj} + \mu_{1j}(\mathrm{X_{ij}} - \bar{X}_j) + \gamma_{ij} \quad (8)$$

There are four data assumptions that must be met first before GLM can be used. These four assumptions are: (a) normality, (b) homogeneity of variance, (c) linearity, and (d) independence (Sedgwick, 2015). Normality refers to the property of a random

variable that is distributed according to the normal distribution and this can be tested using a Kolmogorov-Smirnov test (Siddiqi, 2014). I tested the normality using a a Kolmogorov-Smirnov test. Homogeneity of variance assumes that the distribution of the scores around the mean of two or more samples are equal and this can be tested using Levene's test (Parra-Frutos, 2013). I tested the homogeneity of variance using Levene's test. In addition, a plot (residuals versus predicted values) was generated. The scatterplots are patternless. It indicates that the error is consistent across the range of predicted values hence the assumption is met. Linearity assumes that there is a linear relationship between the variables, and this can be tested by producing scatterplots in order to make sure the mean of the outcome variable for each increment falls on a straight line (Sedgwiek, 2015). I generated scatterplots for linearity testing. The results shows this assumption is met. Lastly, I generated histograms and box-and-whisker plots to check for any data outliers in the sample.

A 95% confidence level is used for hypothesis testing (Weakliem, 2016). This means that all p-value output of the hierarchical multiple regression is assessed using a 0.05 level of significance. A p-value of less than 0.05 dictates that there is a statistically significant relationship between the variables that the null hypothesis is rejected, whereas a value greater than 0.05 dictates that there is no statistically significant relationship between variables.

Threats to Validity

In a quantitative study, the systematic error is caused by questionable methodology in the study design or data analysis. The consequences of systematic error

result from distortion conclusions and threaten the validity of the study (Kleinbaum et al., 1982). In general, the threats to validity are classified into two classes, internal and external threats to validity. Internal validity is concerned with the validity of inferences about the target population, evaluating whether a difference in the outcome is truly caused by a difference of exposure or a systematic error. Whereas, external validity is concerned with generalization of the study, evaluating whether the study population could generalize to the target population (Carlson & Morrison, 2009).

Three important statistical considerations of threats to internal validity are selection bias, information bias, and confounding (Kleinbaum et al., 1982). Selection bias refers to a distortion result that was drawn from a biased study population. Typical selection biases in the epidemiological study include selective survival, a flaw in the choice of sampling frame or compared groups, and nonresponse/lost follow-up during data collection. information bias refers to a distortion in the estimate of effect due to measurement error or misclassification of subjects. Confounding is a bias that results when the study factor effect is mixed with extraneous variables (Kleinbaum et al., 1982).

In this study, the target population was a subset of HRS population who completed the question regarding AD and dementia. HRS is a national panel survey of individuals over age 50 with well representative data on health, cognition, family, employment, and wealth. The HRS has selected a set of measures related to cognitive function consistently and has imputed values for missing value (Chair et al., 2011). A well-defined reference population minimizes selection and information bias in this study.

Research regarding neurodegenerative disease need to address age-dependent patterns of within- or between individual change in traits during a lifetime. The extraneous variables, such as genetic factors, could potentially confound with AD risk factors and outcome variables. The genetic data consortia collaboration report of HRS stated that genetic variants that are common in populations usually have small individual effects on complex traits like behavior (Faul & Smith, 2017). Therefore, the confounding risk to this study was small. I conducted the sensitivity analysis for other potential confounders.

External validity refers to how well the findings or results of the study can be expected to apply to other settings (O'Dwyer & Bernauer, 2016). The design and thus the results of the study may limit the application to other settings or in other populations beyond the chosen target population. This is because this study specifically is concerned with patients having a specific disease or condition that may have a different effect on different settings (Roe & Just, 2009). Roe and Just (2009) stated the interaction of relationship with settings asks whether one kind of setting will hold if done in a different setting or other words whether the findings of this study will hold if another disease or condition is considered other than AD. As this study's population was based on adult patients (50 years old and above) diagnosed with AD or dementia, the interaction of relationship with setting was a threat to generalize for other population based on location.

Ethical Procedures

The researcher secured first and foremost an IRB approval from Walden University before any data extraction begins. Provided the nature of the study where

secondary data were used, it is believed that there is no harm to any participants. No personal identifying information were collected and therefore there is no chance that the data can be linked to a certain participant. Instead, pseudo-codes were used to designate each patient, i.e. P01 for case number one and so on.

The researcher ensured that only authorized personnel have access to the relevant data for this study. All documents were securely kept in a locked filing cabinet inside the personal home office. Soft copies of the documents were saved in a password-protected flash drive. All data and documents related to the study will be destroyed seven years after completion. Hard copies will be shredded while soft copies will be deleted.

Summary

The purpose of this quantitative non-experimental correlational study was to examine the relationship between early year ADL and the development of AD in later years while accounting for the influence of key sociodemographic factors. The independent variables were the sociodemographic factors (health, health services, labor force, economic status, family structure, and retirement expectations), past ADL, and past change in ADL. The dependent variable was the onset of AD diagnosis. The target population for this study was adults 50-years old years old in the United States who participated in the HRS study and completed the survey questionnaire about AD and dementia. All data for this study were retrieved from the HRS dataset. A four-step multilevel model by Aguinis et al. (2013) was used to address the research questions and test the study hypotheses via R software. Chapter 4 presents the study findings by first

characterizing the study sample using descriptive statistics and reporting statistical tests using inferential statistics organized by the research question.

Chapter 4: Results

Introduction

A few promising studies have indicated that ADL may be a useful way of predicting AD (Cass, 2017; Roehr et al., 2019). However, modifiable factors, such as social characteristics, moderate the protective effect and relationship between protective factors and AD development (Beydoun et al., 2014; Shih et al., 2018; Sutin et al., 2019). The purpose of this quantitative study was to examine the relationship between early years' ADL and the development of AD in later years. The study population was U.S. adults 50 years old. I extracted this population data through the HRS dataset. The following are the research questions and corresponding hypotheses that were addressed and tested, respectively:

Research Question 1 (RQ1): What is the relationship between different specific early years' ADLs and later onset of AD?

$H_0$1: There is no relationship between early years' ADLs and the later onset of AD.

H_a1: There is a significant relationship between early years' ADLs and the later onset of AD.

RQ2: What is the relationship between changes in early years' ADL and later onset of AD?

$H_0$2: There is no relationship between changes in early years' ADL and the later onset of AD.

H_a2: There is a significant relationship between changes in early years' ADL and the later onset of AD.

RQ3: To what extent do sociodemographic factors moderate the relationship(s) between early years' ADL and AD?

$H_0 3$: None of the sociodemographic factors moderate the relationships between early years' ADL or ADL changes and AD.

$H_a 3$: One or more of the sociodemographic factors moderate the relationships between early years' ADL and/or ADL changes and AD.

Aguinis et al. (2013) introduced a four-step multilevel model approach. I used this approach to address the research questions. The independent variables were early years' ADL while the dependent variable was the onset of AD diagnosis in the later years. The control variables were sociodemographic factors (medical condition, mental health, economic status, degree of education, and years of education). Data analysis was performed via R software to address the research questions and test the study hypotheses.

In this chapter, I include data collection and analysis results.s First, I describe the data extraction process. Then, I provide descriptive statistics of the study sample for both categorical and continuous variables. I discuss the results from the four-step multilevel model as well as the results of evaluating the assumptions of this model. I also include the results from a sensitivity analysis. Finally, I include a summary of the results.

Data Collection

The study population was U.S. adults 50 years old from HRS study. HRS is a representative national multilevel panel study by the RAND Corporation Center for Study of Aging (RAND, 2021). I extracted this population data through the RAND HRS Fat files. The RAND HRS Fat data are available for public research and free to download at the HRS website. There is no need to secure permission to use the data from HRS administrators. Patients included in the study were adults 50 years old in the United States who had participated in the HRS study and completed the survey questionnaire about AD and dementia. This dataset contains information from 42,233 patients. I only included the respondents who provided responses on AD and ADL indices in the analysis. In the analysis dataset, I only included relevant data to measure the study variables from the HRS data. Data contained the following sociodemographic factors: medical condition, mental health, economic status, degree of education, and years of education. I screened the missing values. All patients with more than 50% missing data on the sociodemographic variables were excluded from the analysis. I used the mean imputation to replace missing values for the remainder of the participants. Following this procedure, a total of 4,526 patients were selected for the analysis. In addition, I created box and whisker plots to detect any extreme outliers in the data. Visual examinations of these plots indicated the presence of univariate outliers on the study variables. However, after checking the accuracy of the responses, no erroneous responses were detected in the data. The clean data set included data from 4,526 patients and was exported to R software for data analysis.

