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An Examination Between Neighborhood Characteristics and Alzheimer's Disease and Related Dementias and Caregiver Mental Health in South Carolina

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DEDICATION

I dedicate this dissertation to my *watan*, my *balad Filistine*.

على هذه الأرض ما يستحق الحياة.

محمود درويش.

ACKNOWLEDGEMENTS

I would like to thank my committee members, Maggi Miller and Bo Cai, for helping move my research along, giving me meaningful advice about interpretation of my findings, and encouraging me to pursue career options of interest to me. I especially felt motivated whenever I met with Maggi, who met my research goals with enthusiasm. I appreciate all the statistical help from Bo, and his prompt responses to my questions. I would also like to give special thanks to my mentors, Matthew Lohman and Jana Hirsch, because I would not have completed this work without their support. They always encouraged me and challenged me to be the epidemiologist and scientist I have become and am becoming. I would also like to thank the Office of Study for Aging, led by directors Daniela Friedman and Lee Peterson, for partially financially supporting this dissertation through the Graduate Scholar of Aging Award.

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ABSTRACT

Research has examined the relationship between neighborhood environments and cognitive decline, yet few have investigated the role of neighborhood characteristics specifically on incident Alzheimer's disease and related dementias (ADRD), on severity of Alzheimer's disease (AD) including neuropsychiatric symptoms (NPS), and on caregiver mental health including depressive symptoms. This dissertation aimed to 1) ecologically examine the geographic distribution of ADRD and investigate ecologic associations between census-tract neighborhood characteristics and diagnosed ADRD case incidence from 2010-2014 in the South Carolina (SC) Alzheimer's Disease Registry; 2) estimate the cross-sectional association between neighborhood characteristics and NPS among those with AD in 2010 in SC; and 3) estimate the cross-sectional association between neighborhood characteristics and mental health outcomes among AD caregivers co-habited with their care recipient in 2010 in SC.

This dissertation utilized the SC Alzheimer's Disease Registry, which is unique and comprehensive in its documentation of ADRD cases from many different sources. Additionally, this dissertation utilized collected secondary data from the Registry in 2010. Analyses for the first aim took place on the census-tract level (n=1,089) with population ≥50. Analyses for the second and third aims took place on the spatial buffer level defined as ½-mile and 1-mile, respectively. Neighborhood measures came from the Decennial Census, American Community Survey, Rural Urban Commuting Area Code, and County Health Rankings. To estimate the ecologic association for the first aim, a

Poisson mixed-effects model was estimated. To estimate the cross-sectional associations for the second and third aims, negative binomial models were estimated.

Overall, we observed that those living in high poverty and low-income neighborhoods had greater incidence of ADRD, NPS, and poor caregiver mental health compared to those living in low poverty and high-income neighborhoods. Contrary to previous findings, our results suggest that those living in rural areas had lower incidence of ADRD, NPS and poor caregiver mental health compared to those living in urban areas. The potential reasons for these findings remain unclear.

Collectively, this dissertation suggests that the neighborhood environments may be an important new consideration in research exploring risk for and management of ADRD, NPS, and caregiver mental health. Future research should investigate additional neighborhood characteristics, such as green space, pollution rates, or psychosocial stress, that contribute to greater ADRD, NPS, and caregiver health.

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LIST OF ABBREVIATIONS

AD ..... Alzheimer's Disease

ADRD ..... Alzheimer's Disease and Related Dementias

GIS .....Geography Information Skills

MDR ..... Multidrug Resistance

NPS .....Neuropsychiatric Symptoms

CHAPTER 1:

INTRODUCTION

Alzheimer's disease, the most common form of dementia, impacts an estimated 5 million adults and is the sixth leading cause of death in the US (1). Additionally, Alzheimer's disease and other related dementias, collectively termed ADRD, have been shown to negatively affect health of those who care for people with ADRD, also referred to as caregivers (2). This burdensome disease makes understanding factors that influence onset and progression of ADRD a significant public health problem. Research suggests that characteristics of the neighborhood environment may significantly impact the progression of ADRD (e.g., such as increasing presence of neuropsychiatric symptoms) (3) and the ability for caregivers to effectively manage the disease (4). However, while extensive research has focused on biological and social factors related to the incidence and progression of ADRD as well as caregiver health (5,6), little is known about influence of neighborhood characteristics.

There is a growing body of literature illustrating the importance of neighborhood characteristics influencing health behaviors and health status across the general population (7). More recently, researchers have examined how neighborhood characteristics influence health among older adults, those 65 years and older (8). Neighborhood characteristics are especially important for the health and well-being of older adults (9), whose more limited mobility results in more time in their immediate

geographic environments. In a similar fashion, neighborhood characteristics are also thought to be important for caregivers, who may rely on accessible care-providing resources (10).

Neighborhood characteristics are hypothesized to influence health outcomes by determining access to resources, medical services, food, parks, and by encouraging or discouraging health behaviors. Furthermore, studies report that neighborhood characteristics may specifically influence ADRD (11–13) and cognition among older adults (14,15). For instance, studies suggest that that greater neighborhood area deprivation are associated with lower cognition (9,15–18). A similar relationship was observed between more disadvantaged neighborhoods are associated with greater depressive symptoms (19,20). Although there is limited research regarding neighborhood characteristics influencing ADRD and caregiver health, such studies could have implications for the development of aging-friendly communities, the promotion of functional independence among older adults, and the ability of caregivers to provide quality care.

STATEMENT OF THE PROBLEM

Although evidence suggests that neighborhood environments may influence health outcomes and cognition of older adults, there is little known about how neighborhood characteristics might be associated with ADRD incidence and progression (21). Further, there is a lack of research examining how neighborhood characteristics may influence the health and well-being of the caregivers (10). We utilized and expanded upon the measures and research done by previous studies by focusing on ADRD and their caregivers in South Carolina (SC). We used the SC Alzheimer's Disease Registry (22),

which is a comprehensive statewide registry of diagnosed cases of ADRD compiled from various sources including but not limited to inpatient hospitalizations, mental health records, and emergency departments. The availability of this unique registry allowed us to conduct this research on a state scale using population-based data to identify neighborhoods with greater ADRD incidence. Further, the availability of this unique registry allowed us to conduct statewide research among those with ADRD and their caregivers in order to contribute to the literature regarding how neighborhood characteristics may influence ADRD incidence, AD progression (e.g., neuropsychiatric symptoms) and caregiver mental health (e.g., depression).

In summary, conducting research to learn how neighborhood characteristics may influence both ADRD and caregiver health in SC is both novel and critical because 1) ADRD is highly prevalent (23), 2) ADRD poses a huge burden to the healthcare system (24), 3) there is no current treatment for ADRD (25), 4) neighborhood policies can have implications in delaying ADRD incidence (26), 5) neighborhood characteristics may also influence the burden experienced by caregivers for those with ADRD (27), 6) neighborhood policies can have implications in reducing negative health outcomes among caregivers as well as alleviating burden on the healthcare system (10).

AIMS AND HYPOTHESES

The goal of this dissertation was to identify neighborhood characteristics associated with ADRD incidence and neuropsychiatric symptoms as well as and depression among caregivers. To address these known gaps in the literature, we utilized a comprehensive Alzheimer's Disease registry in SC from 2010-2014 and secondary data from the Registry subsample in 2010 (28). Specific aims were:

Aim 1: Investigate the ecologic associations between census-tract and county-level neighborhood characteristics and ADRD incidence from 2010-2014 in SC.

Hypothesis 1: We hypothesized the following neighborhood characteristics will be associated with greater ADRD incidence: higher poverty level, higher proportion of non-Hispanic black residents, limited access to healthy food, more rural areas, and higher levels of air pollution. We hypothesized the following will be associated with lower ADRD incidence: higher ranked quality of care.

Aim 2: Estimate the associations between neighborhood characteristics (median household income, residential instability, and rurality) and neuropsychiatric symptoms (NPS) among those with AD cohabitated with their caregiver in 2010 in SC.

Hypothesis 2: We hypothesized that lower income neighborhoods, higher percent residents that moved the past year, and more rural areas are associated with greater NPS score.

Aim 3: Estimate the associations between neighborhood characteristics (median household income, residential instability, and rurality) and caregiver mental health (depression, burden and distress) among caregivers who live in the same household with the patient in 2010 in SC.

Hypothesis 3: We hypothesized that lower income neighborhoods, higher percent residents that moved the past year, and more rural areas are associated with greater depressive, burden, and distress symptoms among caregivers cohabitating with the person with AD.

IMPORTANCE OF RESEARCH

ADRD has been recognized as one of the leading causes of mortality among the US population (1). ADRD also burdens the healthcare system with an estimated $259 billion of total direct medical payments in 2017 (1). Additionally, ADRD places a heavy burden on caregivers; each person with ADRD is estimated to have up to 4 caregivers (2). They are mentally affected through emotional exhaustion often associated with the work and are affected financially through an estimated $5,155 out-of-pocket average spending per year (2). In spite of the widely appreciated magnitude of this problem, unfortunately, little progress has been made in understanding how ADRD can be prevented through medical or pharmacological means (25). Therefore, a growing body of research has focused on social and behavioral approaches to slow the progression of ADRD or to improve functioning of those with ADRD (25). Less research has focused on the influence of the neighborhood environment (29).

The rationale that underlies the conducted research was that understanding how neighborhoods affect ADRD may inform public health policy and future research aimed at mitigating ADRD progression and optimizing management of the disease. Understanding modifiable neighborhood characteristics (e.g., specific physical or social resources), which promote not only physical but cognitive health, may inform the development of broad policies and changes aimed at improving health among older adults (30). By understanding how ADRD is distributed in the population by neighborhood locations, these results can inform allocation of public health resources for ADRD and can inform researchers of which geographic areas to target for intervention. Information learned about specific neighborhood characteristics influencing ADRD can inform

researchers and urban planners the design construction of neighborhoods with high concentrations of older adults. By optimizing neighborhoods with high prevalence of ADRD by ensuring access to health care and features conducive to healthy behaviors, individuals can better manage their disease. Likewise, these results can help researchers focus on addressing poor health experienced by ADRD caregivers. Such macro-level changes to the environment to encourage health behavior changes have the potential to have more lasting and widespread impacts on the cognitive health of communities than specific targeted interventions (31).

One proposed strategy to delay cognitive impairment and reduce risk for ADRD is exposure to complex, stimulating neighborhood environments (29) that promote good vascular health, an established protective factor against ADRD (32). The influence of interventions aimed at modifying neighborhood characteristics on health behaviors can readily be seen through adoption of Silver Sneakers Program and similar exercise programs for older adults that have successfully increased physical activity among this population (33). Likewise, introducing farmers' markets has increased availability of healthy food options and lowered overall food costs within neighborhoods (34). These examples demonstrate the role neighborhood characteristics play in promoting healthy lifestyle choices while reducing preventable diseases. Hence, this research allowed us to identify neighborhood characteristics that may contribute to lower ADRD incidence in order to design effective interventions.

CHAPTER 2:

LITERATURE REVIEW

The goal of this scoping literature review was to: 1) provide a brief overview of important concepts and definitions related to studying the influence certain neighborhood characteristics have on Alzheimer's disease and related dementias (ADRD) and generally on cognition as well as mental health; 2) define and describe dissertation outcomes of interest: ADRD incidence, Alzheimer's disease (AD) neuropsychiatric symptoms (NPS), and mental health (e.g., depression) among ADRD caregivers; and 3) describe what is currently known about how certain neighborhood characteristics influence dissertation outcomes and precursor outcomes.

SEARCH METHODS

A comprehensive literature review was conducted to aid in defining and describing the influence of exposures (neighborhood characteristics) on the outcomes of interest (ADRD incidence, NPS among those with AD, and depression among caregivers). The following databases were used: Google Scholar, PubMed, Web of Science, and CINAHL complete. Cited references and studies published only in English were included. There were no limits set for publication date, although more recent articles (e.g., published within the past seven years) were favored. The following search terms were used to locate studies evaluating the association between neighborhood characteristics and ADRD: ("neighborhood* effects" OR "built environment" OR "social

environment" OR "walkability" OR "environment design" OR "neighborhood* characteristic*") AND ("dementia" [Mesh] OR (Alzheimer* OR dement* OR frontotemporal lobar degeneration* OR "FTD" OR "FTLD" OR lewy bod* OR "AIDS dementia" OR "HIV dementia" OR "ADRD"). The following search terms were used to locate studies evaluating the association between risk factors and NPS: ("neuropsychiatric symptom*" OR "inventory" OR "progress*" OR "severity" AND "Alzheimer* OR dement*). The additional search terms were used to locate studies evaluating the association between neighborhood characteristics and depression among ADRD caregivers: ("depression" OR "depressive disorder" OR "depressive symptoms") AND (caregiver* OR care giver* OR carer* OR "families" OR "family" OR friend* OR spouse* OR personal care aide* OR personal care worker*). Because of the limited research available on neighborhood and ADRD, studies assessing the association between neighborhood and cognition, cognitive impairment, cognitive decline, and cognitive function were also included.

FINDINGS

An estimated 120 articles were included in the literature review, with majority focusing on outcomes related to cognition. Most of the studies evaluated were cross-sectional studies, and seven were longitudinal studies. A majority of the studies were conducted in the US with several conducted internationally including but not limited to England, Spain, and Japan.

OUTCOME: ADRD AND NPS AMONG THOSE WITH AD

Alzheimer's disease and related dementias (ADRD) is the sixth leading cause of death in the US (1). Currently, an estimated 5.4 million adults in the US have AD (1). As

the older adult population (≥65 years) will rapidly increase in the next forty years, the prevalence of ADRD will also increase tremendously (35). This growing prevalence of ADRD makes understanding the risk factors of ADRD a significant public health problem, and there is a strong need to develop effective prevention strategies. This is especially true since there are no current cure or effective medication to treat ADRD. It also places a large economic burden on the healthcare system with an estimated total direct medical cost of $259 billion in 2017 (1). However, studies have shown that even modest delays in the onset of ADRD may significantly reduce the prevalence of and high levels of health care associated with ADRD (36).

The strongest risk factors for ADRD are age, family history, and genetics. The vast majority of those with ADRD are 65 and older (1). Because women have a longer life expectancy than men, more women than men have ADRD (1). Epidemiological profiles also show nonwhites to be at greater risk for ADRD. Recently, a systematic review of 1,215 studies found that black and African Americans have significantly higher ADRD incidence rates compared to all other racial groups (37). Established modifiable risk factors that can be intervened on during mid-life have recently been identified by the Lancet International Commission on Dementia Care: education, exercise, social engagement, hearing loss, depression, smoking, diabetes, hypertension, and obesity (32). Low education has consistently been shown to be associated with poor cognition and ADRD risk, regardless of race (38,39). A systematic review of 16 prospective studies concluded that those who engage in physical activity have a lower risk of ADRD (35). Another meta-analysis of 29 randomized controlled trials found cognitive benefits among adults who exercise regularly (40). Moreover, studies suggest that remaining socially

active supports brain health and thus can reduce the risk of ADRD (41). Furthermore, factors associated with poor cardiovascular health are also associated with a higher risk of ADRD including but not limited to smoking, diabetes, hypertension, and obesity (32).

This dissertation also includes the outcome of neuropsychiatric symptoms (NPS), which are non-cognitive symptoms that are present during AD and persist throughout disease progression (42). Common NPS include apathy, agitation, irritability, delusions, and hallucinations. Clinical studies estimate that 70-90% of AD patients experience at least one NPS (42). Additionally, NPS have recently emerged as predictors of disability, faster cognitive decline, and greater mortality (6). For example, apathy has been found to be associated with increased risk of mortality, as well as more severe cognitive and physical decline (43,44). Moreover, NPS are cited to be one of the most challenging behavioral symptoms caregivers deal with (4). NPS increase caregivers' risk of poor health (45) and consequently their caretaking abilities. As such, the Lancet Commission has also reported the need to manage NPS via psychological, social and environmental intervention with pharmacological management reserved only for those with more severe NPS (32).

SECONDARY OUTCOME: DEPRESSION AMONG ADRD CAREGIVERS

ADRD also places a heavy burden on informal caregivers. Informal caregivers are those who attend to the needs of people with ADRD and tend to be a family member, usually a spouse or daughter. For the purposes of this dissertation, the term 'caregiver' is specific to those who care for someone with ADRD unless stated otherwise. Caregiving assistance ranges from bathing and dressing to paying bills, shopping and transportation (46). There are an estimated 15 million caregivers in the US (46). These caregivers are

disproportionately women, representing approximately two-thirds of all caregivers (47). According to BRFSS data in 2017, among all caregivers, 10% are ADRD caregivers (48). An anticipated increase in the aging population as well as ADRD prevalence in the next forty years will lead to a greater reliance on caregivers (49). Hence, it is vital to understand risk factors of caregiver health.

Caregivers experience negative health problems, stress, and burden (50,51) ranging from poor emotional and social well-being to worsening physical health (52). Approximately 30-40% of caregivers suffer from depression, compared to 5-17% of non-caregivers of similar ages (1). Prevalence of depression is also higher among ADRD caregivers compared to other types of caregivers (53). Caregivers looking after someone with severe NPS are most at risk for depression (54). Caregivers depressive symptoms and poor mental health impacts both the individual and the person with AD as well as wider society since caregiver depression predicts care breakdown and consequently institutionalization (55). Because those with AD experience a better quality of life when they live at home (56), it is important to know how to effectively prevent or manage NPS as well as caregiver health.

EXPOSURES: OVERVIEW OF NEIGHBORHOOD CHARACTERISTICS

Neighborhood characteristics can be contextualized in several ways including social and built environment attributes. The social environment can include socioeconomic status, social disorder, social climate and other related sociodemographic characteristics (20). The built environment can include placement and configuration of roads, homes, commercial buildings, public spaces, and other related physical characteristics (29).

Social environment attributes are hypothesized to affect health via influences on social support and cohesion (i.e., social norms of reciprocity and trust within communities) (57). For example, neighborhood security has been shown to positively influence social cohesion among community-dwelling older adults (58). Social environment attributes are also hypothesized to affect health via influences on education, employment and wealth. For example, racial residential segregation and school segregation (that have been maintained for generations due to historical context) limits educational and job opportunities (39). Likewise, explicit discrimination in the labor market earnings continues to persist and thus reinforces existing low socioeconomic status in neighborhoods (39). In fact, the current substantial social and residential stratification by race and intergenerational transmission of both individual-level and neighborhood-level socioeconomic status reinforces existing neighborhood socioeconomic status (39), which in turn impacts health.

Built environment attributes are hypothesized to affect health via influences on many factors. For example, residential distance to major roadways and highways increases exposure to toxic air pollution (29,59). Similarly, high traffic volume and noise can cause anxiety (29). Presence of grocery stores and/or supermarkets can promote healthy eating, thus decreasing risk for poor health (29). Graffiti, shade, greenery and other aesthetics of the built environment are hypothesized to influence recreational walking and physical activity as well as depression (60).

EXPOSURES: OVERVIEW OF NEIGHBORHOOD DEFINITION

Neighborhoods, defined as geographical places that can have social and culture meaning to residents (61), can be conceptualized via different ways. Neighborhood

conceptualization, however, is contingent upon the research question (61). Due to ease of data collection and processing, census tracts are traditionally the most common neighborhood definition in neighborhood health research in the US (61). Census tracts are subdivisions of a county with an average population of 4,000 residents that are purposefully designed to capture homogenous areas with respect to population characteristics, economic statuses, and living conditions (62). These boundaries are drawn by the US Census Bureau. Thus, census tracts are especially useful for identifying geographic disparities and determining resource allocation (61,63). Given these boundaries are arbitrarily drawn by administrative agencies, they do not reflect an individual's mobility patterns, especially for those living at the edge of boundaries where spatial misclassification (e.g., incidents beyond the boundary of each areal unit would affect the estimate accuracy of the issue and yield biased results in subsequent statistical analyses using aggregated data) is more likely to occur (61). Studies aiming to focus on a more personalized neighborhood definition that is well suited for the assessment of personal exposure areas often use GIS-based spatial buffers. Spatial buffers define neighborhoods as radii around a particular location, often participants' home addresses. There are different types of buffers, but circular-base (also known as Euclidean buffers) have been traditionally used because they work well for analyzing distances in relatively small areas, such as one U.S. state (61). Another common type includes geodesic buffers that account for the actual shape of the earth and thus are typically used when analyzing distances in large regions, such as the whole U.S. Buffers vary in size with no standardization being possible to define the neighborhood; instead, researchers determine the size of the buffer based on the research question and sample population (64). For

example, a recent study examining the association between the built environment and cognition among older adults used a spatial buffer size of 0.5 mile (65). This small size reflects the area closer to the participants' homes that is more important for older adults (65). While still utilizing available secondary data (e.g. Census) to create neighborhood measures, buffers are more accurate compared to census tracts in reflecting an individual's mobility patterns. However, buffers are static and still do not completely reflect an individual's mobility pattern. Some of these limitations can be overcome with GPS-derived activity space neighborhood definitions (66), which are beyond the scope of this dissertation work.

EXPOSURE: NEIGHBORHOOD SOCIOECONOMIC STATUS

There are a wide variety of measures used to represent neighborhood socioeconomic status (NSES); however, one of the most commonly used is median household income (16,62). Median household income is often operationalized by dividing the income distribution into two equal parts with one-half falling below and the other half above the median. Another common measure used is poverty, defined as the percentage of families living below federal poverty threshold within a census tract. This measure is recommended to use for monitoring socioeconomic inequalities in health across a region (67). Alternatively, studies have indexed neighborhood socioeconomic advantage or disadvantage via a principal component analysis. For example, Clarke averaged six census indicators to calculate neighborhood socioeconomic disadvantage: percent households with income less $15,000 annually, percent households with incomes over $50,000 annually that was reverse coded, percent of working age adults who are unemployed, percent families in poverty, percent households on public assistance

income, and percent female-headed families (68). Because of the imprecision and difficulty in interpreting SES indices, it has been previously argued to rely on univariate measures, like annual household income, instead (69). This approach avoids statistical issues of multicollinearity that are common with neighborhood variables and allows easier comparison with other studies.

EXPOSURE: RESIDENTIAL INSTABILITY

Residential instability is defined as the movement of people in and out of neighborhoods. This measure has been previously used in research assessing the relationship between residential instability and depressive symptoms among adults and child caregivers (19). Most studies, however, have measured residential stability (defined as the proportion of people who live in the same house for the past five years) (70). Greater residential stability has been found to be associated with better self-rated health after controlling for individual demographics (71). Residential stability allows residents more opportunities to form friendships, participate in local affairs, and produce social capital compared to residents living in less stable areas and thus residential stability is a proxy measure for residents' ability to maintain shared values (72).

EXPOSURE: RURALITY

There are many measures to capture rurality; a common measure used in SC at the census-tract level is the US Department of Agriculture Rural-Urban Commuting Area code (RUCA) from the 2010 decennial census. By the US Census definition, in 2010 SC ranked 17th state with percent of the population living in a rural area at 33.7% whereas 28.8% of the US population lives in a rural area (73).

Since a majority of neighborhood research has largely focused on adults living in suburban and urban areas (74), conceptualization of neighborhoods used for urban areas does not apply for rural areas for several reasons (75). Rural neighborhoods tend to be more automobile dependent compared to urban neighborhoods and are typically characterized by low residential density; mainly single land use and low street connectivity (76). As a result, studies revealed that those living in rural areas define their neighborhood based on social relationships, structural features, and shared resources (75).

This differing view in neighborhood space is reflected in behavior. For example, studies have shown that those living in rural neighborhoods tend to walk for leisure whereas those living in urban neighborhoods tend to walk for transportation. A study conducted in a rural setting in Georgia among adults averaging 55 years old who are physically active found that lack of sidewalks was irrelevant to one's decision to exercise (75). Given the light traffic in rural settings, most participants walked on their property or parts of a road (75). The aesthetically pleasing demeanor of one's neighborhood was found to play an influential role in determining exercise decisions (75). Also, conflicting results reported difficulty in examining how neighborhood characteristics influence health among those living in rural areas when examining neighborhood walkability (74). Contrasting urban versus rural views on neighborhood definitions coupled with the issues in examining how neighborhood characteristics influence health in rural areas demonstrate the difficulty in measuring attributes of the social and built environment in a rural context.

EXPOSURE: OTHER NEIGHBORHOOD VARIABLES

Quality of care can be defined in different ways, such as resident-to-staff ratio (77). Another definition is obtained from the County Health Rankings that defines quality of care as the preventable hospital stays per 1,000 Medicare enrollees, percent of diabetes patients that receive HbA1c screening, and percent of females that receive mammography screening, that has been previously used (78).

EXPOSURE AND OUTCOME

Rarely have neighborhood studies or neighborhood design considered the needs of people with ADRD (79). Instead, most neighborhood research among people with ADRD has focused on the design of the home, internal environment, and ADRD-care facilities (80). Yet, those with ADRD regularly interact with their outside environment and engage in activities in the public space (81). Walking is reported to be the most frequent mode of transportation among those with ADRD (81); walking to access the bank, buy groceries, or visit a healthcare professional, for example. Such services are tend to be closer in proximity among those living in high-income and urban neighborhoods compared to low-income and rural neighborhoods. This may contribute to walking at greater lengths among those living in low-income and rural neighborhoods. Unfortunately, reports show that pedestrians who die from traffic accidents had greater amounts of ADRD-related changes (81). Therefore, it is imperative to understand how those with ADRD interact with their neighborhood, especially in low-income and rural neighborhoods, in order to promote a comfortable, safe environment (81).

Little research has been done regarding how people with ADRD interact with their neighborhood. Most of research has examined attributes of the social environment,

namely components of NSES, and cognition (29,82). Attributes of the built environment have largely been unconsidered (29). For example, a recent review looking at attributes of the built environment and cognition only identified six studies, with one of them examining park space (29). That study found no association between neighborhood park area and cognition (68).

Because individual-level behavior change strategies are expensive and largely unsuccessful, public health advocates have taken a more ecological approach to examine how social and built neighborhood attributes influence established risk factors of ADRD (32), such as physical activity (83). It is imperative to understand how the environment acts as a facilitator or barrier to physical activity and other factors associated with ADRD, and how this can inform the design of policy interventions as well as influence those with influence over urban design to create environments that promote physical activity (84).

EXPOSURE AND OUTCOME: NSES AND ADRD

Most studies focusing on cognition and ADRD have looked at neighborhood socioeconomic status (NSES) (82), which is a broader measure to capture income, education, accessibility of resources, strength of social network, and more. Although the vast majority of those who experience either poor cognition or cognitive decline are not diagnosed with ADRD, we still consider these studies for our literature review because we hypothesize similar mechanisms from NSES to poor cognition or to ADRD or NPS are at play.

Overall, studies examining NSES (measured via various methods) have demonstrated an association with poor cognition. A review found significant

relationships between community-level SES and cognitive function among 11 studies out of 14; specifically, seven studies reported greater area deprivation to be associated with lower cognitive function (82). Studies using other measures of low NSES- deprivation, poverty, socioeconomic position, and education- have also reached similar conclusions in relation to poor cognition (9,16,62,85,86).

Studies also show that high NSES to be associated with higher cognitive function (68,87,88). For instance, higher NSES was associated with higher MMSE scores (mini mental state examination) among 3,595 older adults (88). Similarly, another study found that high NSES is associated with higher cognitive functioning beyond individual-level demographic characteristics among older women (15). These findings could be due to neighborhood resources promoting cognitive reserve for older adults who are aging in urban settings (68). A study found that those living in neighborhoods with a proper proportion of laborers and employed- indicating high income neighborhoods- were found to be associated with a lower risk of ADRD (11). High county-level SES was also found to be associated with higher cognition level (89). These results indicate that attributes of the social environment and specifically NSES may influence risk for ADRD by improving the overall neighborhood quality (11).

Generally, longitudinal studies examining the relationship between low NSES and cognitive decline did not find any association (87,90). For example, Meyers et al. (90), did not find any significant relation between low NSES and cognitive decline longitudinally. After six years of follow-up, another study no longer observed a significant association between high NSES and higher cognitive function (88). The disappearance of the significant cross-sectional association observed longitudinally is

consistent with AlHazzouri's findings previously described (87,88). Another study found that those who lived in higher NSES had greater initial gains in everyday cognition but not long-term gains (90). Even the association between high county-level SES was unrelated to cognitive decline (89). The consistent association between high NSES and baseline high cognition but not with rate of cognitive decline suggest that NSES conditions in early life are associated with level of cognitive function in old age but not with rate of cognitive decline. That neighborhood characteristics may have a stronger role with initial gains but not long-term rate of change or response to cognitive interventions (87,90).

EXPOSURE AND OUTCOME: RESIDENTIAL INSTABILITY AND ADRD

There is little research regarding the association between residential instability, or low social cohesion broadly, and ADRD. Nonetheless, reviews report that high social cohesion and collective efficacy are associated with better health outcomes and lower risk of cardiovascular diseases among older adults, such as hypertension (30,91). A systematic review concluded that larger social networks were associated with higher cognitive function while social isolation was associated with lower cognitive function (92). A longitudinal study also demonstrated the relationship between having a large social network and lower risk of dementia (93).

EXPOSURE AND OUTCOME: RURALITY AND ADRD

Given the heterogeneity in defining rurality, it is difficult to compare study findings regarding ADRD prevalence by rurality, yet most studies have observed higher rates in rural areas (94). This is not surprising as older adults tend to live in rural areas (95). Also, this geographic pattern is commonly found globally. A study in Japan found

that the age and sex adjusted prevalence of cognitive impairment among those 65 years and older was higher in rural areas (8.4%) compared to urban areas (2%), even after adjusting for lifestyle factors (94). On the other hand, ADRD prevalence rates have also been found to geographically cluster in urban areas compared to rural areas (96). In addition to prevalence disparities by rurality, a study also found AD-related services disparities by rurality (97). There were less AD-related services in community pharmacies located in rural compared to urban counties where individuals with AD and their caregivers face barriers to obtaining quality pharmaceutical care (97). Likewise, it has also been noted that community-dwelling veterans with ADRD in rural counties experience disparities due to lack of quality ambulatory care (97).

Attributes of the social environment can be contributing to these higher rates among older adults living in rural areas (94). For instance, a study examining 29 rural communities in Canada found that an age friendly index (measured via built environment, housing, social environment, opportunities for participation, transportation options, and communication/information) were positively related to life satisfaction among older adults (98). These results indicate how an age-friendly city that provides support and opportunities for older adults encourages them to engage in physical activity and social activities, and thus neighborhood characteristics should also be taken into account for a rural context (98). Furthermore, another study found that those living in affluent areas were more likely to have high levels of social activity independent of individual demographic and SES characteristics (99). Poor local facilities have also been shown to be associated with less social activities (99). Rurality is hypothesized to

progress AD severity and NPS by contributing to low social functioning among older adults (99).

EXPOSURE AND OUTCOME: OTHER NEIGHBORHOOD VARIABLES AND ADRD

There is growing evidence that older adults living in areas with higher concentrations of outdoor air pollution have worse cognitive function and are at greater risk of cognitive decline. Air pollution and other neighborhood environmental stressors tend to cluster together geographically, as historically determined by the structurally racist, capitalist society we live in (100,101).

Although limited research has examined the relationship between quality of care and cognition, a recent article demonstrated that greater quality of care was associated with presence of psychiatric services including a psychiatric hospital and outpatient psychiatry at the county-level (78).

There is a wealth of literature demonstrating the association between limited access to healthy food and greater risk of health outcomes, such as diabetes (102), hypertension (103), and obesity (104). As previously mentioned, these health outcomes are risk factors for ADRD (32). More recently, a study noted neighborhoods with less grocery stores to be associated with greater dementia among Japanese older adults (12). No other studies examining the food environment and cognition or ADRD have been found.

EXPOSURE AND SECONDARY OUTCOME: NSES AND DEPRESSION

Because of the diverse measures used to capture NSES, it is difficult to compare study findings, yet there is evidence that links neighborhood characteristics, namely

components of low NSES, and mental health, including depression (20). A recent review identified neighborhood socioeconomic disadvantage to be associated with greater depression among adults, although not specific to caregivers (19). One study reported significant findings at the census-tract level between low neighborhood socioeconomic disadvantage and greater depression among older adults (105). Similarly, another study showed that living in a poor neighborhood is associated with reporting more depressive symptoms among older adults, while adjusting for individual-level variables (106). Because approximately one third of caregivers are older adults (50), neighborhood characteristics can especially influence health among this age group (9).

Extant literature on neighborhood environments and caregiver mental health is limited. One study found that neighborhoods with higher levels of crime were associated with higher glucose levels among caregivers compared to non-caregivers, thereby increasing risk for diabetes (107). On the other hand, a recent study conducted in Philadelphia among caregivers found greater neighborhood disadvantage to be related to lower depressive symptoms (10).