I used a retrospective 10-year average ADL measurement prior to the baseline was utilized as the early years' ADL variable. In order to establish a meaningful interpretation across the models, the items measuring early years' ADL (ADLA) and change in early years' ADL (ADLC) were re-scaled in to [0, 1]. The scale of all covariates was standardized with Mean 0 and Variance 1. Because the questionnaire of whether or not a doctor has told the respondent they had AD was collected by HRS from Wave 10 and afterward. I used the data in Wave 10 data as baseline. The measures prior to baseline were used for covariates as early years' value. The overall scores for the continuous variables of the study (early years' ADL, changes in early years ADL, health condition, mental health, household income, and adjusted family) were obtained by taking the average of their respective indices for the Waves 3 through 9. Wave 3 through 5 were included for early years' measures and Waves 6 through 9 were included for further sensitivity analysis. Therefore, Waves 10, 11, are 12 were not included as this study aimed to determine the effects of the past values of these variables on the future diagnosis of Alzheimer's disease, and the questions about AD and dementia are first asked in Wave 10. The dependent variable (onset AD diagnosis) was derived from Waves 10, and later wave. I created a second data set was provided for sensitivity analysis. I took the average of ADL indices from Waves 6 through 9 as independent variables for this sensitivity analysis. In each data set, the scales of all covariates were standardized with Mean 0 and Variance 1, and the ADL measurements were rescaled into [0,1].

Descriptions of the Sample

The study sample included data from 4,526 patients who had participated in the HRS study and completed the survey questionnaire about AD and dementia. The age of these patients in Wave 3 ranged from 31 to 83 and had a mean of 59.17 (*SD* = 6.77). Tables 1 through 5 show the demographic characteristics of the sample. As shown in Table 1, 42.5% of the patients were male while 45.5 were female.

Table 1

Frequency Analysis for Gender

Gender	Frequency	Percent
Male	1,922	42.5
Female	2,604	57.5
Total	4,526	100.0

Table 2 shows that a vast majority of the patients were married (95.7%), 2.5% were partnered, 1.1% were separated/divorced, 0.5% were widowed, and 0.2% were married but their spouses were absent. As reported in Table 3, the place of birth with the highest frequency was the East North Central region (19.0%), followed by Mid-Atlantic (13.4%), South Atlantic (13.3%), and West North Central (12.7%). Regarding race/ethnicity, 88.3% were White/Caucasian, 8.5% were Black/ African American, and 3.2% were from other races (see Table 4).

Table 2

Frequency Analysis for Married Status

Marital Status	Frequency	Percent
Married	4,331	95.7
Married Spouse Absent	10	0.2
Partnered	111	2.5
Separated/divorced	49	1.1
Widowed	22	0.5
Never married	2	0.0
Total	4,526	100.0

Table 3

Frequency Analysis for Place of Birth

Place of Birth	Frequency	Percent
New England	179	4.0
Mid Atlantic	607	13.4
East North Central	860	19.0
West North Central	575	12.7
South Atlantic	603	13.3
East South Central	369	8.2
West South Central	424	9.4
Mountain	174	3.8
Pacific	251	5.5
Not from the US	474	10.5
Total	4,526	100.0

Table 4

Frequency Analysis for Race/Ethnicity

Race/Ethnicity	Frequency	Percent
White/Caucasian	3,995	88.3
Black/African American	385	8.5
Other	146	3.2
Total	4,526	100.0

Table 5 shows the results of the frequency analysis for highest level of education. This table shows that 18.4% had no degree, 33.7% had a high school diploma, 5.0% had a general education diploma, an additional 17.5% had either a general education or a high school diploma, 3.6% had an associate degree, 12.6% had a bachelor's degree, and 9.2% had a master's/MBA or a higher degree.

Table 5

Frequency Analysis for Education Level

Education Level	Frequency	Percent
No degree	834	18.4
General Educational Diploma	227	5.0
High School Diploma	1,523	33.7
General Education/High School Diploma	794	17.5
Associate Degree	163	3.6
Bachelor's Degree	570	12.6
Master's /MBA Degree	312	6.9
Law/MD/PhD Degree	103	2.3
Total	4,526	100.0

Frequency analyses for the categorical variables of the study are provided in Tables 6 through 9. Table 6 shows the frequency analysis for years of education. The year of education with the highest frequency was 12 (36.4%). As reported in Table 7, the degree of education with the highest frequency was high school degree (33.7%), followed by no educational degree (18.4%), high school degree, or a GED (17.5%), and bachelor's degree (12.6%). Regarding household income, 10% of the patients were identified to be below the poverty threshold (see Table 8). Amongst 4,526 patients who completed the AD and dementia questionnaire, 4,385 (96.9%) were not diagnosed with AD. A small portion of the participants (3.1%, n = 141) were diagnosed with Alzheimer's disease (see Table 9).

Descriptive statistics for the covariates are provided in Table 10. The frequency distributions are illustrated in Figures 1 through 4. These variables are provided by HRS. The statistics are calculated based on the raw data on these variables. It can be seen that medical conditions had an approximate normal distribution (Figure 1) with a mean of 1.704 (SD = 1.194), mental health had a skewed left distribution (Figure 2) with a mean of 1.098 (SD = 1.243), activities of daily life had a skewed left destitution (Figure 3) with a mean of 0.142 (SD = 0.391), changes in the activities of daily life had a approximate normal distribution (Figure 4) with mean of 0.019 (SD = .095), household income had a mean of $68,400.707 (SD = 626,445.029), adjusted family income compared to the poverty threshold had a mean of $72,372.549 (SD = $67,774.501).

Table 6

Frequency Analysis for Years of Education

Years of Education	Frequency	Percent
0	20	0.4
1	10	0.2
2	10	0.2
3	45	1.0
4	20	0.4
5	38	0.8
6	79	1.7
7	46	1.0
8	149	3.3
9	132	2.9
10	207	4.6
11	192	4.2
12	1,649	36.4
13	327	7.2
14	417	9.2
15	171	3.8
16	465	10.3
17	549	12.1
Total	4,526	100.0

Table 7

Frequency Analysis for Degree of Education

Degree of Education	Frequency	Percent
No Degree	834	18.4
GED	227	5.0
HS	1,523	33.7
HS/GED	794	17.5
AA/LtBA	163	3.6
BA	570	12.6
MA/MBA	312	6.9
Law/MD/PHD	103	2.3
Total	4,526	100.0

Table 8

Frequency Analysis Household Income Status Relative to Poverty Threshold

Category	Frequency	Percent	Valid Percent
Above Poverty	4,074	90.0	90.0
Below Poverty	452	10.0	10.0
Total	4,526	100.0	100.0

Table 9

Frequency Analysis for AD Diagnosis

	Frequency	Percent
No AD	4,385	96.9
Diagnosed with AD	141	3.1
Total	4,526	100.0

Table 10

Descriptive Statistics for the Continuous Variables

Variable	Minimum	Maximum	Mean	Std. Deviation
Medical Condition	0.000	7.286	1.704	1.194
Mental Health Condition	0.000	7.714	1.098	1.242
Early Years' ADL	0.000	4.286	0.142	0.391
Changes in Early Years'	-0.571	0.714	0.019	0.095
Household Income	$0.000	$748,290.43	$68,400.70	$62,645.029
Adjusted Family Income	$0.000	$811,873.44	$72,372.54	$67,774.501