EXPOSURE AND SECONDARY OUTCOME: RESIDENTIAL INSTABILITY AND DEPRESSION

Few studies have examined the relationship between residential instability, and more broadly social cohesion, and mental health among ADRD caregivers. However, a review found that larger caregiver network and support was related to lower caregiver burden (108). Caregiver network, social support, and social institutions are largely determined by one's neighborhood (27), thus illustrating the role neighborhoods may influence health among caregivers. A longitudinal study among those ≥50 years old,

found neighborhood social cohesion to be associated with fewer depressive symptoms independent of demographic and socioeconomic factors (109). In a similar fashion, another review identified greater social cohesion to be related to lower rates of depressive symptoms while greater residential instability was related to higher rates of depressive symptoms among adults (19). Although no studies to our knowledge have specifically been conducted among ADRD caregivers, we hypothesize to find similar relationships between areas characterized by greater instability to be associated with greater depressive symptoms and poor mental health among ADRD caregivers.

CONCEPTUAL DIAGRAM

Neighborhood characteristics play a role in influencing health outcomes by largely determining access to resources, medical services, food- whether its grocery stores or fast food restaurants- parks and other recreational facilities, shops, and much more (20). These resources and establishments contribute to health via biological, social, and mental mechanisms. Availability of such resources and presence (or absence) are determined by institutional and structural factors at the local, regional, and national level (110). Although these various- and rather invisible- structural forces are not the primary focus of this dissertation, their role in determining financial allocation, affecting business growth and impacting residential segregation, to name a few, are kept in mind when discussing the mechanisms in which neighborhood characteristics influence health, specifically ADRD incidence, NPS, and depression.

Further, the relationship between people and place is reciprocal and mutually enforcing (111). Neighborhood characteristics do not operate in a linear fashion when influencing ADRD but instead work in circular motions. There are certain instances

where this top-down approach is true; however, individuals also influence their neighborhoods, and individuals' autonomy can overpower neighborhood effects. However, for the purposes of this dissertation, linear non-causal pathways are described in order to clearly articulate how a neighborhood characteristic may influence health. Specific mechanisms through which neighborhood characteristics affect an individual and influence their behavior (112), which in turn impacts ADRD, NPS, and depression, will be examined.

The exact causes of ADRD and specifically AD are unknown (32). There are, however, several physiological responses that cause cognitive impairment and in turn ADRD: increase risk of neurodegeneration, dysregulation of stress hormones, and hardening of arteries (113,114). These few examples of physiological responses are caused by psychosocial stress responses and psychological distress (114). Psychosocial stress responses and psychological distress are influenced by individual-level risk factors, such as physical inactivity, social disengagement, poor diet, smoking and toxin exposure- to name a few (32). Psychological distress manifests itself physiologically resulting in dysregulation of stress hormones as well as activation of neural and endocrine reactions that in turn activate the hypothalamic-pituitary-adrenal axis, which overproduces glucocorticoid hormones (e.g., cortisol) (113). This overproduction has been linked to brain damage that is consistent with cognitive dysfunction (59). Similarly, chronic activation of stress increases risk for hardening of arteries, which causes hypertension and cardiovascular diseases (100). These diseases have also been linked to ADRD risk (32).

Neighborhood characteristics are then hypothesized to influence ADRD indirectly by influencing individual-level health behaviors. Local laws and policies that govern organizational-level structures impact neighborhood characteristics (115), which in-turn operate as mediators through individual-level behaviors to affect health. Although neighborhood characteristics can also impact ADRD directly as contextual factors, this is omitted from the conceptual diagram for simplicity purposes.

There are several pathways from built environment attributes to poor cognition and ADRD risk. The food environment, specifically presence or absence of grocery stores and other healthy food outlets, influence diet and consequently have been demonstrated to influence diabetes (102), hypertension (103), and obesity (104), which all increase risk for ADRD (32). Also, there is less availability of healthy food outlets in rural compared to urban areas (116). Built environment attributes (e.g. proximity to highways or power plants) also increase exposure to air pollution and other environmental toxicants, which in turn increase risk for cognition (100) and are hypothesized to influence ADRD risk (59) as well as progress AD severity, namely NPS (3). Moreover, rural areas, which are characterized by geographic isolation, are often associated with low social engagement, which in turn influences ADRD (32) and hypothesized to progress AD severity (117,118). Other built environment attributes that are not considered for this dissertation but hypothesized to influence poor cognition and thus perhaps ADRD risk are related to green space. For example, parks influence recreational walking and total physical activity, which in turn influences ADRD risk (32). General lack of green space is also hypothesized to cause depression (119), which is also associated with ADRD risk (32).

There are several pathways from social environment attributes to poor cognition and ADRD risk. Low NSES and disadvantaged neighborhoods increase exposure to multiple, negative stressors (e.g. crime, drug use, and social disorder), which can interact to worsen both depressive symptoms (19) and cognitive function (82), and consequently ADRD (32). Low NSES also tend to lack stimulating environments and resources (e.g. libraries), which can increase levels of stress that may increase ADRD risk (120).

Also, the social environment attributes are hypothesized to affect ADRD by acting as mediators impacted by built environment attributes (Figure 2.1). For example, built environment attributes increase or limit access to structures that promote health (e.g., health centers) as well as spaces that encourage socializing (e.g., community parks). Vice versa, social environment attributes also act on the built environment and sequentially influence health. For example, high NSES influences a community's ability to leverage desirable changes (e.g., construction of a park or employment opportunities) or prevent undesirable changes (e.g., introduction of a waste facility) (110). A community having stronger social ties, usually characterized by high residential stability, also can leverage desirable changes (121). A low NSES community that is unable to prevent undesirable changes due to inadequate resources and lack of political clout results in community stress, which in turn negatively influences health (110). Low NSES community may also be characterized by residential instability (i.e. high proportion of residents moving) that reduces a community's ability to exercise social control through strong social ties (121). High residential instability is thought to hinder the formation of social cohesion (122) and decreases social engagement that can increase ADRD risk (32), NPS (6,42), and depression (19).

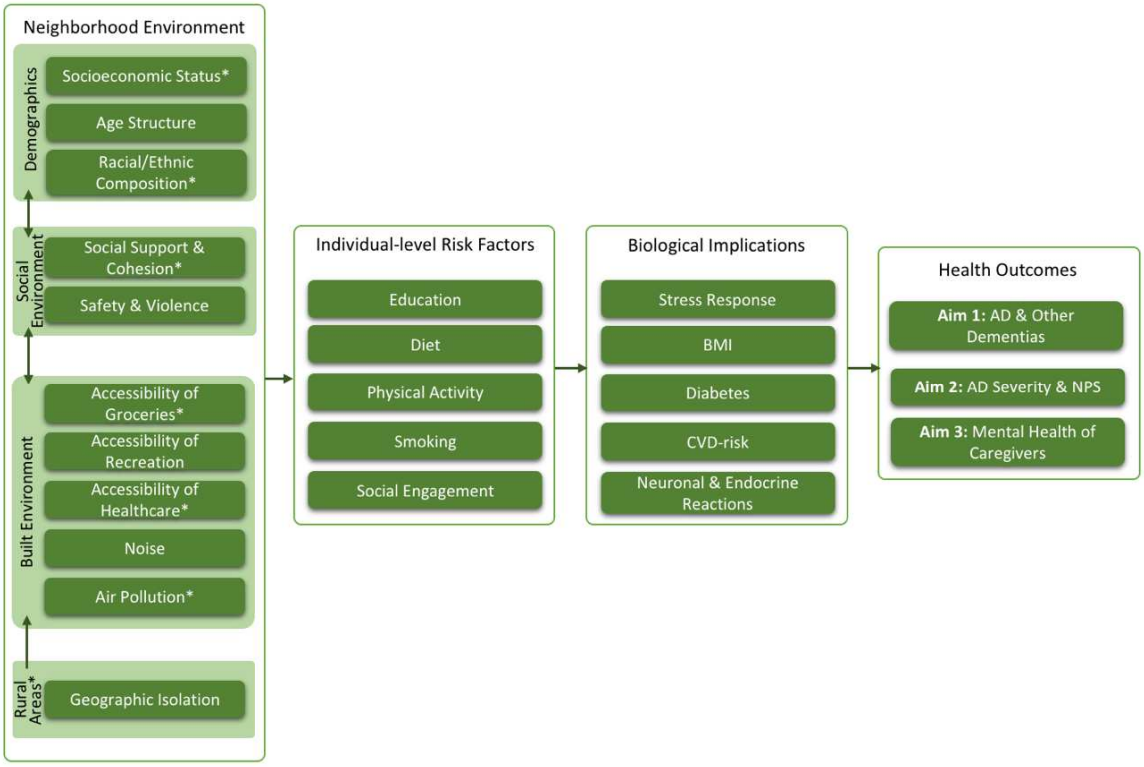

Figure 2.1. Conceptual Framework of the Potential Influences of Neighborhood Characteristics on Health Outcomes for Aims 1, 2, and 3

*Denotes measured exposures
BMI = Body mass index
CVD = Cardiovascular disease
AD = Alzheimer's disease
NPS = Neuropsychiatric symptoms

CHAPTER 3:

AIM 1: AN ECOLOGICAL ANALYSIS EXAMINING THE ASSOCIATION BETWEEN NEIGHBORHOOD CHARACTERISTICS AND INCIDENCE OF ALZHEIMER'S DISEASE AND RELATED DEMENTIAS

INTRODUCTION

Alzheimer's disease (AD) impacts an estimated 5.7 million adults in the US (46) and is ranked, along with other dementias, as the sixth leading cause of death (123). The prevalence of AD, together with related dementias (collectively termed ADRD) in South Carolina (SC) affects an estimated 11% of older adults (those aged 65 and older) in 2015 (22), similar to the national rate among older adults (11%) (23). Also in 2015, SC had the highest AD-related mortality rate in the country (46). As the older adult population is projected to rapidly increase in the next forty years, the prevalence of ADRD will also increase (124), which places a heavy burden on those who must act as caregivers to such individuals impacted by this disease. In SC, all types of caregivers provide an estimated 737 million hours of service each year (125). Additionally, ADRD is one of the costliest conditions to society, with an estimated total direct medical cost of $259 billion in 2017 – half of which was covered by Medicare (1). Long-term care comprises a substantial proportion of the cost of ADRD, so preventing or delaying the onset of ADRD deserves attention (126). Health economists have estimated that delaying the onset of AD by five

years could reduce the economic impact of the disease by 40% (127). Given that there are no current effective treatments for ADRD, identifying novel factors that influence the incidence of ADRD at macro-levels is necessary to determine resource allocation (e.g., age-related health services) and to identify potential area-level interventions. Research has identified candidate characteristics of the neighborhood environment, such as poverty (29), rurality (13), air pollution (59), access to healthy food (12), and access to health care (90) as well as neighborhood demographic variables, such as race (128), as potentially playing a role in ADRD development.

Neighborhood economic and racial conditions have a significant influence on health (129,130). For example, economically disadvantaged neighborhoods have fewer resources (e.g., healthy food outlets), lower quality of care, and more environmental toxicants (82,120). An increased exposure to a cluster of these risk factors is associated with poorer well-being (131), which is especially important among older adults who are more dependent on resources within their immediate environments due to financial and mobility constraints (9). A recent review demonstrated that older adults who lived in greater disadvantaged neighborhoods, as defined by various measures from the US Census that aggregate individual-level data, had poorer cognitive functioning (29). This further suggests the role disadvantaged neighborhoods may play in increasing ADRD risk. Disadvantaged neighborhoods are also usually spatially patterned by racial/ethnic composition (39), in which persistent racial residential segregation limits educational and job opportunities, thus reinforcing existing low socioeconomic status in neighborhoods (39,63,132). Therefore, measures of proportion of minority residents may serve as proxies for systemic disparities in access to healthcare, education, and employment

opportunities (88). Conversely, several studies have noted that affluent neighborhoods are associated with better cognitive function among older adults (15,68,88). Past research shows that greater density of neighborhood resources can promote protective health behaviors (e.g., physical activity) and facilitate mental stimulation (e.g., social interaction), both of which can ultimately improve cognitive function (87,90,133) and protect against ADRD (32).

Two characteristics of disadvantaged neighborhoods – namely, increased exposure to environmental toxicants and limited availability of healthy food options – are both potentially associated with greater ADRD risk (12,59). High levels of air pollution increase brain damage, and thus can increase ADRD risk (100,131). Although SC does not experience as high pollution levels as other places, a recent report found some SC cities are plagued by unhealthy levels of air pollution (134). Similarly, limited access to healthy food increases risk for hypertension (103), obesity (104) and diabetes (102), all of which can increase risk for ADRD (32). This was demonstrated by a longitudinal study in Japan that found lower access to grocery stores selling fresh produce (defined by the number of food stores selling fruits and vegetables within 500 meters of residence), was associated with an increased risk of ADRD (12).

Rural neighborhoods may also increase ADRD risk via similar mechanisms to economic deprivation. Studies report higher ADRD rates in rural compared to urban areas (24). One potential reason for this observation is that there are more geographic distances between people and places in rural areas, yielding higher rates of social isolation, which can increase risk for ADRD (92). On the other hand, studies suggest that remaining socially active supports brain health and can reduce the risk of ADRD (41).

Given the known rural health disparities in SC (135), further work is required to determine whether a similar pattern of ADRD risk by rural neighborhoods exists.

Understanding the role that various neighborhood characteristics play in contributing to ADRD incidence is vital. Like other studies that have used an ecological approach for identifying high disease burden and relevant predictors to inform policy (63,130), our approach will help develop research knowledge on how neighborhood characteristics may be related to the onset of ADRD. While there is a growing body of evidence regarding the potential links between neighborhood characteristics and cognition (82), little research has focused on how neighborhood environments might influence cognitive disorders, such as ADRD. This study will help fill the gap in the literature by exploring which neighborhood characteristics relate to greater incidence of ADRD in SC and by utilizing a unique source of diagnosed ADRD cases from the SC Alzheimer's Disease Registry. More specifically, the aims of this study are 1) to examine the geographic distribution of ADRD incidence rate and 2) to investigate the ecologic association between census tract characteristics and ADRD incidence from 2010-2014 in SC. We hypothesize the following to be associated with greater ADRD incidence: higher poverty levels, higher proportion of black residents, limited access to healthy food, more rural areas, and higher levels of air pollution. On the other hand, we hypothesize the following to be associated with lower ADRD incidence: higher ranked quality of care.

METHODS

Study Setting

We analyzed data from SC, a state in the southeastern region of the US. Unlike most areas in which neighborhood studies have been conducted -- densely populated

urban areas such as New York City, NY, Chicago, IL, and Seattle, WA -- SC is generally rural. By the US Census' definition, in 2010, South Carolina ranked 17th in terms of the percent of the population living in a rural area: 33.7% rural compared to 28.8% of the overall US population that lived in a rural area (136). SC is also unique to having one of three statewide population-based registries of ADRD in the US, allowing for geographic examination by ADRD incidence rates. Established in 1988, it is the oldest and most comprehensive registry in the country. The Registry is managed by the Office for the Study of Aging housed within the Arnold School of Public Health at the University of South Carolina. Data from the Registry comes from a variety of sources to capture as many diagnoses as possible: inpatient hospitalization, emergency departments, mental health records, Medicaid, memory clinics, chart abstracts, vital records, and sources that contain clinical data, such as long-term care evaluations.

Study Design

An ecological analysis was conducted to examine the relationship between neighborhood characteristics and the rate of ADRD incidence among SC residents ≥50 years old between 2010 and 2014 at the census tract level.

Data Sources

Data for this study came from several publicly available sources. The US Census Topologically Integrated Geographic Encoding and Referencing (TIGER) Line Files (137) were used to collect information on geographic features in the state. The 2010 US Decennial Census Summary File 1 (Census) (138) and the 2010-2014 American Community Survey (ACS) (139) were used to collect census tract level population estimates and other covariates. The 2010 US Department of Agriculture Rural-Urban

Commuting Area (RUCA) (136) was used to measure rurality. To collect other important covariates not available at the census tract level, the 2013 County Health Rankings (CHR) were used (140). ADRD cases were obtained from the SC Alzheimer's Disease Registry (22). As this study uses only secondary deidentified data, it was deemed exempt by the Institutional Review Board at the University of South Carolina (ID = Pro00076582).

Dependent Variable: Tract-Level ADRD Incidence Rate

Only hospital-based sources (e.g., in-patient hospitalization), which make up 60% of the Registry sample, are available at the address level. The remaining sources (e.g., Medicaid) adhere to federal requirements that mandate patient deidentification to avoid release of patients' protected health information. Therefore, incident cases from these non-hospital-based sources are available only at the zip code level, given that there are at least 10 cases per zip code. The Registry provides information on each case, type of ADRD (e.g., diagnostic data based on International Classification of Diseases 9/10 Clinical Modifications codes), source from which records were obtained, location of case (e.g., community or facility), age of diagnosis, sex, and race.