Figure 1

Histogram of the Rescaled Scores for Medical Health

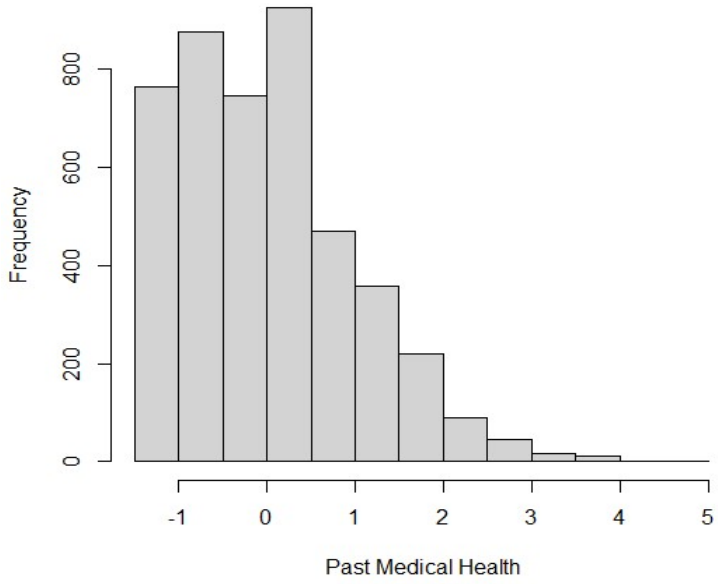


Figure 2

Histogram of the Rescaled Scores for Mental Health

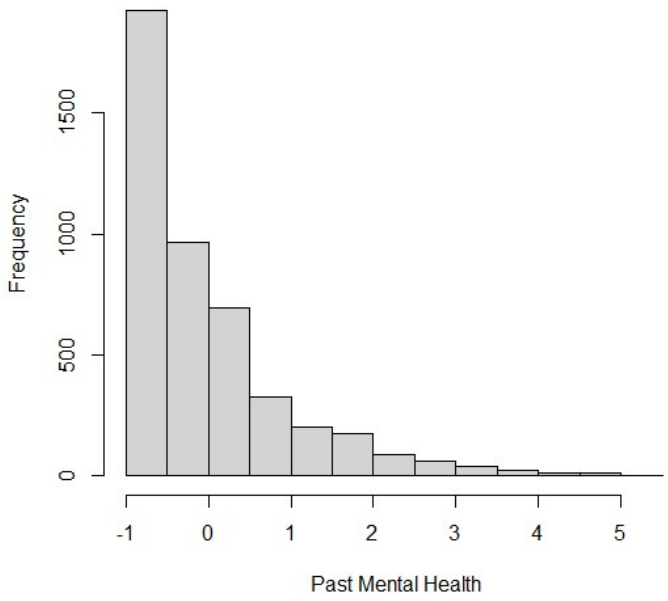


Figure 3

Histogram of the Rescaled Scores for Early Years Activities of Daily Life

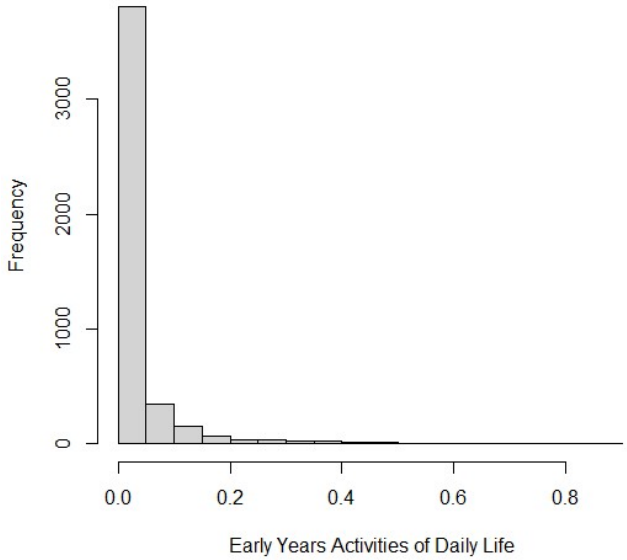
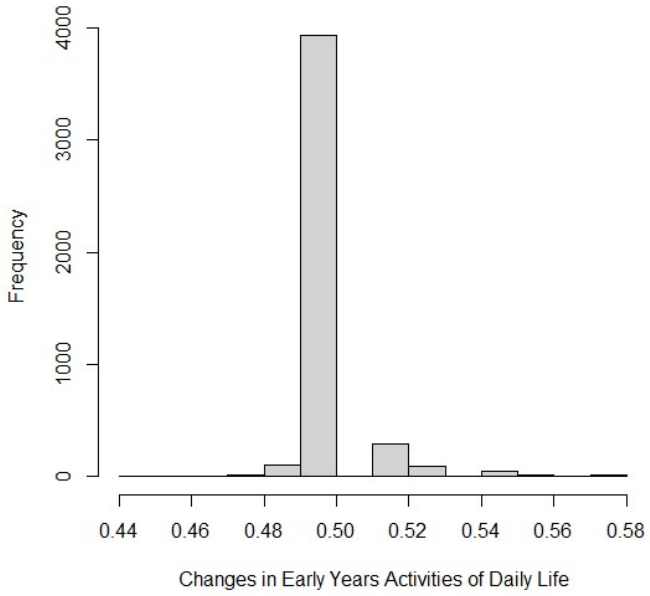


Figure 4

Histogram of the Rescaled Scores for Changes in Early Years Activities of Daily Life



Results

Inferential Analysis

Aguinis et al. (2013) introduced a four-step multilevel approach for multilevel model analysis. This four-step approach estimates cross-level interaction effects using multilevel modeling to test different hypotheses and evaluates the hierarchical structure relationships using a generalized linear model (Aguinis et al., 2013). In this study, the dependent variable was the AD diagnosis. The Level-1 variables included in the model were early years' ADL and changes in early years' ADL, and the following covariates: previous medical condition, previous mental health, household income, and adjusted family income relative to the poverty threshold. The Level-2 variables were years of education, degree of education, and household income status compared to the poverty

threshold. I conducted data analysis using R software to address the research questions and test the study hypotheses. Prior to running this model, the following assumptions were evaluated:

1. Absence of outliers in the data.

2. Absence of multicollinearity in the data.

3. Presence of linearity between each independent variable and the log odds ratio of the independent variable.

I used boxplots of each of the variables included in the model to evaluate the absence assumption (see Figures 5-10). I assessed the absence of multicollinearity assumption by examining the VIF values for each independent variable. VIF values greater than 10 are considered problematic and indicate a multicollinearity issue in the data. Additionally, I used the Box-Tidwell (1962) approach to assess the linearity assumption. I present the results in the next sections.

Assessment of Assumptions

Absence of outliers

I assessed the absence of outliers' assumption by creating boxplots for each predictor variable included in the model. The results are shown in Figures 5 through 10. These plots indicate the presence of multiple significant outliers on each predictor variable. After checking the data for accuracy, no erroneous responses were found in the dataset. Transformation methods such as different *log* transformations did not help mitigate these problems. Thus, the analyses were performed based on the full dataset.