We calculated census tract level ADRD incidence rate per 100,000 people ≥50 years old in SC from 2010-2014. ADRD incident cases among those diagnosed during the study's time frame, and not previously diagnosed from another place, were retrieved from the SC Alzheimer's Disease Registry (n=65,984) (Figure 3.1). We did not differentiate between types of ADRD diagnosis due to poor validity of the individual diagnoses (46). Assignment of incident cases to census tracts was done via two different processes: 1) incident cases from inpatient hospitalization and emergency departments

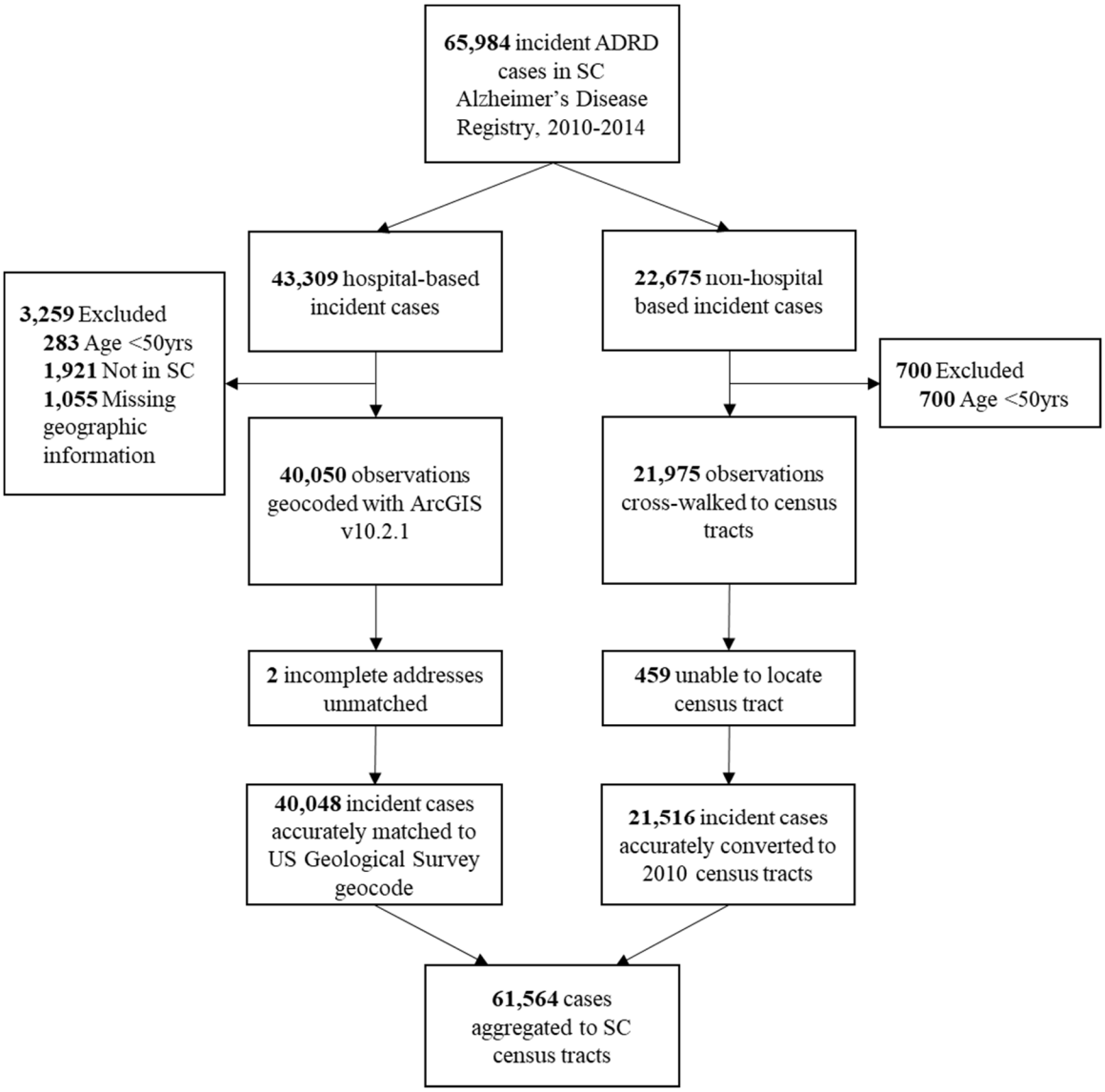

Figure 3.1. Flow Chart of Alzheimer's Disease and Related Dementias Incident Case Selection

included addresses (n=43,309) that were geocoded and assigned their respective census tracts they reside in; 2) non-hospital-based sources, like Medicaid, included zip codes only (n=22,675) that were assigned census tracts using the US Department of Housing and Urban Development (HUD) Crosswalk Files.

Individual ADRD cases were excluded from the analysis based on the following characteristics: cases <50 years old, as this typically is attributed to early-onset ADRD that is greatly associated with a genetic predisposition (n=983; 283 from hospital-based and 700 from non-hospital-based sources); and addresses not located in SC (n=1,921), or that were missing geographic information (i.e. 42 missing addresses, 7 experiencing homelessness, 22 incarcerated, and 984 unverifiable addresses, e.g., PO Box). The remaining 40,050 observations from hospital-based sources were geocoded using ArcGIS Desktop Version 10.2.1 for Windows (Environmental Systems Research Institute, Redlands, CA). A total of 58 addresses were tied (i.e., had more than one assigned location) and re-matched using the "Interactive Rematch Dialogue" feature in ArcGIS. Two addresses were unmatched and removed due to incomplete addresses, leaving 99% of the hospital-based sources' addresses accurately matched to a US Geological Survey geocode with 40,048 incident cases, which were included in subsequent analyses. Next, the geocoded ADRD incident cases were joined to a census tract polygon using the "Spatial Join" tool in ArcGIS.

The remaining 21,975 incident cases from non-hospital-based sources available at the zip code level were cross-walked (i.e. assigned a census tract with the greatest proportion of residents) to 2010 census tracts using HUD's Office of Policy and Development and Research Zip Code Crosswalk Data Files. Each year was cross-walked

from zip code to the 2010 census tract based on the first quarter of the respective zip code's year, except for data from 2010 and 2011, which were cross-walked using the 2012 zip code files, because HUD's 2010 and 2011 cross walk files are for the 2000 census tract geographies. We were unable to locate census tracts for 459 incident cases; therefore, the remaining 21,516 incident cases were successfully cross-walked to census tracts. Combined with incident cases from hospital-based sources, a total of 61,564 incident cases were aggregated to the census tract level.

Estimates of census tract population sizes ≥50 years were obtained from the Census. Fourteen census tracts were removed due to having no population estimates for ≥50 years old. The final sample for analysis included 1,089 census tracts (98.7% of tracts in SC). Incident cases were divided by population estimates to calculate ADRD specific incidence rates.

Independent Variables

The following information came from Census data for SC census tracts: the proportion of population ≥50 years old and the proportion of non-Hispanic black residents, which was divided by ten to represent differences in percentage of residents in 10% increments. Additional information regarding poverty came from ACS data: percent of families below the federal poverty line, which was categorized into tertiles considering recommended standard cut points (141): low (0-9%), medium (9.1-19.9%), and high (20-71%).

Rurality of each census tract was determined using information from the RUCA. Rurality was measured on a 10-point scale. For the purposes of our analysis, we divided census tracts into three rurality categories: 1) large urban (metropolitan area core;

n=635); 2) small urban (metropolitan area high commuting and metropolitan area low commuting; n=241); and 3) rural (micropolitan area core, micropolitan high commuting, micropolitan low commuting, small town core, small town high commuting, small town low commuting, and rural areas; n=213).

The following county-level neighborhood information came from the CHR: quality of care, air pollution, and limited access to healthy food. All variables were ascertained using 2013 CHR data; however, the years that the data was collected from is reflected below. Quality of care rank was defined as preventable hospital stays per 1,000 Medicare enrollees (2010), percent of diabetes patients that receive HbA1c screening (2010), and percent of females that receive mammography screening (2010), as has been used in previous studies (78). Air pollution particulate matter was defined as the average daily measure of fine particulate matter in micrograms per cubic meter and represented using z-scores (2008). Limited access to healthy food, also represented using z-scores, was defined as the percent of population who lives in poverty and more than 1 or 10 miles from a grocery store (2012).

Data Analysis

Age-sex standardized incidence rates were calculated by the direct method for two age groups (50-74, ≥75) specific to females and males, using the 2010 Census US population as the standard population. The overall standardized rate and 95% confidence interval (CI) was calculated using SAS PROC STDRATE, Version 9.3 (SAS Institute, Inc., Cary, NC). The standardized incidence rates were mapped at the census tract level.

To assess the crude relationship between each neighborhood characteristic and ADRD standardized incidence, Spearman rank correlation coefficients and the Kruskal

Wallis Test were computed for continuous and categorical variables, respectively. To analyze the association between neighborhood characteristics and ADRD incidence, a mixed-effect regression model for the Poisson count data was implemented. ADRD counts were the dependent variable and the log of expected cases were the offset. A random intercept with census tracts (Level 1) nested within counties (Level 2) was included.

Counties were used here because there are an adequate number of counties (n=46) to allow for analysis, with the population size in each also being sufficiently large to examine even with low incidence rates. Moreover, counties are a useful unit of analyses because they are used for planning and policy purposes by the SC Department of Health and Environmental Control, who are responsible for the provision of health and community services in the state.

In our multi-level analysis, we considered the following census tract-level covariates: percent of ≥50 years, percent of non-Hispanic black residents, poverty, and rurality. We also considered the following county-level covariates: air pollution, quality of care, and limited access to healthy food as well as a random parameter clustered by county. Initial variable selection was based on known relationships and then variables were removed from the model due to statistical insignificance in our sample defined as $\alpha < 0.05$. Goodness of fit was assessed using the likelihood ratio test. Results obtained from these regression analyses are presented as incidence rate ratios (IRR).

RESULTS

Age-Sex Standardized Incidence Rate

Figure 3.2 displays the ADRD standardized rates per census tract. Overall, we observed ADRD incidence rates geographically distributed across the state with higher rates observed in the Low Country region (Figure A.1). The overall age-sex standardized incidence rate was 4.43% (95% CI: 4.34-4.47) per census tracts from 2010-2014 in SC, resulting in an average annual standardized rate of 0.89%.

Descriptive Statistics

Descriptive statistics of the considered neighborhood characteristics are presented in Table 3.1 as means with standard deviations (SDs) and percentages with numbers for continuous and categorical variables, respectively. Among the 1,089 census tracts in SC considered for our analysis, 557 tracts (51%) had at least one ADRD case.

Nonparametric Tests

Spearman rank correlations between each neighborhood characteristic and ADRD standardized incidence rate are presented in Table 3.2. Although all neighborhood characteristics reached statistical significance at the 0.05 level (except for air pollution and limited access to healthy food), they were weakly correlated with ADRD incidence. The highest correlation coefficient was observed between proportion non-Hispanic black residents and ADRD incidence (r=0.18; p-value = 0.0029).

We also observed statistically significant differences among all poverty levels (H=37.91, p = <.0001) and all rurality levels (H=36.07, p = <.0001) by ADRD standardized incidence rate respectively via a Kruskal Wallis Test.

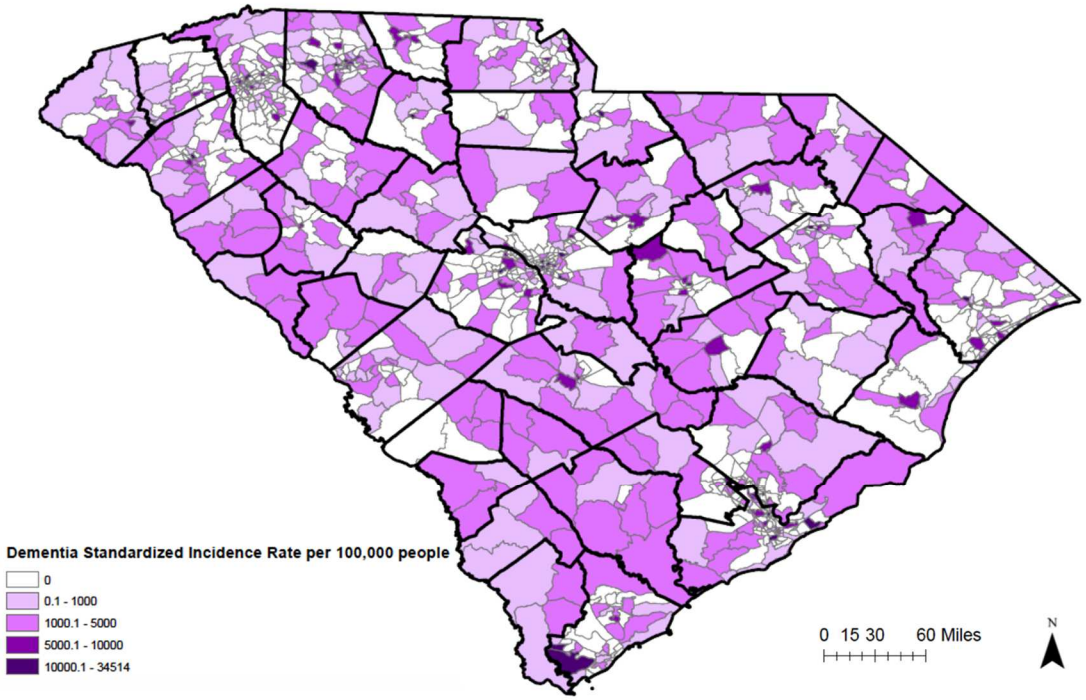

Figure 3.2. Alzheimer's Disease and Related Dementia Standardized Incidence Rate by Census Tract (n=1089), 2010-2014, SC

Table 3.1. Distribution of Neighborhood Characteristics, SC, 2010-2014

Neighborhood Characteristics	Mean (SD) or Percentage (N)
Percent non-Hispanic black	29.23 (23.9)
Quality of Care Rank[a]	14.5 (12.9)
Air Pollution Z-score[b]	0.42 (1.00)
Limited access to healthy food Z-score[c]	0.25 (0.87)
Rurality[d]	
Rural, % (N)	19.52 (213)
Small Urban, % (N)	22.09 (241)
Large Urban, % (N)	58.39 (635)
Poverty[e]	13.6 (10.9)
Low (0-9%), % (N)	33.39 (362)
Medium (9.1-19.9%), % (N)	33.30 (361)
High (≥20%), % (N)	33.30 (361)

[a]Quality of care rank was defined as preventable hospital stays per 1000 Medicare enrollees, percent of diabetes patients that receive HbA1c screening, and percent of females that receive mammography screening and ranged from 1-46.
[b]Air pollution particulate matter was defined as the average daily measure of fine particulate matter in micrograms per cubic meter.
[c]Limited access to healthy food was defined as the percent of population who lives in poverty and more than 1 or 10 miles from a grocery store.
[d]Rurality was measured based on the RUCA (Rural Urban Commuting Area codes). Large urban area was defined as metropolitan area; small urban area was defined as metropolitan area high commuting and metropolitan area low commuting; and rural defined as micropolitan area core, micropolitan high commuting, micropolitan low commuting, small town core, small town high commuting, small town low commuting, and rural areas.
[e]Poverty is defined as the percent of families below the federal poverty line categorized in terciles.

Table 3.2. Spearman Rank Correlations Between Neighborhood Characteristics and ADRD Standardized Incidence Rate in SC Census Tracts, 2010-2014

Neighborhood Characteristic	Correlation	P-value
Percent non-Hispanic black	0.18	0.0029[d]
Quality Care Rank[a]	0.16	<.0001[d]
Air Pollution Z-score[b]	-0.01	0.6737
Limited access to healthy food[c]	-0.05	0.1246

[a]Quality of care rank was defined as preventable hospital stays per 1000 Medicare enrollees, percent of diabetes patients that receive HbA1c screening, and percent of females that receive mammography screening and ranged from 1-46.
[b]Air pollution particulate matter was defined as the average daily measure of fine particulate matter in micrograms per cubic meter.
[c]Limited access to healthy food was defined as the percent of population who lives in poverty and more than 1 or 10 miles from a grocery store.
[d]Correlation is significant at the 0.05 level.
N=1,089 census tracts.