Figure 5

Boxplot of the Rescaled Scores for Medical Health

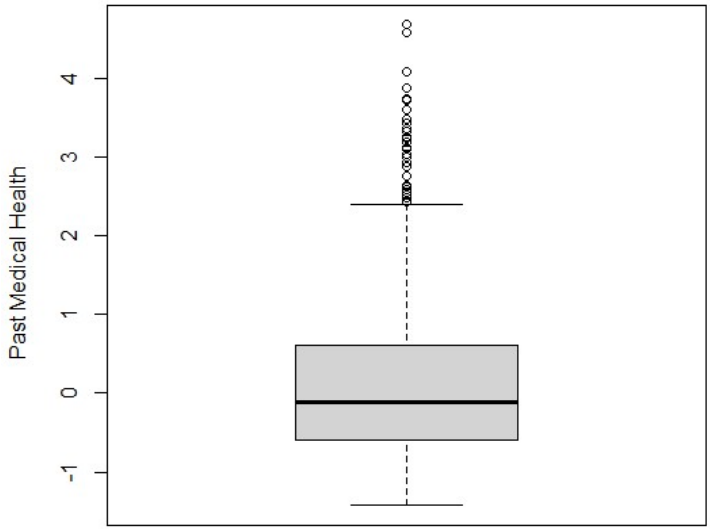


Figure 6

Boxplot of the Rescaled Scores for Mental Health

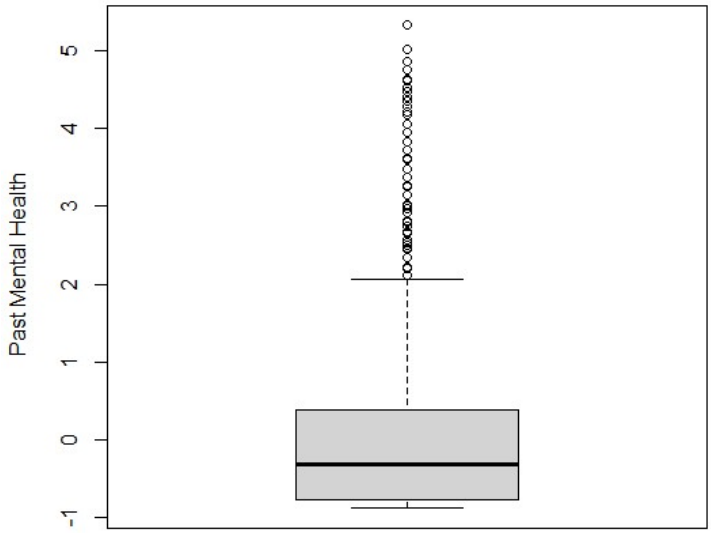


Figure 7

Boxplot of the Rescaled Scores for Household Income

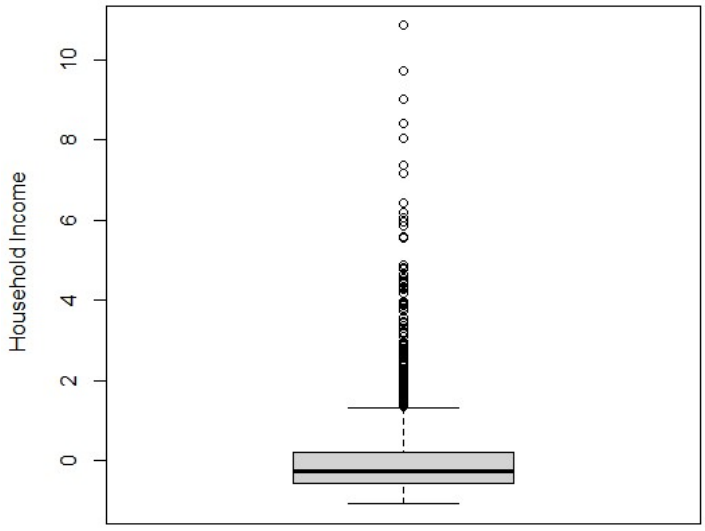


Figure 8

Boxplot of the Rescaled Scores for Adjusted Family Income

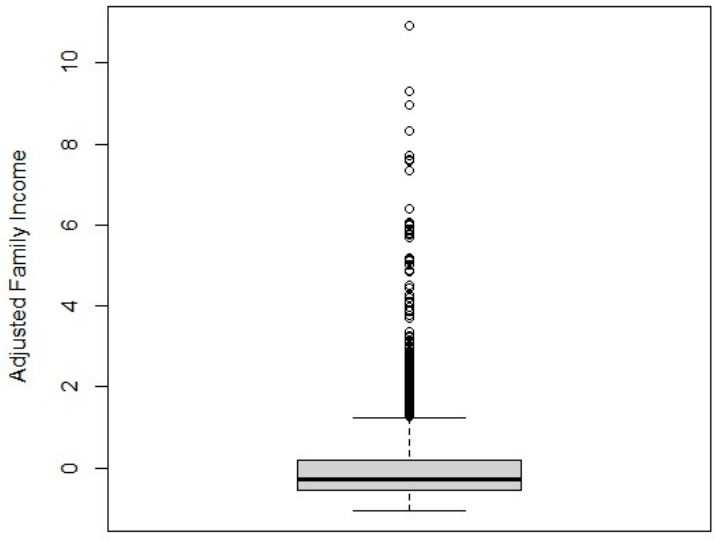


Figure 9

Boxplot of the Rescaled Scores for Early Years Activities of Daily Life

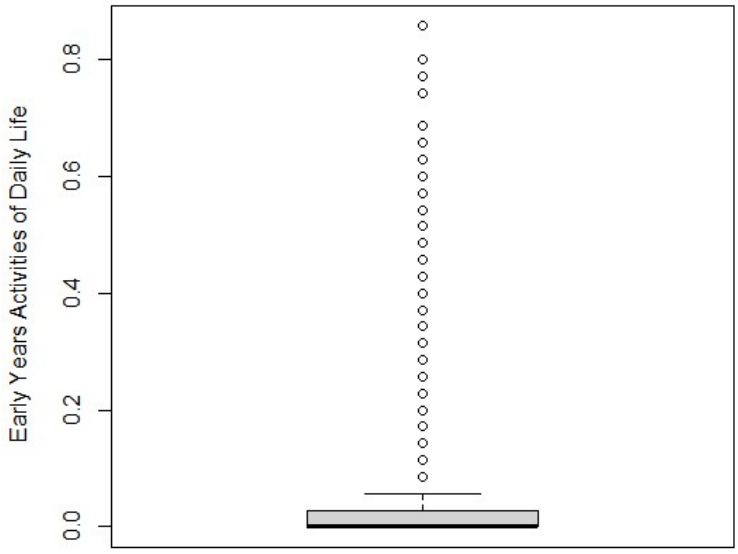
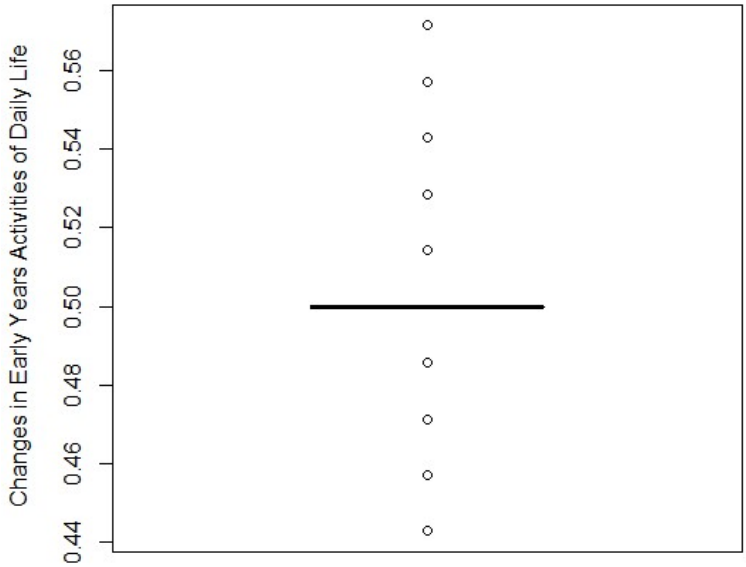


Figure 10

Boxplot of the Rescaled Scores for Changes in Early Years Activites of Daily Life



Assessment of Multicollinearity

I checked the absence of multicollinearity assumption using the VIF values calculated for each predictor variable in the model. As reported in Table 11, the VIF values of household income status and adjusted family income were greater than 5, which showed the high influence on other independent variables. However, all VIF values were less than the threshold of 10, indicating that there was no issue regarding multicollinearity in the data.

Table 11

VIF Values for the Predictor Variables

Variable	*VIF*
Health Condition	1.049103
Mental Condition	1.280446
Early Years'ADL	1.651468
Changes in Early Years' ADL	1.356238
Household Income	5.512088
Adjusted Family Income	5.443945

Assessment of Linearity

I assessed the linearity assumption using the Box Tidwell approach. Following this approach, the interaction term between each predictor variable and its natural log transformation were included in the model. The coefficient estimates for these interaction terms are provided in Table 12. The linearity assumption was satisfied for health conditions (CONDE), mental health (CESD), household income (ITOT), early years' ADL (ADLA), and adjusted family income (POV). However, it was violated for changes in early years' ADL (ADLC), as the interaction term between this variable and its natural

log transformation was statistically significant ($p < .05$). Transformation methods such as different log transformations did not help resolve this issue.

Table 12

Assessment of the Linearity Assumption

Interaction Term	Estimate	Std. Error	z value	p-value
CONDE*ln(CONDE)	-0.1227	0.132	-0.926	.354
CESD*ln(CESD)	-0.115	0.101	-1.139	.255
ITOT*ln(ITOT)	0.147	0.144	1.020	.308
ADLA*ln(ADLA)	-3.166	5.312	-0.596	.551
ADLC*ln(ADLC)	758.311	310.329	2.444	.014
POV*ln(POV)	-0.123	0.177	-0.699	.485

The results from four-step multilevel model evaluation are provided as follows:

Step 1: Null Model

The null model was evaluated to determine whether the intercept of the model varies by years of education, degree of education, and household income status relative to the poverty threshold. For this purpose, the variances associated with the random slopes of these Level-2 variables were examined. It was found that the estimates of the variances associated with years of education and household income status were approximately zero, suggesting that the intercept of the model was not influenced by these Level-2 variables. The estimate of the variance associated with the random intercept of the degree of education was 0.002. Therefore, the intercept of the model was allowed to vary by level of education in the following steps. The result shows in Table 13.

Table 13

Estimates of Random Effects for Step 1

Group (Name)	Variance	Std.Dev.
Years of Education (Intercept)	0.000	0.000
Degree of Education (Intercept)	0.002	0.04542
Household Income Status (Intercept)	0.000	0.000

Step 2: Random Intercept and Fixed Slope Model

In the second step of the model-building process, I was interested in determining what variables were significant predictors of the onset of AD while allowing the intercept of the model to vary by level of education. The results of fixed effect estimate for the predictor variables included in this model are provided in Table 14. These results suggested that the only significant predictor of the onset of AD was changes in early years' ADL ($b = 20.253$, $z = 2.761$, $p < .05$), indicating that an increase in changes in ADL leads to an increase in the probability that a patient is diagnosed with AD in the future. The Akaike information criterion (AIC) and the Bayesian information criterion (BIC) provide measures of model performance. AIC and BIC combine a term reflecting how well the model fits the data with a term that penalizes the model in proportion to its number of parameters. AIC and BIC were provided by the multilevel models. The AIC value for this model was 1228.6. The result shows in Table 14.

Table 14

Fixed Effect Estimates for Step 2

Variable	Estimate	Std. Error	*z*-value	*p*-value
Intercept	-13.755	3.677	-3.741	<.001
Health Condition	0.0820	0.084	0.976	.329
Mental Condition	0.137	0.083	1.664	.096
Early Years' ADL	0.909	0.985	0.923	.356
Changes in Early Years' ADL	20.253	7.337	2.761	.006
Household Income	-0.206	0.285	-0.724	.469
Adjusted Family Income	-0.140	0.283	-0.496	.619

Step 3: Random Intercept and Random Slope Model

In the third step of the model-building process, I was interested in determining whether the slopes of early years' ADL and changes in early years' ADL vary by different Level-2 variables. For this purpose, error terms were included in the model to allow these slopes to vary by years of education, degree of education, and household income status. However, it was found that the variances associated with all these random slopes that were introduced in the model were approximately zero, suggesting that the relationship between early years' ADL and changes in early years' ADL were not influenced by these Level-2 variables. Considering that the presence of random slopes was not supported, conducting the fourth step of the analysis was irrelevant as none of the Level-2 variables explained significant amounts of variance in the regression slopes. Therefore, the research hypotheses were evaluated based on the findings from Step 2. The AIC value for this model was 1,263.3. It was less than the AIC value in Step2,

indicating that the model estimated in Step 2. The model in Step 2 provided a better fit to the data as compared to Step 3. The result shows in Tables 15 and 16.

Table 15

Random Effects Estimates for Step 3

Group (Name)	Variance	Std.Dev	Corr
Years of Education (Intercept)	2.420e-02	0.156	
Changes in Early Years' ADL	9.365e-02	0.306	-1.00
Years of Education 1 (Intercept)	4.632e-06	0.002	
Early Years' ADL	3.096e-03	0.056	-1.00
Degree of Education (Intercept)	2.249e+01	4.742	
Changes in Early Years' ADL	8.862e+01	9.414	-1.00
Degree of Education 1 (Intercept)	0.000e+00	0.000	
Early Years' ADL	9.444e-06	0.003	NA
Household Income Status	8.050e+00	2.837	
Changes in Early Years' ADL	3.212e+01	5.668	-1.00
Household Income Status 1	0.000e+00	0.000	
Early Years' ADL	2.393e-07	0.000	NA

Table 16

Fixed Effect Estimates for Step 3

Variable	Estimate	Std. Error	z-value	p-value
Intercept	-14.770	4.823	-3.062	.002
Health Condition	0.084	0.084	1.002	.316
Mental Condition	0.144	0.082	1.759	.079
Early Years' ADL	0.925	0.980	0.944	.345
Changes in Early Years'	22.259	9.615	2.315	.021
Household Income	-0.191	0.284	-0.674	.500
Adjusted Family Income	-0.162	0.283	-0.574	.566

Sensitivity Analysis

To increase the generalizability of the results, two more independent variables, and average ADL scores over the waves 6 through 9 were included for further sensitivity analysis. All four steps of the multilevel analysis are evaluated here. The results from Step 1 are not provided as there was no change in the outcome variable, and therefore the results are the same as those presented in Step 1 for the main analysis.

Step 2 (Sensitivity Analysis): Random Intercept and Fixed Slope Model. The second step of the model-building process involved determining what variables were significant predictors of the onset of AD while allowing the intercept of the model to vary by degree of education. The results of fixed effect estimate for the predictor variables included in this model are provided in Table 17. Contrary to the results obtained based on the primary analysis, it was found that changes in early years' ADL was not a significant predictor of the onset of AD ($p > .05$). However, it was found that early years' ADL had a positive significant effect on AD. The AIC value for this model was 1225.6.

Table 17

Fixed Effect Estimates for Step 2 of the Sensitivity Analysis

Variable	Estimate	Std. Error	*z*-value	*p*-value
Intercept	-7.432	1.996	-3.723	<.001
Health Condition	0.108	0.084	1.282	.200
Mental Condition	0.113	0.081	1.395	.163
Early Years' ADL	1.624	0.718	2.261	.024
Changes in Early Years' ADL	7.562	3.980	1.900	.058
Household Income	-0.815	0.364	-2.241	.025
Adjusted Family Income	0.393	0.334	1.178	.239

Step 3 (Sensitivity Analysis): Random Intercept and Random Slope Model. In the third step of the model building process in the sensitivity analysis, I aimed to determine whether the slopes of early years' ADL and changes in early years' ADL vary by different Level-2 variables. To do this, error terms were included in the model to allow these slopes to vary by years of education, degree of education, and household income status. However, as reported in Table 18, the variances associated with all these random slopes were approximately zero, indicating that the relationships between early years' ADL or changes in early years' ADL were not influenced by these Level-2 variables. Therefore, conducting the fourth step of the analysis was irrelevant as none of the Level-2 variables explained significant amounts of variance in the regression slopes. Furthermore, the AIC value for this model was 1257.3, indicating that the model estimated in Step 2 provides a better fit to the data as compared to Step 3.

Evaluation of the Research Hypotheses

Hypothesis 1

Null Hypothesis 1 in present study was that there is no relationship between early years' ADLs and the later onset of AD. The relationship was estimated in the multilevel model of Step 2. The statistical significance of regression coefficients and variance of intercept across groups were tested. The estimate of the early years' ADLs from the multilevel model of the analysis were $b = 0.909$, $p = 0.356$. It indicates the effect of early years' ADL on the onset of AD was not significant and that can be interpreted as one unit of increase in early years ADL did not significantly lead to an increase in the probability that a patient is diagnosed with AD in the late year. The results from the sensitivity

analysis that evaluated whether the slopes of changes in early years' ADL vary by different Level-2 variables found that early years' ADL had a positive significant effect on AD. These results still did not provide strong evidence to reject this null hypothesis. I failed to reject the Null Hypothesis 1.

Table 18

Random Effects Estimates for Step 2 of the Sensitivity Analysis

Group (Name)	Variance	Std.Dev
Years of Education (Intercept)	3.190e+01	5.648e+00
Changes in Early Years' ADL	1.230e+02	1.109e+01
Years of Education 1 (Intercept)	8.637e-08	2.939e-04
Early Years' ADL	3.165e-05	5.626e-03
Degree of Education (Intercept)	2.292e+01	4.787e+00
Changes in Early Years' ADL	9.081e+01	9.530e+00
Degree of Education 1 (Intercept)	0.000e+00	0.000e+00
Early Years' ADL	1.241e-06	1.114e-03
Household Income Status (Intercept)	8.976e+00	2.996e+00
Changes in Early Years' ADL	3.606e+01	6.005e+00
Household Income Status 1 (Intercept)	0.000e+00	0.000e+00
Early Years' ADL	2.101e-05	4.583e-03

Hypothesis 2

Null Hypothesis 2 in present study was that there is no relationship between changes in early years' ADL and the later onset of AD. The relationship between changes of early years' ADL and AD was estimated in the multilevel model in Step 2. The statistical significance of regression coefficients and variance of intercept across groups were tested in the model. The estimate of the change of early years' ADLs from the

multilevel model of the analysis were $b = 20.25$, $p = 0.006$. It indicates the effect of changes in early years' ADL on the onset of AD was positive and statistically significant while allowing different group means of degree of education from the total mean in the second level groups. The results suggest that a unit increase in changes of early years ADL significantly leads to an increase in the probability of onset AD in the late year. However, this finding was not supported based on the results from the sensitivity analysis that evaluated whether the slopes of changes in early years' ADL vary by different Level-2 variables. As the result were $b = 3.98$, $p = 0.58$. The coefficient for this variable was non-significant. Additionally, given that there were violations of the linearity and absence of outliers' assumptions, the findings from Step 2 of the primary analysis were deemed insufficient to provide support to reject the null hypothesis. I failed to reject Null Hypothesis 2.

Hypothesis 3

Null Hypothesis 3 in present study was that none of the sociodemographic factors moderate the relationships between early years' ADL or ADL changes and AD. The influence of sociodemographic factors was estimated in the model in Step 3 that is to understand whether the relationships (random slopes) vary across Level-2 variables. In this step, the intercept of sociodemographic factors (years of education, degree of education, and household income status) on early years' ADL and changes in early years' ADL were added respectively. Based on the results, the variances and standard deviation corresponding to the random slopes were approximately zero, indicating that the relationships between early years' ADL or changes in early years' ADL and the onset of

AD were not influenced by years of education, degree of education, and household income status. Thus, these results did not provide support to reject the null hypothesis. I failed to reject the Null Hypothesis 3.

Summary

This study aimed to examine the relationship between early years' activities of daily life (ADL) and the development of Alzheimer's disease (AD) in later years. This chapter presents the results from the data analyses that were carried out to fulfill the purpose of the study. This study was guided by three research questions and their related research hypotheses. A four-step multilevel model proposed by Aguinis et al. (2013) was evaluated to address the research questions. However, the analyses did not provide sufficient support to accept any of the research hypotheses. It was found that changes in early years' ADL was significantly and positively associated with the later onset of AD. However, this finding was not supported by the sensitivity analysis. No significant relationship was found between early years' ADLs and the later onset of AD. Furthermore, no evidence was found indicating the moderating role of any of the sociodemographic factors in the relationship(s) between early years' ADL and/or ADL changes and future AD diagnosis.