Table 3.3. Poisson Mixed Effects Regression Model, 2010-2014, SC (n=1,089 census tracts)

Variable	Crude IRR (95% CI)	Adjusted IRR[e] (95% CI)
Percent non-Hispanic black	1.00 (0.99-1.01)	1.02 (1.01-1.03)
Quality of Care Rank[a]	1.00 (0.99-1.01)	0.99 (0.98-1.00)
Air Pollution Z-score[b]	1.04 (0.96-1.11)	1.09 (1.02-1.16)
Rurality[c]		
Rural	1.00 (0.97-1.04)	0.91 (0.88-0.95)
Small Urban	0.65 (0.62-0.67)	0.62 (0.59-0.64)
Large Urban	1.0	1.0
Poverty[d]		
High (≥20%)	0.99 (0.97-1.02)	1.17 (1.15-1.20)
Medium (9.1-19.9%)	1.11 (1.09-1.14)	1.15 (1.13-1.17)
Low (0-9%)	1.0	1.0

[a]Quality of care rank was defined as preventable hospital stays per 1000 Medicare enrollees, percent of diabetes patients that receive HbA1c screening, and percent of females that receive mammography screening and ranged from 1-46.
[b]Air pollution particulate matter was defined as the average daily measure of fine particulate matter in micrograms per cubic meter.
[c]Rurality was measured based on the RUCA (Rural Urban Commuting Area codes). Large urban area was defined as metropolitan area; small urban area was defined as metropolitan area high commuting and metropolitan area low commuting; and rural defined as micropolitan area core, micropolitan high commuting, micropolitan low commuting, small town core, small town high commuting, small town low commuting, and rural areas.
[d]Poverty is defined as the percent of families below the federal poverty line.
[e]Model controls for age.

Multivariable Model

Table 3.3 presents unadjusted and adjusted results from the multilevel Poisson model predicting ADRD IRRs per census tract. Limited access to healthy food was dropped from the model because it was not significantly related to ADRD incidence in our sample. We controlled for the following variables in our final model: percentage ≥50 years, percentage non-Hispanic black residents, poverty, rurality, quality of care, and air pollution. Compared to census tracts with low proportion of residents living below the poverty level, tracts with medium and high proportion of residents living in poverty had 15% (IRR= 1.15; 95% CI= 1.13-1.17) and 17% (IRR= 1.17; 95% CI = 1.15-1.20) greater incidence of ADRD, respectively after adjustment. Compared to urban census tracts, we found that rural and small urban tracts had 9% (IRR=0.91; 95% CI = 0.88-0.95) and 38% (IRR=0.62; 95% CI= 0.59-0.64) lower ADRD incidence, after adjustment. For every ten percent increase in percent of non-Hispanic black residents, ADRD incidence rate increased by 2% (IRR=1.02; 95% CI= 1.01-1.03) after adjustment. For every unit increase in levels of air pollution z-scores in the adjusted model, ADRD incidence rate increased by 9% (IRR=1.09; 95% CI= 1.02-1.16).

DISCUSSION

This study examined the geographic patterning of ADRD incidence and ecologically explored the relationship between neighborhood characteristics and ADRD incidence in SC, a state with high ADRD incidence and mortality (46). The overall age-sex standardized incidence rate was similar compared to previous research (37). Our calculated average annual incidence rate (0.88%) is similar to a recent study (0.73%) conducted in Chicago among older adults with AD only (2.1% from 2010-2012; 95% CI

=1.6-2.8) (142). This study also confirmed our hypotheses that higher poverty levels, higher proportion of non-Hispanic black residents, and higher air pollution levels are related to greater ADRD incidence, while greater quality of care is related to lower ADRD incidence although not statistically significant. This study did not support hypothesis that more rural areas are related to greater ADRD incidence; instead, we found more rural areas to be related to lower ADRD incidence. Given the expected projection of ADRD cases in the US (23) coupled with both increasing trends of AD-related mortality (143) and SC ranking the highest mortality rate due to AD (46), prevention efforts of ADRD is warranted.

Results from the multivariable model indicated that the neighborhood environment is associated with ADRD incidence in this sample. Specifically, neighborhood variables related to poor, disadvantaged neighborhoods (e.g., higher poverty levels) were associated with greater ADRD incidence, in the adjusted model. This observation is similar to previous studies that reported greater ADRD incidence (11) or poorer cognitive functioning (29,82) in neighborhoods with greater socioeconomic disadvantage. Previous research has suggested several ways in which neighborhood disadvantage may be related to ADRD incidence. These include greater clustering of environmental toxicants, such as air pollution, pesticides and lead, and through fewer resources and/or lower quality health care (144,145). In support of the hypothesized influence of environmental toxicants, we found that higher air pollution was associated with greater ADRD incidence, comparable to previous findings (146,147). Similarly, we observed that higher quality of care was associated with lower ADRD incidence, although this did not meet statistical significance. Our findings are similar to a previous

study that found greater quality of care (e.g., better resident-to-staff ratio at the county level) was associated with higher late-life well-being (77). Because previous studies note the uneven, spatial distribution of health care resources where physicians tend to concentrate in areas of greater economic wealth (145), we would expect to see greater quality of care statistically associated with lower ADRD. The lack of a statistical significant association between ADRD incidence and quality of care may reflect a lifetime influence of living in areas with greater quality of care that prevent risk of cerebrovascular diseases and other risk factors for ADRD (32) as well as increasing opportunities for diagnosis given the more frequent contact with healthcare providers. Lifespan influence and detection may explain the null findings of living in areas with greater quality of care. It may also reflect the aggregate level of measurement of quality of care in our study, assessed at the county level. Counties are large geographic units with varying degrees of heterogeneity within them; therefore, depending on where one lives within the county, their access to care may differ. Considering the non-restrictive boundaries of counties, it is also likely that people travel between counties, or even across state lines, for care. While providers are available in each county, one's provider might not be within the same county and thus requires people to travel across county boundaries. Use of alternative measures to capture quality of care at a smaller, more meaningful scale, may result in different estimates of association.

Contrary to our original hypothesis, we found that rural census tracts had lower ADRD incidence compared to urban census tracts. One explanation for this finding is detection bias. In other words, fewer health care resources and providers in rural settings (148) may translate to an inability to properly diagnose ADRD, which would then

translate to a lower reported incidence of these conditions in rural census tracts. Most studies have reported both incidence and prevalence of ADRD to be higher in rural compared to urban areas (146,147). For instance, a meta-analysis found greater incidence and prevalence of ADRD in rural areas (13). Another study noted lower AD-related services among community pharmacies in rural compared to urban counties (97). Fewer resources can also influence migration; that is, older adults diagnosed with other comorbid health conditions from age often migrate to urban areas to seek care, yielding more geographic clusters of ADRD prevalence in urban compared to rural areas, as has been noted in past research (96). Thus, our findings could reflect the influence of health and disease on the choice of neighborhood rather than the influence of neighborhoods on cognitive health.

Implications for Research and Practice

The current study adds to a growing body of research investigating the environmental correlates for ADRD incidence. Our study demonstrates the association between neighborhood characteristics and ADRD, namely the influence of poverty on ADRD incidence. The measure of poverty has been recommended to use as the standard for capturing low neighborhood socioeconomic status (141). Hence, our findings are critically important given the known health harms, including ADRD risk, associated with poverty, thus shedding light on policy and programmatic relevance. Because we think that high poverty neighborhoods with fewer resources and services compared to low poverty neighborhoods might increase ADRD risk or lead to cognitive impairment (149), promoting opportunities for social and cognitive stimulation can potentially help lower ADRD prevalence in the future. Specifically, our results indicate the need for more

services catered to areas with higher proportion of older adults, such as senior centers and/or activities offered by local organizations, access to affordable meal programs, and accessible health services including home care. These services are vital to older adults by promoting social support and social cohesion (17,41,72).

Given the concurrent finding that higher proportion of non-Hispanic black residents was associated with greater ADRD risk, this further warrants an examination by race. Because SC has a higher population of black residents (30% compared to the US average of 12%), that black individuals are reported to be at greater risk for ADRD (38,39), and that neighborhoods are spatially patterned by race, it is important to further explore areas with high ADRD incidence by race (Figure A.2-3). Future research can specifically examine the relationship between residential segregation and ADRD risk. The Index of Concentration at the Extremes can be used to measure both racial residential segregation and racialized economic residential segregation, as done in previous studies (130).

Future avenues of research meriting pursuit include 1) replicating this study in other ADRD registries; 2) exploring the use of additional measures to capture other neighborhood dimensions; and 3) designing etiologic studies to test hypotheses about specific pathways by which disadvantaged neighborhoods structure population risk of ADRD. Conducting this research on larger geographic areas may increase the generalizability of these results, as our sample is specific to SC, which has a unique neighborhood context (e.g., predominantly rural) where people may seek treatment outside the state (e.g., edge effect). As our results showed a differential impact according to rurality, researchers in this field should endeavor to develop separate measures on

environmental ADRD risk between urban and rural neighborhoods. Focus on defining, operationalizing, and measuring specific neighborhood features (e.g., local access to services), exposures (e.g., crime), and social processes (e.g., social cohesion) can help us better understand the underlying mechanism by which high poverty is associated with adverse health outcomes, including ADRD incidence. Because ADRD does not have a cure and the social, emotional, economic, and physical cost of these conditions remain significant, research must continue to investigate the role of environmental drivers for ADRD.

Strengths

This study uses a unique data source, the SC Alzheimer's Disease Registry, allowing for population-based statewide research. Using multiple data sources with a history of validity checks (e.g., an algorithm to capture duplicate entries), the Registry is able to capture almost all diagnosed cases of ADRD in SC. This study also drew on diverse sources to include several neighborhood measures related to access to health promoting resources and demonstrated how environmental risk may come from multiple neighborhood characteristics that interact with each other. Specifically, we employed a recommended measure to capture neighborhood socioeconomic status (percentage of families living below federal poverty threshold within a census tract) that has been noted to be the most apt for monitoring socioeconomic inequalities in health (67). Furthermore, the use of an ecologic study design identifies areas of high disease burden in need of resources, which are more effectively intervened on through policies and public health initiatives.

Limitations

A limitation of our study concerns the assignment method of incident cases to census tracts, and specifically the fact that non-hospital-based sources were only available at the zip code level due to the need to protect personally identifiable health information. Since zip codes are designed for mailing purposes, they frequently change and thus greatly overlap with census tracts, which reduces the accuracy of the crosswalk procedure (150). However, this was the only geographic information available from these data sources. Furthermore, considering the passive nature of the Registry, it is possible that those with low income, who have limited access to care, and/or that live in a rural area may not visit a doctor until they are very sick or not visit at all, and thus might not be captured by the Registry. Similarly, the age of diagnosis reported in the Registry may be inaccurate because often people are diagnosed long after disease onset, as the AD symptoms may remain subclinical for decades (151). Also, use of measures from ACS like poverty can be a limitation because data are based on probability samples, for which sampling frames change annually. To mitigate this problem, we used five-year data estimates. Lack of a stratified analysis by race/ethnicity is another limitation to note. Because there may be different effects of neighborhoods by race, future work to analyze this relationship by race is warranted. A final limitation to note includes factors inherent to the ecologic study design, including the inability to directly determine whether differences across areas are due to characteristics of the area themselves or to differences between the types of individuals living in different areas. As such, we cannot evaluate the role of individual-level factors, like socioeconomic status (152), as confounders or mediators, because individual-level variables were not available. Also, our study is

interested in identifying areas of high disease burden and not necessarily focused on disentangling the effects of living environments on health from influence of individual level risk factors.

CONCLUSION

We found that neighborhood characteristics are associated with ADRD incidence. This emphasizes the need for a macro-level approach by allocating age-related services to areas with high proportions of older adults and disadvantaged neighborhoods, which can improve older adults' cognitive and physical health. While not in alignment with our hypothesis, another interesting finding was the association between rural neighborhoods and greater ADRD incidence. Given that older adults primarily make up rural areas, understanding the role of rurality is essential. Understanding how ADRD is distributed in the population by neighborhoods and locations informs both allocation of public health resources and direction of potential public policy initiatives. Future research can determine whether the causes of the observed variation can be identified, and how to highlight modifiable environmental risk factors, to work towards making ADRD a preventable disease.

CHAPTER 4:

AIM 2: ASSOCIATION BETWEEN NEIGHBORHOOD CHARACTERISTICS AND NEUROPSYCHIATRIC SYMPTOMS AMONG ALZHEIMER'S DISEASE COMMUNITY-DWELLING OLDER ADULTS

INTRODUCTION

Alzheimer's disease (AD) is a neurodegenerative, debilitating disease that is consistently ranked as the sixth leading cause of death in the United States (123,153). With no cure for AD, limited possibilities for its treatment, and a growing older adult population, the prevalence of AD is expected to substantially increase over the next forty years (124). As AD is one of the costliest conditions to society, with an estimated total direct medical cost of $259 billion in 2017, half of which was covered by Medicare, the projected increase in AD prevalence will further burden our healthcare systems (1). In addition to the excessive financial cost, AD exacts a cognitive, physical, and socioemotional toll on its sufferers and their caregivers. The burden impacts the caregiver's ability to take care of both the person with AD and themselves. Hence, delaying AD progression is beneficial to both those experiencing AD and their caregivers. Furthermore, delaying progression to late-stage AD can reduce the negative impact on quality of life and well-being of people with AD (126) and can potentially increase meaningful time spent with those afflicted by the condition (154). As such,

novel factors influencing the progression and severity of AD at the macro-level must be identified and addressed in order to better meet needs of people with AD.

Research suggests that there are several individual-level factors related to greater AD severity, including cognitive decline, physical impairment, younger age of onset, higher education, and extrapyramidal signs (e.g. continuous spasms and muscle contractions) (6). Neuropsychiatric symptoms (NPS) of AD are also greatly associated with AD severity (154). NPS are non-cognitive symptoms that are present during AD and persist throughout disease progression (42). Common NPS include apathy, agitation, irritability, delusions, and hallucinations. Clinical studies estimate that 70-90% of AD patients experience at least one NPS (42). Literature has also identified certain NPS associated with greater AD severity, particularly highlighting apathy (154) and agitation (155). Apathy is consistently the most frequently reported symptom among those experiencing AD (6). The prevalence of agitation among community-dwelling older adults with a severe clinical profile of AD is about 60% (156). Additionally, NPS in general have recently emerged as predictors of disability, faster cognitive decline, and greater mortality (6). For example, apathy has been found to be associated with increased risk of mortality, as well as more severe cognitive and physical decline (44,157). Moreover, NPS are cited to be one of the most challenging behavioral symptoms caregivers deal with (4). NPS increase caregivers' risk of poor health (45) and consequently their caretaking abilities.

The consistent association between NPS and poor health outcomes has led to the widespread acknowledgement of NPS as a priority for research in neurodegenerative diseases including AD (156). Although the biological basis of NPS is poorly understood

(158,159), NPS are hypothesized to be influenced by psychological, social, and environmental factors (6). For example, chronic psychological stress, limited social engagement and mental stimulation, and exposure to environmental toxicants and stressors, such as air pollution, pesticides, and noise, are hypothesized to influence NPS (8). Because previous literature has demonstrated the role of these factors with poor cognition and risk of AD (3,59), similar factors may contribute to NPS and AD severity. Yet, few studies have investigated factors correlated with NPS, especially in terms of neighborhood environment characteristics (155). Evaluating whether different neighborhood-level characteristics are associated with NPS can help understand the potential mechanisms by which neighborhood environments influence AD severity. This approach, the crux of our work, is one advocated for chronic conditions, like AD, in which primary prevention has failed (126).

Disadvantaged, rural, and weak social cohesive neighborhoods are theorized to influence NPS by increasing stress levels, impeding mental stimulation, and lacking opportunities for social engagement (19). Neighborhood environments are also theorized to have a contextual effect, beyond individual-level risk factors, on NPS by determining access to resources (e.g., senior centers), health care services, and transportation (68). While limited neighborhood resources and insufficient healthcare services are hypothesized to exacerbate NPS, areas with high neighborhood resources and sufficient healthcare services may alleviate these symptoms (71). Disadvantaged neighborhoods are also characterized by more environmental toxicants and stressors, such as air pollution, pesticides, and excessive noise (160), which are theorized to influence NPS (161,162). This proposed NPS-environment relationship among those with AD has been

demonstrated in outcomes related to AD severity, such as poor cognition, cognitive decline, and physical impairment (163). Research suggests, for instance, that environment may contribute to exposure to stressful factors (e.g., noise), which may lead to NPS among individuals with AD, such as agitation (164,165).