Chapter 5: Discussion, Conclusions, and Recommendations

Introduction

AD is the most common cause of dementia in the world's growing elderly population (Weller & Budson, 2018), affecting over six million people in the United States and constituting the third leading cause of death in the elderly (Alzheimer's Association, 2021; National Institute on Aging, 2021, July 08). Biomedical efforts to treat AD have typically produced mixed to poor results (Cummings, 2018), while more lifestyle-focused treatments such as exercise may fare better than existing biomedical treatments (Cass, 2017). Despite this, most research on lifestyle factors such as ADL in relation to AD has focused on how AD impairs ADL (Kamiya et al., 2018; Kawaharada et al., 2019), or on how ADL impairment affects the progression of AD (Fuentes et al., 2020).

However, a few promising studies have indicated that ADL may be a more broadly useful way of predicting AD (Roehr et al., 2019). This perspective aligns with the theory of social epidemiology (Krieger, 2001a). Therefore, the problem is that it is not known how early years' ADL and change of early years' ADL may predict AD diagnosis at a later point in time. Further research is needed to examine the extent to which changing ADL can predict the development of AD (Weintraub et al., 2018), especially from a longitudinal perspective (Alberdi et al., 2018) and using both baseline and change over time data (Li et al., 2017).

The purpose of this quantitative historical correlational study was to examine the relationship between early years' ADL and the development of AD in later years. The

population under study was U. S. adults who were 50 years old. I extracted this population data through the RAND HRS Fat files, which contains a representative national multilevel panel study by the RAND Corporation Center for Study of Aging. Data from the Health and Retirement Study (HRS) dataset are freely available for use in research. The independent variables were early years' ADL while the dependent variable is current AD diagnosis. The control variables were sociodemographic factors (health, health services, labor force, economic status, family structure, and retirement expectations). Examining the relationships between these variables may create positive social change through identifying risk and protective factors relating to AD onset.

Aguinis et al. (2013) introduced a four-step multilevel model approach. I used this approach to address the research questions.. The study sample included data from 4,526 patients who had participated in the HRS study and completed the survey questionnaire about AD and dementia. RQ1 was: What is the relationship-between different specific early years' ADLs and later onset of AD? $H_0$1 was: there is no relationship between early years' ADLs and the later onset of AD. Based on the results from the multilevel model provided in Step 2 of the analysis, the effect of early years' ADL on the onset of AD was not significant. Thus, this study failed to reject this null hypothesis.

RQ2 was: What is the relationship between changes in early years' ADL and later onset of AD? $H_0$2 was: There is no relationship between changes in early years' ADL and the later onset of AD. Based on the results from the multilevel model provided in Step 2 of the analysis, the effect of past changes in ADL on the onset of AD was positive and statistically significant, indicating that an increase in the past changes in ADL is

associated with a higher probability that a patient has diagnosed with AD in the future. However, this finding was not supported based on the results from the sensitivity analysis as the coefficient for this variable was non-significant. Additionally, given that there were violations of the linearity and absence of outliers' assumptions, the findings from Step 2 of the primary analysis were deemed insufficient to provide support to reject the null hypothesis. Thus, I failed to reject the second null hypothesis.

RQ3 was: To what extent do sociodemographic factors moderate the relationship(s) between early years' ADL and AD? $H_0$3 was: none of the sociodemographic factors moderate the relationships between early years' ADL or ADL changes and AD. Based on the results from the multilevel model provided in Step 3 of the analysis, the variances corresponding to the random slopes were approximately zero, indicating that the relationships between early years' ADL or past changes in ADL and the onset of AD were not influenced by years of education, degree of education, and household income status. Thus, I failed to reject the third null hypothesis.

The remainder of this chapter includes a discussion of these findings. An interpretation of the findings is provided first, based on the extent to which they aligned with literature presented in Chapter 2. Limitations that were identified in Chapter 1 and the extent to which they are believed to have influenced study outcomes are then discussed. Recommendations are then made for future research and practice, based on these limitations and the significance of the findings. Implications of the research for practice, research, and social change are then considered. This chapter concludes with a summary and outline of key points.

Interpretation of the Findings

This section contains an interpretation of the findings, based on the extent to which they aligned with literature presented in Chapter 2. Each hypothesis is presented and discussed individually below, and the extent to which the result corresponds with literature presented in Chapter 2 is considered. Results from this study and their alignment with the theoretical framework underpinning this research are then discussed.

Aguinis et al. (2013) introduced a four-step multilevel model approach. I used this approach to address the research questions. The study sample included data from 4,526 patients who had participated in the HRS study and completed the survey questionnaire about AD and dementia. $H_0$1 was that there is no relationship between early years' ADLs and the later onset of AD. Based on the results from the multilevel model provided in Step 2 of the analysis, the effect of past ADL on the onset of AD was not significant. Thus, I failed to reject this null hypothesis.

Results from this hypothesis test expanded upon much of the literature presented in Chapter 2 associated with the age of onset in early years AD. Along a similar line of research, Alberdi et al. (2018) studied the ability to use data regarding factors like ADL to predict the onset of AD. Their model was good but imperfect, and they called for more similar research that makes use of longitudinal data. In a systematic review of modeling approaches used in such research, Li et al. (2017) found that few prior researchers had used a combination of baseline and change over time factors. Therefore, they called for more research using such an approach. In addition, Mauricio et al. (2019) reviewed and summarized the proceedings of the G8 dementia summit; the most significant conclusion

was a need for more—and more innovative—research into dementia, of which AD is the primary cause. The present study fulfills all these calls for research by examining the predictive power of early years' ADL on AD and with both baseline and change over time data.

Clinical trials demonstrated that Aβ pathology is present before clinical symptoms of AD, lined with mitochondrial change by the onset of symptomology (Albensi, 2019). Researchers studying the mitochondrial effect indicated that variables such as epigenetic dysregulation and environmental modifications might be linked to AD diagnosis (Albensi, 2019). Rahman et al. (2019) synthesized genetic, medical, societal, and lifestyle risk, focusing on the role of hormonal changes in a systemic review study. The authors noted that the female sex is the major risk factor for late-onset AD (Rahman et al., 2019). This study's primary research question pertained to the extent to which the level exists between the earlier life sociodemographic predictors and the later onset of AD, and an enhanced understanding of this topic was obtained based on the findings.

$H_0$2 was: there is no relationship between changes in early years' ADL and the later onset of AD. Based on the results from the multilevel model provided in Step 2 of the analysis, the effect of past changes in ADL on the onset of AD was positive and statistically significant, indicating that an increase in the past changes in ADL is associated with a higher probability that a patient has diagnosed with AD in the future. However, this finding was not supported based on the results from the sensitivity analysis as the coefficient for this variable was non-significant. Additionally, given that there were violations of the linearity and absence of outliers' assumptions, the findings from Step 2

of the primary analysis were deemed insufficient to provide support to reject the null hypothesis.

AD is an increasing epidemic in the United States (Alzheimer's Association, 2021). Although AD's underlying mechanism is not known, increasing evidence emerges that lifestyle factors have profound effects on the brain's neurochemistry, which could potentially influence the development of AD (Lista & Sorrentino, 2010; Serrano-Pozo & Growdon, 2019). Many previous epidemiological studies have demonstrated that dementia was associated with ADL difficulty (Pakstis et al., 2018). A few promising studies have indicated that ADL may be a useful way of predicting AD (Alberdi et al., 2018; Mauricio et al., 2019; Weintraub et al., 2018). Although ADLs are studied as a risk factor epidemiologically or neurophysiological, the underlying mechanism and relationship between ADL and AD development are still unclear (Liu et al., 2019). The findings of present study showed the evidence of the relationship between ADL in the early years and AD presence in the later years. However, this relationship found in the model was not significant. I failed to reject the hypothesis

$H_0$3 was that none of the sociodemographic factors moderate the relationships between early years' ADL or ADL changes and AD. Based on the results from the multilevel model provided in Step 3 of the analysis, the variances corresponding to the random slopes were approximately zero, indicating that the relationships between early years' ADL or past changes in ADL and onset of AD were not influenced by years of education, degree of education, and household income status. Thus, these results did not provide support to reject this null hypothesis.

Research on AD-related brain function shows that gender and genetic factors are confounded with other risk factors (Thibeau et al., 2019). Thibeau et al., (2019) investigated whether the association between nondemented executive function trajectories and physical activity is moderated by sex and AD genetic risk factors. The results showed that everyday physical activity had a significant effect on executive function in females and a significant effect on mobility in both females and males, and a significant effect on the interaction of gender and APOE factors (Thibeau et al., 2019). A systemic review by Rahman et al. (2019) synthesized genetic, medical, societal, and lifestyle risk, focusing on the role of hormonal changes. The authors noted that the female sex is the major risk factor for late-onset AD (Rahman et al., 2019). The present study's findings lead to a precision health approach to research of effects of physical activity.

Sutin et al. (2020), studied whether these sociodemographic factors or mental status moderated the associations. The results of his study showed that some shared mechanisms are likely to contribute to the associations between personality and cognition. Still, specific mechanisms are more relevant for some traits than others (Sutin et al., 2019). A longitudinal study showed that everyday physical activity had a significant effect on executive function in women and a significant effect on mobility in both women and men, and a significant effect on the interaction of gender and APOE factors (Thibeau et al., 2019). Although the previous studies have expounded that personality factors are associated with AD and dementia, they have not been examined against markers of brain functioning, such as regional brain glucose metabolism. Results from this study offer increased insight into this issue.

In addition to extending the literature presented in Chapter 2, findings of the present study also align with the theoretical framework underpinning the research. The theoretical framework for this study was that of social epidemiology. The theory of social epidemiology is used to study society and biology simultaneously, with a focus on how social conditions produce patterns of health and disease (Honjo, 2004; Krieger, 2001a). In the present study, social epidemiology was an appropriate framework because the research addresses the impact of both social factors and individual risk factors on the incidence of AD. One such factor is the diverse set of sociodemographic factors included under RQ1, including health services, labor force, economic status, family structure, and retirement expectations (Bugliari et al., 2016). Grounded in the social epidemiology theoretical framework, this study addresses key research questions through its multilevel hierarchical analyses. These findings may be used to meaningfully help reduce AD or offer incremental progress toward isolating causes and risk factors can contribute significantly to positive social change.

Secondly, ADL is an individual risk factor, given that the daily activities of individuals differ from person to person. However, daily activities undertaken by persons from different social contexts appear to differ significantly. For example, white-collar worker from an upper socioeconomic stratum, on average, engaged in different daily activities than blue-collar workers from a low socioeconomic stratum (Pieczyńska et al., 2019). This includes both physical and mental activities. Nonetheless, they are significantly influenced by social context and sociodemographic factors (Krieger, 2001a). Therefore, the theoretical framing of social epidemiology theory is an apt perspective

from which to discuss the issues in this study. Aligning with the theory of social epidemiology, I included the socioeconomic factors as level 2 predict variables . Additionally in this two level model, I evaluated the relationship between ADL indices change with AD diagnosis in a later years and revealed the extent of socioeconomic factors influences in this relationship.

Further research is still needed to examine the extent to which changing ADL can predict the development of AD (Weintraub et al., 2018), especially from a longitudinal perspective (Alberdi et al., 2018) and using both baseline and change over time data (Li et al. 2017). The purpose of the present study was to evaluate the relationship between ADL in the early years and AD presence in the later years. Social epidemiology provides a strong theoretical basis to guide the multilevel interaction relationship. This study was grounded in social epidemiological frameworks and link together the distribution of structural factors and individual risk factors that determine the incidence and prevalence of the disease and investigate the hierarchical relationships among the effect of the factors. The following section contains a discussion of the limitations that were present in this study and the extent to which they were believed to have influenced study outcomes.

Limitations of the Study

Although I believed that findings from this study improve understanding of the relationship between the development of AD and sociodemographic factors involved, there were some limitations that may have influenced the results. In contrast to deliberately chosen delimitations, limitations are weaknesses related to research designs and methodologies (Balnaves & Caputi, 2001; Vogt, 2011). Firstly, although the analysis

dataset included all desired variables, the scope of what data was potentially limited by HRS study design. The HRS is a longitudinal panel study that surveys 20000 Americans over the age of 50 and their spouses. The demographic characteristics shows that 95.7% were married in the study population, compared with 43.6% and 61.9% respectively for females and males respectively in the US population (Yahidy et al., 2021). It indicates that some level of selection bias exists in the HRS dataset. The characters of panel survey data is prone to several biases of AD observed. It has been indicated that there is unobserved transitions in the HRS data (Dudel et al., 2021). These limitations may explain the low AD rate (3.1%) in the study population, compared with prevalence of AD (10%) in US population (Alzheimer's Association, 2021).

Secondly, the study may have limited quantitative approach's focus on testing hypothesized relationships; the study was not able to explore or uncover new relationships. This limitation was offset by the advantages of a quantitative approach, particularly the statistical power it affords. The study may limit in that it only considers a key subset of variables. However, these particular variables are supported in the literature (Fuentes et al., 2020; Kamiya et al., 2018; Kawaharada et al., 2019). Moreover, the use of statistics such as the generalized least squares approach helped to determine the degree to which the variables included in the study can explain the variance in AD onset. The following section contains a discussion of recommendations that was based, in part, on these limitations and also the significance of the findings for practice and research.

Recommendations

Based on the results of this study and their significance, several recommendations can be made for practice and future research. Research by Matthews et al. (2019) researched the AD and related dementias prevalence among population subgroups. The finding of significant disparities in prevalence leaded to further future research of individual risk estimations for subgroups (Matthews et al., 2019). However, it is important to discuss how individual characteristics such as gender, age, race, and ethnicity may play a role in AD's burden to address treatment options and address high-risk patients (Matthews et al., 2019). Various dietary approaches are recommended and explored for AD patients, including the ketogenic diet tested by researchers discussed in Chapter 2, such as that of Taylor et al. (2018). According to Taylor et al. (2018), a ketogenic diet can mildly impact AD patients in a clinical sample of 11 participants. Overall, lifestyle changes were recommended as a predictive and preventative factor for AD patients (Khoury et al., 2019).

It is also recommended a more broader representive target population to address the limitations identified previously. Additionally, it is recommended that research associated with the evidence of inflammatory treatment models be conducted. Liu et al. (2019) noted a lack of evidence for the efficacy of inflammatory treatment models. Research is also needed regarding dietary factors associated with AD. A limitation of understanding dietary changes for AD is the lack of empirical assessments such as controlled or randomized studies.

Hill et al. (2019) advocated for dietary changes. But he found limited number of randomized trials to support dietary change and biomarkers of AD. The meta-analysis performed by Hill et al. (2019) only identified 13 studies that demonstrated a significant positive result on AD patients. Hill et al. argued that while diet may be an important nonpharmacological approach, extensive clinical assessments are required for demonstrated efficacy. Thus, further empirical trials and meta-analyses of these findings is still needed. Research regarding neurodegenerative disease needs to address age-dependent patterns within or between individual changes in traits during a lifetime. Because of the lack of longitudinal and adequate data on neurodegenerative diseases, existing studies are mostly cross-sectional. Thus, this study is good attempt to address age-dependent patterns usign longitudinal data.

Implications

Results from this study have significance academically, practically, and in terms of creating positive social change. These findings address the problem associated with the lack of understanding regarding the prediction of AD based on cognitive functioning. The academic significance of the study derives from addressing the research gap. This gap is highlighted by three calls for research. Firstly, Weintraub et al. (2018) studied the ability of cognition and function to predict the development of AD. Although their results offered a promising model, they called for further research into the ability of functional-related issues such as ADL to predict AD.

Findings from this study also extend the theory of social epidemiology by offering insight into the social determinants of AD. Along a similar line of research, Alberdi et al.

(2018) studied the ability to use data regarding factors like ADL to predict the onset of AD. Their model was good but imperfect, and they called for more similar research that makes use of longitudinal data (Alberdi et al., 2018). Finally, in a review of modeling approaches, Li et al. (2017) found that few prior researchers had used a combination of baseline and change over time factors. Therefore, they called for more research using such an approach. In addition, Mauricio et al. (2019) reviewed and summarized the proceedings of the G8 dementia summit; the most significant conclusion of the summit was a need for more—and more innovative—research into dementia, of which AD is the primary cause. The present study fulfills all these calls for research by examining the predictive power of ADL on AD longitudinally and with both baseline and change over time data.

The practical implications of the study derive from the importance of combatting AD. As noted above, the incidence of AD is quite high, and it represents one of the most significant threats to the health of older Americans today (Weller & Budson, 2018). Over 6 million Americans suffer from AD as of 2021 (Alzheimer's Association, 2021; National Institute on Aging, 2021, July 08). Therefore, there is an urgent need to help identify both which factors may be predictive of AD and which factors may protect against it. Identifying the predictors of AD may help isolate causes and target screening at those at the highest risk. Identifying protective factors, on the other side of the issue, and especially those as straightforward as ADL factors may allow for people to practice such protective habits and fight AD.

These findings may contribute to social change regarding the prevention of AD or the delay of symptoms. The significance for positive social change inherent in the study is bound up in these practical implications. If the results can help combat AD, either by reducing its prevalence or better targeting screening and early treatments, then the study will contribute to the ongoing and essential battle against AD. AD represents one of the most significant health threats to older Americans and causes great emotional harm to families who must cope with a relative still being technically alive yet not remembering them (Weller & Budson, 2018). Therefore, any results that meaningfully help reduce AD or offer incremental progress toward isolating causes and risk factors can contribute significantly to positive social change.