In rural neighborhoods, even greater distances to resources and healthcare, coupled with limited transportation methods, may exacerbate NPS. Moreover, people living in rural areas, compared to urban areas, experience greater social isolation, which is speculated to indirectly speed NPS development (94). The growing need to understand the burden of those with AD in rural areas not only due to limited resources but also greater social isolation makes it imperative to understand the impact of rurality on AD (166). Further, caregivers, especially those living in rural areas, are also thought to experience social exclusion (166), which can indirectly impact NPS among those with AD via their caretaking abilities. Given that social isolation and fewer opportunities for social engagement are hypothesized to increase risk of NPS, weaker social cohesion may exacerbate NPS. High neighborhood social cohesion provides opportunities for social engagement, and thus is hypothesized to slow NPS development via cognitive stimulation and social support (27).

Despite the potential links between neighborhood characteristics and NPS, the association between them, to our knowledge, has not been evaluated by previous work. In accordance with the environmental stress concept argued by Wainaina et al. (3), this study aims to understand AD from a contextual perspective rather than an individualized one. Understanding how the neighborhood environment influences progression and severity of AD is important because public health and other practitioners can intervene on

the environmental level (i.e., using environmentally-based interventions, for instance) to improve the health of people experiencing AD. Such a macro-level approach to interventions also have potential to positively influence more people's health compared to individual-level interventions (31). The aim of this study is to estimate the association between neighborhood characteristics (median household income, rurality, and residential instability, defined as the percent of residents that moved the past year) and NPS among community-dwelling older adults with AD living with a caregiver in South Carolina (SC). We hypothesize that those with AD living in lower income neighborhoods, more rural areas, and higher percent of residents that moved the past year will be associated with greater NPS.

METHODS

Study Setting

Data generated from participants for this study were from SC. SC has markedly higher racial and economic health disparities compared to other states (167). In 2018, SC ranked the highest state with AD-associated mortality rate in the US (168). The median household income for SC ($48,781) is below the national average ($59,039) (169). SC's population is also more rural than the national average. By the US Census definition, in 2010, SC ranked 17th in the percent of the population living in a rural area at 33.7%, compared to 28.8% of the US population living in a rural area (169).

Study Design

A cross-sectional study was conducted to estimate the association between neighborhood characteristics (median household income, rurality, and residential instability) and NPS (measured via the Neuropsychiatric Inventory Questionnaire, NPI-

Q) (170) among community-dwelling older adults with AD living with a caregiver in 2010 in SC.

Data Sources

Participant data for this study came from a subset of data collected from the SC Alzheimer's Disease Registry (28). The Registry is a comprehensive statewide registry of diagnosed cases of Alzheimer's disease and other related dementias compiled from inpatient hospitalizations, mental health records, emergency departments, Medicaid, memory clinics, chart abstracts, vital records, long-term care evaluations, and other sources. Data from the Registry subsample were collected in 2010 by trained interviewers who asked caregivers by phone about those with AD for whom they cared. Those with AD were diagnosed between 2005 and 2010. All participants were enrolled in a Medicaid waiver program and eligible for nursing home level of care (e.g., can receive additional care services while still residing within the community). Most of the caregivers were family members (e.g., children) of those they cared for and reported feeling a duty or responsibility to care for the person with AD. Further information regarding study details and eligibility criteria have been reported elsewhere (28).

Neighborhood characteristics at the census tract level data came from two secondary sources available online: the 2006-2010 American Community Survey (ACS) (171), and the 2010 US Department of Agriculture Rural-Urban Commuting Area (RUCA) codes (172). Shapefiles and geographic features for SC data came from the US Census Topologically Integrated Geographic Encoding and Referencing (TIGER) Line Files (137). This study was deemed exempt by the Institutional Review Board at the University of South Carolina (ID = Pro00076582).

Dependent Variable: Neuropsychiatric Symptoms

NPS were measured using the NPI-Q, a shortened version of the original questionnaire. The NPI-Q consists of 12 domains: delusions; hallucinations; agitation/aggression; depression/dysphoria; anxiety; elation/euphoria; apathy/indifference; disinhibition; irritability/lability; motor disturbance; sleep and nighttime behavior disorders; and appetite/eating changes. Within each of these 12 domains, a respondent caregiver is asked if these characteristics are present or absent. For the characteristics that are present, the caregiver is asked to rate both the severity of the symptoms on a 3-point scale (1=mild, 2=moderate, and 3=severe), and the frequency of the symptoms on a 4-point scale (1=occasionally, 2=often, 3=frequently, and 4=very frequently). Multiplying the severity and frequency scores in each domain produces a domain score. The domain scores, when summed across all 12 categories, yield a composite NPS score. Each domain score ranges from 0-12, and, when the composite scores are summed for total NPI-Q, they range from 0-144.

Study Sample

Among the 283 community-dwelling older adults with AD from the Registry subsample, 224 cohabitated with their caregiver; thus, their addresses were available. Twelve cases were removed because we were unable to verify participants' actual place of residence (e.g., PO Box). The remaining 212 observations were geocoded using ArcGIS Desktop Version 10.2.2 for Windows (Environmental Systems Research Institute, Redlands, CA). Only one address was tied (i.e. had more than one assigned location with the same best match score) and re-matched using the "Interactive Rematch Dialogue" feature in ArcGIS. A sensitivity analysis was conducted to compare those who

were excluded and those who were included in terms of age, sex, race, and NPI (Table B.1).

Independent Variables

Participant demographic information was obtained from the Registry subsample including sex (male or female), current age, race/ethnicity (non-Hispanic black or other), and caregiver education (>8th grade, 8th-12th grade, High school or more, and unknown).

The neighborhood was defined as ½-mile buffer distance around each participants' geocoded address. Euclidean (or radial) buffers were created by drawing a straight line ½-mile from a home address creating a circle. Because the individual residence-based buffers tend to overlap multiple census tracts, neighborhood characteristics were calculated as the weighted average of intersecting census tracts within the buffer. We chose this smaller buffer size, compared to standard sizes in the field (e.g., 1, 3 and 5-mile), with the consideration that those with AD are not as mobile and do not travel far away from their home. This same buffer size has also been previously used in research among older adults (65). Because of the dependent varying neighborhood definitions, a sensitivity analysis was conducted to define neighborhood at the 1-mile buffer distance. Participant neighborhood characteristics defined as the weighted average within the ½-mile buffer distance were the following: median household income and residential instability. Median household income (median income dollars per family) was categorized into tertiles: low (<$30,500), medium ($30,500-40,000), and high (>$40,000). Residential instability was defined as the percent who moved the past year. Both neighborhood income and residential instability were obtained from the ACS.

Participant rurality was based on the census tract in which the geocoded addresses resided. We defined rurality using information from the RUCA. RUCA measures rurality on a 10-point scale ranging from metropolitan to rural. For the purposes of our analysis, we divided census tracts into three rurality categories: 1) large urban (metropolitan area core; n=105), 2) small urban (metropolitan area high commuting and metropolitan area low commuting; n=41), and 3) rural (micropolitan area core, micropolitan high commuting, micropolitan low commuting, small town core, small town high commuting, small town low commuting, and rural areas; n=66).

Data Analysis

Descriptive statistics were computed; categorical variables were presented as percentages with numbers, and continuous variables were presented as means with standard deviations (SDs). To estimate associations between demographic and neighborhood characteristics and total NPI score, we conducted a negative binomial regression. Because empirical evidence shows that specific NPS are related to greater AD severity, we also conducted a negative binomial regression between the considered covariates and apathy, agitation, and irritability, separately (Tables B.2-B.4). The following covariates were considered for the model: patient age, sex, race/ethnicity, caregiver education, neighborhood income, residential instability, and rurality. Results obtained from these regression analyses are presented as rate ratios (RR), and diagnostics were assessed using the Pearson chi-square test of deviance. No offset parameter was included because the NPI-Q asked about frequency and severity of NPS regarding the past month. There were no noted significant differences between the models using different neighborhood definitions (½- versus 1-mile), and, therefore, the ½-mile buffer

distance is the only one reported. The significance level was set at 0.05. All analyses were completed using SAS software, Version 9.3 for Windows (SAS Institute, Cary, NC).

RESULTS

The study population consisted of 212 community-dwelling older adults with AD living with a caregiver, who were diagnosed between 2005 and 2010. The mean age was 82.42 years, the female: male ratio was 2.5:1, and over half of the study population were non-Hispanic black (55.19%) (Table 4.1). Most participants lived in large urban neighborhoods (49.53%) and lived in average income neighborhoods of $37,485.

Table 4.2 summarizes the mean of total NPI score and each of the 12 domains. The overall total NPI score had a mean of 26.33 (range = 0-95; S.D.=22.35). Domains with the highest means were agitation, irritability, apathy, and motor disturbances. The lowest domain observed mean was euphoria.

Multivariable Model

Table 4.3 presents both unadjusted and adjusted rate ratios (RR) modeling the average scores of total NPI score. The following covariates were adjusted for in the model: AD patient age, sex, race, caregiver education, neighborhood median household income, rurality, and residential instability. We estimated those who live in small urban and rural neighborhoods have 31% (RR=0.69; 95% CI = 0.48-0.98) and 36% (RR=0.64; 95% CI= 0.45-0.90) on average lower NPI scores, respectively, compared to those who live in urban neighborhoods, after adjustment. We estimated those who live in low income neighborhoods (defined as <$30,500) and those who live in medium income neighborhoods (defined as $30,500-40,000) have 1.53 (95% CI= 1.06-2.23) and 1.21

Table 4.1. Demographics and Neighborhood Variables of Community-Dwelling Older Adults with Alzheimer's Disease Living with a Caregiver, 2010, SC (n=212)

Demographics	**Percentage (N)**
Age, mean (S.D.)	82.42 (8.72)
Sex	
Male	27.36 (58)
Female	72.64 (154)
Race/ethnicity	
Non-Hispanic black	58.49 (124)
Other[a]	41.51 (88)
Caregiver Education	
<8th grade	35.38 (75)
8th – 12th grade	25.00 (53)
≥High School[b]	31.33 (66)
Unknown/Refused	8.49 (18)
Neighborhood Variables	**Percentage (N)**
Rurality[c]	
Large Urban	49.53 (105)
Small Urban	19.34 (41)
Rural	31.13 (66)
Median household income, mean (S.D.)	$37,485.21 ($12,867.81)
High (>$40,000)	33.49 (71)
Medium ($30,500-40,000)	34.43 (73)
Low (<$30,500)	32.08 (68)
Residential instability[d], mean (S.D.)	3.89 (2.14)

[a]Other race/ethnicity included non-Hispanic white (n=87), Hispanic (n=1), and Asian (n=1).
[b]Caregiver education high school and more included those who completed the GED (n=46), some college (n=15), and graduated college (n=5).
[c]Rurality was measured based on the RUCA (Rural Urban Commuting Area codes) where large urban was defined as metropolitan area care; small urban was defined as metropolitan area high commuting and metropolitan area low commuting; and rural was defined as micropolitan area core, micropolitan high commuting, micropolitan low commuting, small town core, small town high commuting, small town low commuting, and rural areas.
[d]Residential instability was defined as the percent of residents that moved the past year.

Table 4.2. Mean Scores of NPI-Q[a] Domains in Community-Dwelling Older Adults with Alzheimer's Disease Living with a Caregiver, 2010, SC (n=212)

NPI Domain	**Mean (S.D.)**
NPI total score	26.33 (22.35)
Delusions	1.8 (3.14)
Hallucinations	1.95 (3.07)
Agitation/aggression	3.15 (3.59)
Depression/dysphoria	2.30 (3.52)
Anxiety	1.72 (3.06)
Euphoria/elation	0.77 (1.77)
Apathy	2.83 (3.75)
Disinhibition	1.38 (2.71)
Irritability	2.88 (3.74)
Motor disturbances	2.83 (3.79)
Sleep and nighttime disturbances	2.73 (3.88)
Appetite/eating change	1.95 (3.31)

[a]NPI-Q is the Neuropsychiatric Inventory Questionnaire that assesses neuropsychiatric symptoms.

Table 4.3. Unadjusted and Adjusted Multivariable Negative Binomial Regression Analysis of Neighborhood Characteristics Associated with Total Neuropsychiatric Symptoms Score, 2010, SC (n=212)

Variable	Unadjusted RR (95% CI)	Adjusted[c] RR (95% CI)
Rurality[a]		
Rural	0.81 (0.60-1.08)	0.64 (0.45-0.90)**
Small Urban	0.78 (0.55-1.10)	0.69 (0.48–0.98)*
Large Urban	1.00[d]	1.00[d]
Median household income		
Low (<$30,500)	1.13 (0.82-1.55)	1.53 (1.06-2.23)*
Medium ($30,500-40)	0.98 (0.72-1.34)	1.21 (0.86-1.69)
High (>$40,000)	1.00[d]	1.00[d]
Residential instability[b]	0.94 (0.88-1.00)	0.92 (0.86–1.00)*

[a]Rurality was measured based on the RUCA (Rural Urban Commuting Area codes) where large urban was defined as metropolitan area care; small urban was defined as metropolitan area high commuting and metropolitan area low commuting; and rural was defined as micropolitan area core, micropolitan high commuting, micropolitan low commuting, small town core, small town high commuting, small town low commuting, and rural areas.
[b]Residential instability was defined as the percent who moved the past year.
[c]Model was adjusted for individual AD patient age, sex, race/ethnicity, and caregiver education.
[d]Reference category.
*p<.05; **p<.01

times (95% CI = 0.86-1.69), respectively, as high an NPI score as those who live in high income neighborhoods (defined as >$40,000), after adjustment. Our estimates suggest that a one percent increase in the proportion of residents who moved the past year results in an 8% decrease (RR=0.92; 95% CI= 0.86-1.00) in the average NPI score after adjustment but failed to reach statistical significance.

DISCUSSION

This study estimated the association between neighborhood characteristics and NPS among community-dwelling older adults with AD living with a caregiver. This study found evidence to support the hypothesis that those with AD living in low income neighborhoods experienced greater NPS and refuted the hypothesis that residing in rural neighborhoods is associated with greater NPS. However, we did not find evidence in support of the hypothesis that those with greater average NPS lived in residential instable areas.

While a myriad of studies have evaluated individual-level factors associated with NPS (6), few studies have evaluated factors among those experiencing AD. Therefore, our study replicates and extends prior work. Specifically, we observed a mean NPS score of 26.33 (S.D. = 22.35), similar to average scores found in previous studies of community-dwelling older adults with AD (173,174). Yet the participant sample in our study does have a slightly higher NPS score compared to others. In particular, our observed mean is higher compared to the Cache County Dementia Progression Study, based in Utah, that reported a mean of 8.9 (S.D. = 14.30) among 214 AD patients (175), and the ALSOVA study based in Finland that reported a mean of 8.89 (S.D. = 9.69) among 236 very mild and mild AD patients (159). Given the higher AD rates in SC, as

well as having the highest AD-related mortality rate in 2018 (168), this observation was not surprising. Further, the observation was expected since our sample included those eligible for nursing home level of care, where institutionalization is associated with greater NPS (176).

Among our study's main findings, those living in low income neighborhoods (defined as <$35,000) experienced significantly greater NPS compared to those living in high income neighborhoods (defined as >$40,000), after adjusting for individual AD age, sex, race, and caregiver education as well as rurality and residential instability, which is in line with previous literature (29). A similar study, focusing on dementia incidence, also found that those living in socioeconomically disadvantaged neighborhoods were at greater risk for dementia, independent of age, sex, and individual-level education (11). Previous studies of cognitively healthy individuals found similar results regarding the relationship between greater neighborhood disadvantage and greater physical impairment or cognitive decline, two factors also associated with AD severity (70,131,163,177,178). Even when using various measures to capture disadvantaged neighborhoods, similar results of greater neighborhood disadvantage and greater factors associated with AD severity were observed. For example, one study defined economic disadvantage using five measures (e.g., poverty for total population and older adults, housing units without a vehicle, unemployment, and public assistance) (163); while, another study defined neighborhood problems using six measures (e.g., crime, lighting at night, traffic, excessive noise, trash, and public transportation access) (177).