Conclusion

The purpose of this chapter was to provide discussion of the findings of this study and their implications for practice, future research, and positive social change. An interpretation of the findings was provided first, based on the extent to which they aligned with literature presented in Chapter 2. Limitations that were identified in Chapter 1 and the extent to which they are believed to have influenced study outcomes were then discussed. Recommendations were then made for future research and practice, based on these limitations and the significance of the findings. Implications of the research for practice, research, and social change were then considered.

Aguinis et al. (2013) introduced a four-step multilevel model approach. I used this approach to address the research questions. The study findings indicated that an increase in changes in ADL leads to an increase in the probability of onset AD in later years.

However, this finding is not supported by sensitivity analysis. However, the analyses did not provide sufficient support to accept any of the research hypotheses. It was found that changes in early years' ADL was significantly and positively associated with the later onset of AD. On the contrary, this finding was not supported by the sensitivity analysis. No significant relationship was found between early years' ADLs and the later onset of AD.

Furthermore, no evidence was found indicating the moderating role of any of the sociodemographic factors in the relationship(s) between early years' ADL and/or ADL changes and future AD diagnosis. Based on the results of this study, it is clear that there are numerous sociodemographic factors associated with AD risk, although further research is still needed in regard to identifying the predictive value of each and their combined association with the onset of this disease.

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Appendix: Power Analysis

The common practice of power analysis is using an assumed true effect size based on a prior study then calculate power at a range of sample sizes. However, there is no such research available using hierarchical structure data (Maas & Hox, 2005). In this power analysis, the prior- variance and correlation estimate using a 50 random sample drawn from a legacy HRS sample dataset. The assumed true fixed and random effects values obtained by fitting a generalized linear model using this sample. The results indicated that the intraclass correlation (ICC) is 0.656, which means that differences across level 2 groups account for about 65.6% of the variability in individuals ADL. The fixed intercept and slope of ADL are -4.22 and -0.97, respectively. The random component of the intercept is 0 with 1.33 standard deviation. These results, then, be used in the subsequence simulation as the parameters.

The data used in the power analysis is simulated with the parameters generated in the previous step. Based on the specific prior-, the posterior distributions of random effect are obtained by 1000 simulation. A grid of patients identifier generated by the levels of the second level groups. The fixed effect predictor is created using prior- the coefficient for fixed effect and the simulated ADL measures. The dependent variable is, then, simulated using the makeGlmer function in “SIMER” package, given prior- fixed effect, variance-correlation matrix (Green and MacLeod, 2016). This simulation assumed the residual of the model is zero.

In a multilevel model, the level 1 effects are moderated by the higher-level variables (Chen et al.). Raudenbush and Liu (2000) indicated that level 1 sample size is

most relevant for the statistical power to detect level 1 direct effects, and level 2 sample size is most relevant for the statistical power to detect level 2 direct effects. The intraclass interactions determine the intercept and slope variance across level 2 groups (Raudenbush and Liu, 2000). The power analysis in this study was grounded in these conclusions.

In this power analysis, how the statistical power are impacted by level 2 sample size were assessed on a range of sample sizes. Keeping the value of other parameters constant, the simulation was conducted using the number of groups from 5 to 15. The power and 95% confidence interval on the significance level (alpha=0.05) were simulated. The results of the simulation are illustrated in Table 19. The result shows that with the level 2 sample size of 5, the model has only around 40% power to detect the assuming true effect. When the sample size increases to 15, the power increases to 80% with a 95% confidence interval from 61.43 to 92.29. The power curve illustrates the effects of varying numbers of sample sizes in Figure 11.

How the statistical power are impacted by level 1 sample size were also assessed on a range of level 1 sample sizes from 3 to 80. The essential assumption of the analysis was that the sample size of each group is balance. The simulation was first conducted with a small level 2 sample size of 3. The power and 95% confidence interval on the significance level (alpha=0.05) are displayed in Table 20. The result shows that when the sample size significantly increased to 80, the power of the model is only 53%, with 95% CI from 34 to 72. The power curve illustrates the results of the simulation in Figure 12.

Table 19

Power and 95% Confidence Interval for the Continuous Variables of the Study

Number of groups	Power	95% CI
3	40.0%	(22.66, 59.40)
4	46.7%	(28.34, 65.67)
6	60.0%	(40.60, 77.34)
7	63.3%	(43.86, 80.07)
8	63.3%	(43.86, 80.07)
10	70.0%	(50.60, 85.27)
11	76.7%	(57.72, 90.07)
12	76.7%	(57.72, 90.07)
14	80.0%	(61.43, 92.29)
15	80.0%	(61.43, 92.29)

Figure 11

Power Curve by the Number of Groups

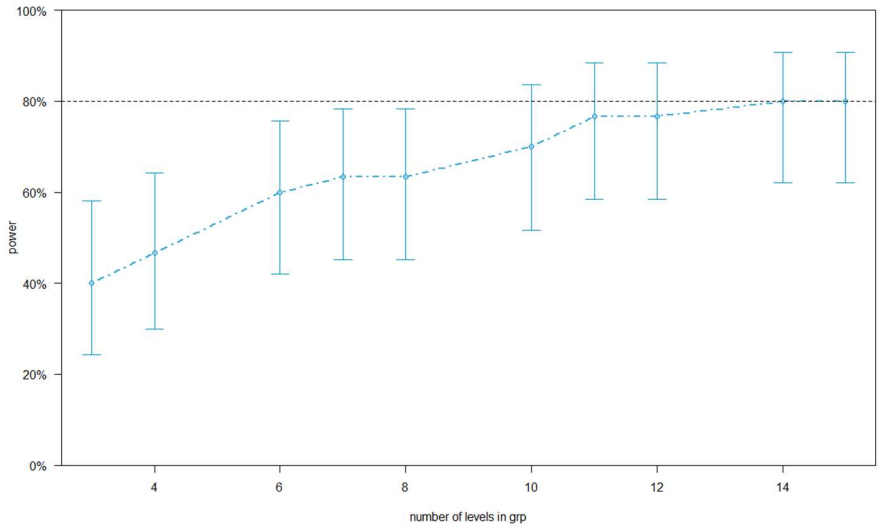


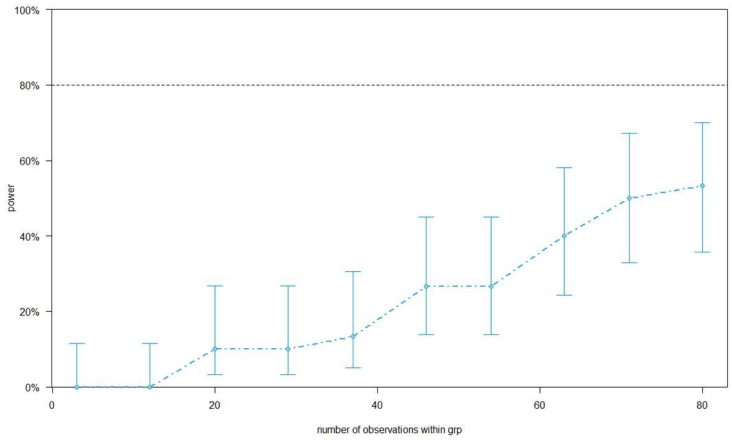
Table 20

Power And 95% Confidence Interval by The Number of Patients With Small Level 2 Sample Size

Number of patients	Power	95% CI
3	0.0%	(0.00, 11.57)
12	0.0%	(0.00, 11.57)
20	10.0%	(2.11, 26.53)
29	10.0%	(2.11, 26.53)
37	13.3%	(3.76, 30.72)
46	26.7%	(12.28, 45.89)
54	26.7%	(12.28, 45.89)
63	40.0%	(22.66, 59.40)
71	50.0%	(31.30, 68.70)
80	53.3%	(34.33, 71.66)

Figure 12

Power Curve By The Number Of Patients With Small Level 2 Sample Size



The simulation was then conducted with a large level 2 sample size. This result is consistent with previous studies that the higher level sample size has a larger contribution in detecting the effect in a multilevel structure data (Maas and Hox 2004; Scherbaum

2009). The third simulation is conducted by changing sample sizes at both levels. The result shows that when the sample size are 15 and 63 at level 2 and level 1 respectively, the model has 83% (95% CI 65, 94) power to detect the assuming true effects. The results is displayed in Table 21. The power curve of this simulation is illustrated in Figure 13.

Table 21

Power and 95% Confidence Interval by The Number of Patients with Varying Level 2 Sample Size

Number of patients	Power	95% CI
3	0.0%	(0.00, 11.57)
12	23.3%	(9.93, 42.28)
20	43.3%	(25.46, 62.57)
29	53.3%	(34.33, 71.66)
37	73.3%	(54.11, 87.72)
46	76.7%	(57.72, 90.07)
54	76.7%	(57.72, 90.07)
63	83.3%	(65.28, 94.36)
71	86.7%	(69.28, 96.24)
80	90.0%	(73.47, 97.89)

Figure 13

Power Curve By The Number Of Patients With Varying Level 2 Sample Size