The finding that those living in rural neighborhoods experienced greater NPS compared to those living in urban neighborhoods did not align with our hypothesis. Rural

neighborhoods are characterized by fewer resources, less access to care, and greater social isolation, which have potential to increase NPS and thus AD progression (94). Nonetheless, because rural neighborhoods have less environmental stressors compared to urban neighborhoods, it is possible that the quiet, serene, and naturalistic settings found in rural neighborhoods are a potential explanation to why we observed lower NPS among those living in rural compared to urban neighborhoods (179). Some studies have found that stressors common in urban areas, such as excessive noise, crime, and incivilities, to be associated with greater dementia, cardiovascular health, and stroke (161) and may be associated with NPS, especially specific symptoms like agitation (36). Although there is no evidence to support this idea among those with AD, some researchers suggest that those with AD may be more sensitive to these stressors (180). Because people with AD have progressive difficulty processing and responding to environmental stimuli, excessive noise can lower the biological stress threshold and increase potential for higher levels of frustration (180). Furthermore, rural neighborhoods have less traffic and street integration (e.g. less turns required to be made from a street segment to reach all other street segments in a defined area) compared to urban neighborhoods, which can make rural areas easier to navigate among those with AD and thus potentially be associated with lower NPS. Watts et al. (21) found that high neighborhood integration (a measure of number of turns required to travel between two points) was associated with a greater decline in attention over a two-year period among those experiencing mild AD (21). There is greater cognitive complexity required to navigate a neighborhood, which can discourage older adults with AD from venturing and walking. In fact, Brorsson et al. (81) found that moving around in a complex and dynamic environment is exhausting for

people with dementia and cognitive limitations. As walking and physical activity in general are proposed methods to delay AD progression (33), while domestic confinement increases disease severity (23), it is possible that rural neighborhoods, with their open and green spaces, allow for those with AD to interact more with their neighborhood environment. Another potential explanation for these findings is that those with greater NPS and experiencing severe AD tend to gravitate to urban neighborhoods because those places have more resources to help caregivers deal with troublesome behavioral and psychiatric issues. Given the average diagnosis period is somewhat recent for our sample (mid-point of 2007), this is an unlikely explanation.

The null findings regarding residential instability and NPS score differ from the literature among children and older adults. A longitudinal study in the UK found greater neighborhood social fragmentation (comprised of four measures including percent of people in a household who moved the last year) at birth to be associated with more negative symptoms, like apathy, in adolescence (OR= 1.43; 95% CI: 1.06-1.85) after individual and maternal level adjustment (181). Furthermore, Beard et al. (70) found residential instability to be associated with higher prevalence of physical disability, a factor associated with AD severity like NPS. In a similar manner, Nguyen et al. (182), found that adults ≥50 years old who lived in neighborhoods with high social cohesion (measured via self-report of feelings of trust, feeling part of the area, feeling that people are friendly or would help them if they were in trouble) experienced lower incidence of limitations in instrumental activities of daily living and activities of daily living after eight years. Studies suggest that even in low-income neighborhoods that are limited in resources, social networks supplement and address the ongoing needs of those

experiencing poor health outcomes, including AD (183). So that, neighborhoods with limited resources, yet high social cohesion, can offer informal assistance from neighbors, creating an indispensable phenomenon by which neighborhoods can offer more support to caregivers (184). Perhaps, our null findings reflect the notion that those with NPS who move to these neighborhoods matter more than the residential instability of the neighborhood having an impact on NPS. Further, our sample consists of those who are eligible for nursing home level of care, where the hinderance of social incohesive neighborhoods may be unrelated to exacerbating NPS. Another potential explanation includes the little variability in percentage of residents that moved the past year (range = 0.6-11.68) that may be too small to capture differences in residential instable areas that might be associated with NPS, especially considering the small neighborhood definition. More commonly, studies used percentages of residents that lived in the same house the past five years to capture stability (70,105); however, this variable was not available in the ACS for our study's timeframe.

Implications and Future Research

The current research adds knowledge regarding the determinants of NPS among community-dwelling older adults with AD, a lacking area of research (185). Because we observed those with AD living in low median household income neighborhoods experienced greater NPS, future research can assess if this relationship is specifically due to lower access to care, traffic, air pollution, pesticide exposure, or other potential mechanisms. By examining the role of additional neighborhood characteristics, future research can focus on the explicit pathways between neighborhood environments and NPS. Identifying neighborhood environments with or at risk of high NPS is important to

delay the progression or severity of AD. NPS are among the most complex, stressful, and costly aspects of care, and they lead to a myriad of poor patient health outcomes, including excess morbidity, mortality, and early placement in nursing homes (4). This way, policy can be driven towards supporting dementia-friendly neighborhoods that will help bring about a society where people with AD and other forms of dementia can continue to engage in everyday activities (186).

NPS are strongly associated with stress and depression in caregivers, as well as with reduced income from employment and lower quality of life (4). Because our sample population of community-dwelling older adults with AD was limited to those who lived with caregivers, a living situation which may impact both NPS and AD severity, future research should examine the association between neighborhood environments and AD severity among community-dwelling older adults who do not live with a caregiver.

Strengths

This study used the NPI-Q, which is a highly validated and reliable questionnaire (187). The merits of the NPI-Q include being comprehensive, avoiding symptom overlap, and easy to use (188). Cummings, the designer of the questionnaire, intended for caregivers to answer the questionnaire, as they are the best person to complete and report behaviors based on the rationale that those with AD are often unable to recall or describe their symptoms (189). Given the gaps presented in NPI distribution, use of parametric methods in analysis is cautioned against (188,190). Instead, it is recommended to employ nonparametric statistics when assessing NPI (190). As most studies treat NPI as normally distributed when it is not, this study, which accounted for the non-normal distribution of NPI scores, can also serve as an example of how to model the natural logarithm of

average number of NPS. Another strength of our work that is worthy of note is the definition of the study participant's neighborhood at a small, spatial scale, given that those with AD are less likely to interact with their environment compared to healthy older adults. This same neighborhood definition has also been previously used (65). Neighborhood income and residential instability, although defined using administrative data, were not defined at the administrative boundary level (e.g. census tracts) but instead at the buffer zone; however, rurality was only available at the census tract level.

Limitations

Our cross-sectional study only provides a snapshot of the relationship between neighborhood characteristics and NPS. Because we did not have any geographic data on whether those with AD has moved since their diagnosis, we were unable to assess how changes in neighborhood environments may impact NPS. Those with AD most likely moved as they were currently living with a caregiver during the time of data collection. Moving after an AD diagnosis is common, especially to areas with healthcare services in order to access such resources. Yet, because the NPI-Q asks about symptoms over the past month, this limits our results being heavily impacted by changes in the neighborhood environment since the timeframe queried is so limited. Further, studies show how NPS persist throughout disease progression (4,44). Another limitation is that there may be selection bias regarding which caregivers chose to participate in the study, in that caregivers with a recipient with greater AD severity might be less likely to respond as they are providing continuous care and do not have time for an hour long interview. Given no data regarding non-response, we were unable to conduct a sub-analysis to see how this impacts our study; however, the initial response rate from the original collected

data was high (72%) (28). Similarly, our sample consists of those enrolled in a Medicaid waiver program, which can limit the generalizability of the results to those of low income. Finally, a fourth limitation to note is lack of individual-level variables, such as individual socioeconomic status (SES), that can potentially mediate the relationship between low income neighborhoods and NPS. Because low income neighborhoods can operate as a compositional variable via proxy for individual-level SES, low income neighborhoods expose individuals to a cluster of risk factors (e.g., unemployment) resulting in increased exposure to stressors and decreased social and physical resources (88). Although individual income and education was not available in our dataset to explore this relationship further, we used caregiver education level in our model, which has been previously shown to be similar to the recipients' education level (191) or slightly higher than the recipients' education level (192,193). For example, one study reported the average of total years of education to be slightly higher among caregivers compared to care recipients (15.4 vs 13.1 years) (192).

CONCLUSION

Our study concerns an important area of research, considering the lack of effective treatments for Alzheimer's disease (AD), and the worldwide projections that this disease is only expected to increase and worsen in ensuing decades. Neuropsychiatric symptoms (NPS) is greatly associated with AD progression and severity. In cases where NPS (e.g. apathy) persist, the increased risk for institutionalization, comorbidities, and mortality occurs (6). Overall, we observed that those living in low income and urban neighborhoods had greater severity of NPS. This study supports an approach to identify neighborhood environment characteristics that influence NPS and AD severity in order to

offer targets for intervention that can slow or diminish AD-associated morbidity. Because the underlying biological mechanisms of NPS are still unknown, there is need for more research to uncover the mechanisms between neighborhood environments and NPS at a macro scale. This study provides insight on the role of the contextual environment and neighborhood characteristics as one avenue to combat AD. As there is significant, yet limited, progress in the pharmaceutical industry, we encourage researchers to look for more viable, cost-effective solutions to fill in the gap for needed treatment (194).

CHAPTER 5:

AIM 3: CAREGIVERS CO-HABITING WITH CARE RECIPIENTS WITH ALZHEIMER'S DISEASE: AN EXAMINATION OF THE RELATIONSHIP BETWEEN NEIGHBORHOOD CHARACTERISTICS AND CAREGIVER MENTAL HEALTH

INTRODUCTION

There are an estimated 15 million people who provide unpaid care for those with Alzheimer's disease (AD) and other forms of dementia (1). AD caregivers, hereafter 'caregivers', bear substantial physical, mental, and financial burdens as they assist with multiple activities of daily living (ADL, e.g., bathing) and instrumental activities of daily living (IADL, e.g., paying bills) as well as provide emotional support (1). Most research on the influence of caregiving on caregiver health has examined individual factors that have an impact on poor caregiver mental and physical health outcomes (5). Yet, little research has focused on the role of neighborhood contextual factors where caregivers reside (10) and how they might influence the ability of caregivers to provide care.

Each person with AD is estimated to have up to four caregivers (46). Caregivers tend to be family members, usually a spouse or daughter, and are disproportionately female (1). In fact, approximately two-thirds of caregivers are women (1,47). Caregivers also are likely to have children of their own who need care, so that they frequently take on several different and, sometimes, conflicting care roles, also known as "sandwich"

caregivers (46). This can place an even greater burden on caregivers as they usually spend long durations providing care (195), complete many ADL tasks (196), and manage difficult behavioral problems (1). Neuropsychiatric symptoms (NPS) (e.g. apathy, delusions, and hallucinations) of AD patients are especially challenging for caregivers, especially when the care recipient is in the later stages of AD experiencing losses in judgment, orientation, and the ability to communicate effectively (1). Caregivers often cover multiple expenses, spending an estimated $5,155 out-of-pocket on average per year (2).

Given the financial and emotional demands associated with caregiving, caregivers often experience negative health problems (47,50,51). Approximately 30 to 40% of caregivers suffer from depression, compared to 5 to 17% of non-caregivers of similar ages (1). Similarly, the prevalence of depression is higher among AD caregivers compared to other types of caregivers (53) given the strong association between NPS in people experiencing AD and depression in caregivers (108). Increased depressive symptoms among caregivers have been linked to greater use of prescription medications (e.g., psychotropic drugs) relative to non-caregivers (197).

Given these realities, the impact of AD on caregivers is often measured as caregiver burden (108), defined as the "extent to which caregivers perceive that caregiving has had an adverse effect on their emotional, social, financial, physical, and spiritual functioning" (198). Based on the 2015 Burden of Care Index, AD caregivers were classified as experiencing higher burden compared to other types of caregivers (195). The anticipated increase in the aging population coupled with the growing

prevalence of AD in the next forty years will lead to a greater reliance on caregivers (49); hence, it is vital to understand the risk factors that impact caregiver health.

Most studies have identified person-level caregiver factors that influence mental health, which include older age, female sex, employed, spouse caregivers, sandwich caregivers, and co-habitation with the person experiencing AD, also known as the care recipient (5). Additionally, the research has identified factors among the care recipient that influence caregiver mental health. One of the most commonly cited problematic behavioral symptoms caregivers manage while taking care of someone with AD are NPS (4). More severe NPS among the care recipients places greater demand on the caregiver, which increases the caregiver's risk of experiencing poor mental health (45,199). Ways in which the neighborhood environment can influence NPS among the AD recipients has been documented (200). Thus, we propose that neighborhood environments also may influence caregiver mental health.

Extant literature on neighborhood environments and caregiver mental health is limited; however, research suggests links between neighborhood characteristics and physical health conditions. For example, one study found that neighborhoods with higher levels of neighborhood crime were associated with higher glucose levels among caregivers compared to non-caregivers, thereby increasing risk for diabetes (107). Studies also have demonstrated the role between neighborhood disadvantage and other poor health outcomes (29) or depressive symptoms (19), making it reasonable to hypothesize that neighborhoods with greater exposure to multiple, negative environmental stressors (e.g., crime, drug use, and tobacco advertisement) (201), may interact to increase risk of adverse physical and mental health outcomes among caregivers (202). Disadvantaged

neighborhoods, often defined by variables from the US Census describing the composition of the people living in the area like median income (7), may also affect a caregiver's vulnerability to stressors, thus potentially increasing their risk of experiencing depressive symptoms (70). While there is emerging evidence of the influence of neighborhood socioeconomic disadvantage on health and mental health in the general population (19,203), little is known about these associations specifically among AD caregivers (10).

Residential instability, or the movement of people in and out of neighborhoods through time, has also been reported to be related with greater depressive symptoms among adults (19). In one study, greater residential instability was documented as a significant factor in increasing depressive symptoms specifically among child caregivers (122). One mechanism by which residential instability is thought to influence depressive symptoms is by hindering the formation of social cohesion and negatively impacting the support networks needed to protect individuals from worsening depressive symptoms (122). This hypothesis was supported by another study in Cyprus that found low social cohesion and fewer connections with neighbors were related to greater caregiver burden among those taking care of someone with AD or a related dementia (204). Conversely, more connections with neighbors and greater social support may also influence aspects of caregiving. A systematic review concluded that larger caregiver network and support was related to lower burden among caregivers compared to caregivers experiencing less social support (108). In a similar manner, neighborhood composition has been shown to buffer depressive symptoms among caregivers. Rote found that depressive symptoms were lower among Mexican-American dementia caregivers living in neighborhoods with a

higher percent of Spanish speaking residents compared to those caregivers living in neighborhoods with a lower percent of Spanish speaking residents, even when care recipients displayed more severe NPS (27).

Rural neighborhoods, generally characterized by limited access to healthcare, scarce resources and geographic isolation, may also negatively impact caregiver mental health (205,206). While no studies to our knowledge have examined the association between rurality and mental health among AD caregivers, a recent study reported demographic differences among all types of caregivers living in rural compared to urban areas (207). All types of caregivers in rural areas experienced lower employment, lower education attainment, and lower income, which are all related to resource gaps and thus suggests a greater likelihood of caregiver burden to be experienced in rural compared to urban areas (207). It is also thought that the larger geographic distances in rural areas may exacerbate social exclusion (166,208) and thus poor caregiver mental health (209). At the same time, geographic and social isolation may inform how caregivers might fill in gaps to provide community-based care (209) or may indicate differing cultural values (207). For example, a recent study reported that caregivers living in rural areas were able to rely on friends and neighbors in their community for support (209). Although rural caregivers face more financial barriers, studies also report that all types of caregivers living in rural areas experienced less caregiving-related difficulties (e.g., not enough time to oneself, interferes with work, and affects family relationships) compared to caregivers living in urban areas (210). A recent meta-analysis demonstrated that urban compared to rural residence was associated with greater depressive symptoms among those ≥60 years old (211), an age demographic that encompasses the majority of AD caregivers (1).

Given this understudied topic (209,212), it is important to understand the impact of rurality on caregiving.

In this study, we seek to understand how neighborhood environments may influence caregiver mental health. The aim of this study is to estimate the association between neighborhood characteristics (e.g., median household income, percent of residents that moved the past year as a measure of residential instability, and rurality) and caregiver mental health, specifically depressive symptoms, caregiver burden, and caregiver distress, among caregivers cohabitating with their AD care recipient in 2010 in South Carolina (SC). We hypothesize that caregivers residing in neighborhoods with lower income and higher percent residents that moved will be associated with greater levels of depression, burden, and distress, while those residing in more rural areas will be associated with lower levels of depression, burden, and distress. We also hypothesize that the associations between neighborhood environments and mental health symptoms will be stronger among caregivers who co-habited with AD care recipients experiencing severe NPS compared to caregivers who co-habited with care recipients without severe NPS (27).

METHODS

Study Design

A cross-sectional study was conducted to estimate the association between neighborhood characteristics (median household income, percent residents that moved the past year, and rurality) and three caregiver outcomes (depressive symptoms, caregiver burden, and caregiver distress). All caregivers were co-habiting with an older adult living

with AD, also described as the care recipient, in 2010 in SC. Those experiencing AD were diagnosed between 2005 and 2010.

Caregiver Participants

Participant data for this study came from a subset of data collected from the SC Alzheimer's Disease Registry (28). The Registry is a comprehensive statewide registry of diagnosed cases of AD and other related dementias compiled from inpatient hospitalizations, mental health records, emergency departments, Medicaid, memory clinics, chart abstracts, vital records, long-term care evaluations, and other sources (22). Data from the Registry subsample were collected in 2010 by trained interviewers who asked caregivers by phone about their caregiving experiences and about the care recipient's behavioral disturbances. Caregivers were defined as the person who spends at least four hours per day and at least four days per week with the recipient. All recipients in the study were enrolled in a Medicaid waiver program and eligible for nursing home level of care. This includes the option of those with AD and their caregivers to receive additional care services and case management while still residing within the community. Most of the caregivers were family members of the recipient (e.g., children) and reported feeling a duty or responsibility to care for the them, despite the recipients' eligibility for long-term, institutionalized care. Further information regarding study details and eligibility criteria have been reported elsewhere (28).

Study Sample

The sample consisted of 224 caregivers who co-habited with care recipients. Twelve caregivers were excluded from the analysis because we were unable to verify their actual place of residence (e.g., PO Box). The remaining 212 caregivers were

geocoded using ArcGIS Desktop Version 10.2.2 for Windows (Environmental Systems Research Institute, Redlands, CA). Only one address was tied (i.e. had more than one assigned location with the same match score) and re-matched using the "Interactive Rematch Dialogue" feature in ArcGIS. We compared those caregivers included in our study (n=212) to those excluded from the study (n=224) in terms of demographic variables (Table C.1).

Data Sources

Caregiver demographic data was obtained from the Registry subsample along with data regarding the cohabited care recipient (22,28). Neighborhood characteristics data came from two secondary sources available online at the census tract level: the 2006-2010 American Community Survey (ACS) (171) and the 2010 US Department of Agriculture Rural-Urban Commuting Area (RUCA) codes (172). Shapefiles and geographic features for SC data came from the US Census Topologically Integrated Geographic Encoding and Referencing (TIGER) Line Files (137). This study was deemed exempt by the Institutional Review Board at the University of South Carolina (ID = Pro00076582).

Dependent Variable: Caregiver Mental Health

There were three caregiver mental health outcomes considered: 1) depressive symptoms, 2) caregiver burden, and 3) caregiver distress (Table 5.1). Depressive symptoms were measured using the Center for Epidemiologic Studies Depression Scale Revised (CESD-R), a validated self-report measure of depression (213), that has also been recently validated among dementia caregivers (214). The CESD-R is made up of ten statements regarding how one felt or behaved in the past week. Caregivers responded

Table 5.1. Instruments Used to Measure Caregiver Mental Health Outcomes

Instrument	0	1	2	3	4	5	Range
Center for Epidemiologic Studies Depression Scale Revised	Rarely/ None of the time	Some of the time	Occasionally	Most of the time	n/a	n/a	0-30
Zarit Burden Interview	Never	Rarely	Sometimes	Quite frequently	Nearly always	n/a	0-16
Neuro-psychiatric Inventory Questionnaire Caregiver Distress	Not distressing at all	Minimal	Mild	Moderate	Severe	Extreme or very severe	0-60

with 0=rarely/none of the time, 1=some of the time, 2=occasionally, and 3=most of the time. Summing each score yielded a composite score that ranges from 0 to 30. Caregiver burden was measured using the shortened Zarit Burden Interview (ZBI-4), a validated measure of caregiver burden (127). The ZBI short version is made up of 4 items which caregivers ranked on a 5-point scale: 0=never, 1=rarely, 2=sometimes, 3=quite frequently, and 4=nearly always. The summed scores range from 0 to 16. Caregiver distress was measured using the Neuropsychiatric Inventory Questionnaire (NPI-Q), a validated measure of caregiver distress in relation to NPS (215). Caregivers reported the presence of 12 domains related to NPS present among their care recipient: delusions; hallucinations; agitation/aggression; depression/dysphoria; anxiety; elation/euphoria; apathy/indifference; disinhibition; irritability/lability; motor disturbance; sleep and nighttime behavior disorders; and appetite/eating changes. For each present domain, caregivers assessed their level of distress by ranking on a 6-point scale: 0=not distressing at all, 1=minimal, 2=mild, 3=moderate, 4=severe, and 5=extreme or very severe. Summing each domain yields a composite score that ranges from 0 to 60.

Independent Variables

Caregiver demographic information obtained from the Registry subsample included current caregiver age, sex (male or female), race/ethnicity (non-Hispanic black or other including non-Hispanic white, Hispanic, and Asian), employment (retired/unemployed, employed, or other), relationship to care recipient (spouse, child, or other), and sandwich caregivers (yes or no). Any caregiver who reported taking care of someone under 18 years old (e.g., grandchild) was considered to be a sandwich caregiver.

The care recipient's NPS were also considered for the analysis. NPS and caregiver distress was measured using the NPI-Q. For each domain present, the caregiver rated both the severity of the symptoms on a 3-point scale (1=mild, 2=moderate, and 3=severe), and the frequency of the symptoms on a 4-point scale (1=occasionally, 2=often, 3= frequently, and 4=very frequently). Multiplying the severity and frequency scores in each domain produces a domain score. The domain scores were summed across all twelve categories to yield a composite NPS score that ranges from 0 to 144.

The neighborhood was defined as a 1-mile buffer distance around each caregivers' geocoded address. Euclidean (or radial) buffers were created by drawing a straight line (a radius) 1 mile from a home address, creating a circle. Because the individual residence-based buffers tend to overlap multiple census tracts, neighborhood characteristics were calculated as the weighted average of intersecting census tracts within the buffer. Because of varying neighborhood definitions, a sensitivity analysis was also conducted to define neighborhood at a 3-mile buffer distance. Caregiver neighborhood characteristics defined as the weighted average of the 1-mile buffer distance were the following: median household income and percent residents moved the past year. Both measures were obtained from the ACS. Median income per family were categorized into tertiles: low (<$31,000), medium ($31-40,758), and high (>$40,758). ACS determines the extent of residential mobility by using data on location of current residence and residence of one year ago.

Caregiver rurality was based on the census tract in which the geocoded addresses resided. We defined rurality using information from the RUCA. RUCA measures rurality on a 10-point scale, ranging from metropolitan to rural. For the purposes of our analysis,

we divided census tracts into three rurality categories: 1) large urban (metropolitan area core; n=105), 2) small urban (metropolitan area high commuting and metropolitan area low commuting; n=41), and 3) rural (micropolitan area core, micropolitan high commuting, micropolitan low commuting, small town core, small town high commuting, small town low commuting, and rural areas; n=66).

Data Analysis

Descriptive statistics were computed; categorical variables were presented as percentages with numbers, and continuous variables were presented as means with standard deviations (SDs). To estimate associations between neighborhood characteristics and caregiver mental health scores, we conducted a negative binomial regression stratified by care recipient NPS severity status. Given the non-normal distribution of NPS, the median of total NPS score (median=19) was used to separate recipients into severe and non-severe status. The following confounders were adjusted for in the model: age, sex, race/ethnicity, employment, relationship with care recipient, and sandwich caregiver status. Results obtained from these regression analyses are presented as rate ratios (RR), and diagnostics were assessed using the Pearson chi-square test of deviance. No offset parameter was included because questionnaires asked about the symptoms occurring during the same time frame. There were no noted significant differences between the models using different neighborhood definitions (1- versus 3-mile), and, therefore, the 1-mile buffer distance is the only one reported. The significance level was set at 0.05. All analyses were completed using SAS software, Version 9.3 for Windows (SAS Institute, Cary, NC).

RESULTS

Table 5.2 summarizes the caregiver mental health scores by neighborhood variables as well as by caregiver and care recipient demographics. The study population consisted of 212 caregivers co-habiting with their recipient. The mean age of caregivers was 58.95 years, majority were female (85%), and over half of the caregivers were non-Hispanic black (55.19%). Most caregivers lived in large urban neighborhoods (49.53%). Overall total depression, burden, and distress scores had a mean of 10.27 (S.D.= 6.36; range= 0-29), 5.91 (S.D.= 3.95; range= 0-16), and 12.17 (S.D.= 10.42; range= 0-45), respectively.

Multivariable Model

Tables 5.3-5.5 presents both unadjusted and adjusted rate ratios (RR) modeling the average scores of total depressive symptoms, burden scores, and caregiver distress scores stratified by the care recipients' NPS status, respectively. With respect to caregivers co-habited with a recipient of severe NPS, we estimated that those caregivers living in low income neighborhoods (defined as <$31,000) and living in medium income neighborhoods (defined as $31-40,458) had 1.61 (95% CI= 1.26-2.04) and 1.45 times (95% CI = 1.17-1.78), respectively, greater distress scores compared to caregivers living in high income neighborhoods (defined as >$40,758), after adjusting for percent residents moved past year, rurality, caregiver age, sex, race/ethnicity, relationship to recipient, employment, and sandwich caregiver status. In contrast, results suggest that caregivers of non-severe NPS recipients exhibited the opposite relationship between neighborhood income and depressive symptoms (low compared to high income: RR= 0.88; 95% CI= 0.55-1.17; medium compared to high income: RR= 0.77; 95% CI= 0.53-1.12). Among

Table 5.2. Descriptive Characteristics of Co-Habited Caregivers' Demographics and Neighborhood Variables, 2010, SC (n=212)

Neighborhood Variables	**Total Percentage (n)**	**Caregiver Depression**		**Caregiver Burden**		**Caregiver Distress**	
		<median	**>median**	**<median**	**>median**	**<median**	**>median**
Percent moved 1 year ago, mean (S.D.)	3.86 (1.86)	3.73 (1.92)	3.98 (1.80)	3.75 (1.71)	3.95 (1.98)	3.96 (1.99)	3.75 (1.73)
Rurality[a]							
Large urban	49.53 (105)	45.71 (48)	53.27 (57)	44.00 (44)	54.46 (61)	42.31 (44)	56.48 (61)
Small urban	19.34 (41)	21.9 (23)	16.82 (18)	18.00 (18)	20.54 (23)	20.19 (21)	18.52 (20)
Rural	31.13 (66)	32.38 (34)	29.91 (32)	38.00 (38)	25.00 (28)	37.5 (39)	25.00 (27)
Median household income							
High (>$40,758)	25.47 (54)	34.29 (36)	31.78 (34)	25.00 (25)	41.07 (46)	32.69 (34)	34.26 (37)
Medium ($31-40,758)	45.28 (96)	32.38 (34)	34.58 (37)	38.00 (38)	29.46 (33)	35.58 (37)	31.48 (34)
Low (<$31,000)	29.25 (62)	33.33 (35)	33.64 (36)	37.00 (37)	29.46 (33)	31.73 (33)	34.26 (37)
Caregiver Demographics	**Percentage (n)**	**<median**	**>median**	**<median**	**>median**	**<median**	**>median**
Age, mean (S.D.)	58.95 (10.33)	58.92 (10.98)	58.98 (9.71)	58.85 (10.95)	59.05 (9.8)	59.27 (10.62)	58.65 (10.1)

Sex							
Male	14.62 (31)	17.14 (18)	12.15 (13)	21 (21)	8.93 (10)	22.12 (23)	7.41 (8)
Female	85.38 (181)	82.86 (87)	87.85 (94)	79 (79)	91.07 (102)	77.88 (81)	92.59 (100)
Race/ethnicity							
Non-Hispanic black	55.19 (117)	62.86 (66)	47.66 (51)	37 (67)	44.64 (50)	61.54 (64)	49.07 (53)
Other[b]	44.81 (95)	37.14 (39)	52.34 (56)	33 (33)	55.36 (62)	38.46 (40)	50.93 (55)
Employment[c]							
Employed	33.02 (70)	33.33 (35)	16.51 (35)	56 (56)	35.71 (40)	38.46 (40)	27.78 (30)
Retired/ unemployed	53.3 (113)	53.33 (56)	53.27 (57)	30 (30)	50.89 (57)	50.00 (52)	56.48 (61)
Other	13.68 (29)	13.33 (14)	14.02 (15)	14 (14)	13.39 (15)	11.54 (12)	15.74 (17)
Relationship to Care recipient							
Spouse	16.51 (35)	11.43 (12)	21.50 (23)	16 (16)	16.96 (19)	14.42 (15)	18.52 (20)
Child	67.92 (144)	68.57 (72)	67.29 (72)	67 (67)	68.75 (77)	69.23 (72)	66.67 (72)
Other[d]	15.57 (33)	20.00 (21)	11.21 (12)	17 (17)	14.29 (16)	16.35 (17)	14.81 (16)
Sandwich caregivers[e]							

Yes	33.96 (72)	38.1 (40)	29.91 (32)	40 (40)	28.57 (32)	34.62 (36)	33.33 (36)
No	66.04 (140)	61.9 (65)	70.09 (75)	60 (60)	71.43 (80)	65.38 (68)	66.67 (72)
Care Recipient Demographics	**Percentage (n)**	**<median**	**>median**	**<median**	**>median**	**<median**	**>median**
Neuropsychiatric symptom severity (NPS) mean (S.D.)	26.3 (22.34)	18.76 (15.6)	33.76 (25.36)	19.75 (20.99)	32.21 (21.98)	10.66 (8.66)	41.43 (21.1)
Severe NPS (>median)	52.83 (112)	40.95 (43)	64.49 (69)	38 (38)	66.07 (74)	16.35 (17)	87.96 (95)
Non-severe NPS (<median)	47.17 (100)	59.05 (62)	35.51 (38)	62 (62)	33.93 (38)	83.65 (87)	12.04 (13)
Age, mean (S.D.)	82.42 (8.7)	82.62 (8.49)	82.22 (8.96)	81.98 (9.0)	82.81 (8.5)	82.47 (9.1)	82.47 (8.4)
Sex							
Male	27.36 (58)	25.71 (27)	28.97 (31)	30 (30)	25.00 (28)	25.96 (27)	28.7 (31)
Female	72.64 (154)	74.29 (78)	71.03 (76)	70 (70)	75.00 (84)	74.04 (77)	71.3 (77)

[a]Rurality was measured based on the RUCA (Rural Urban Commuting Area codes). Large urban area was defined as metropolitan area; small urban area was defined as metropolitan area high commuting and metropolitan area low commuting; and rural area was defined as micropolitan area core, micropolitan high commuting, micropolitan low commuting, small town core, small town high commuting, small town low commuting, and rural areas.
[b]Other race/ethnicity included non-Hispanic white (n=93), Hispanic (n=1), and Asian (n=1).
[c]Retired and unemployed included fully retired (n=64), unemployed (n=31), and homemaker (n=18), and employed included employed full time (n=40), employed part time (n=27), and retired by working part time (n=3).

[d]Other relationship to care recipient included daughter-in-law (n=6), sister (n=5), brother (n=3), grandchild (n=9), niece or nephew (n=2), and other (n=8).
[e]Sandwich caregivers were defined as those who reported taking care of someone under 18 years old (e.g., grandchild).

Table 5.3. Unadjusted and Adjusted Multivariable Negative Binomial Regression Analysis of Neighborhood Characteristics Associated with Caregiver Depressive Symptoms, 2010, SC

Variable	Severe Neuropsychiatric Symptoms (n=112)[c]		Non-severe Neuropsychiatric Symptoms (n=100)[c]	
	Unadjusted RR (95% CI)	Adjusted[d] RR (95% CI)	Unadjusted RR (95% CI)	Adjusted[d] RR (95% CI)
Rurality[a]				
Rural	1.06 (0.83-1.35)	0.98 (0.75-1.27)	0.89 (0.65-1.22)	0.98 (0.69-1.39)
Small urban	0.88 (0.66-1.19)	0.96 (0.71-1.28)	0.89 (0.62-1.28)	1.02 (0.68-1.51)
Large urban	1.00[e]	1.00[e]	1.00[e]	1.00[e]
Percent moved 1 year ago	1.02 (0.96-1.09)	1.04 (0.95-1.12)	0.99 (0.93-1.07)	0.98 (0.89-1.09)
Median household income[b]				
Low	1.18 (0.91-1.53)	1.33 (1.00-1.78)	0.82 (0.59-1.14)	0.80 (0.55-1.17)
Medium	1.19 (0.93-1.54)	1.25 (0.97-1.61)	0.75 (0.53-1.05)	0.77 (0.53-1.12)
High	1.00[e]	1.00[e]	1.00[e]	1.00[e]

[a]Rurality was measured based on the RUCA (Rural Urban Commuting Area codes). Large urban area was defined as metropolitan area; small urban area was defined as metropolitan area high commuting and metropolitan area low commuting; and rural area was defined as micropolitan area core, micropolitan high commuting, micropolitan low commuting, small town core, small town high commuting, small town low commuting, and rural areas.
[b]Median household income categories based on tertiles where low was (<$31,000), medium ($31-40,758), and high (>$40,758).
[c]Severe neuropsychiatric symptoms among those with AD defined as >median.

[d]Model adjusted for caregiver age, sex, race/ethnicity, employment, relationship to care recipient and sandwich caregiver status.
[e]Reference category.

Table 5.4. Unadjusted and Adjusted Multivariable Negative Binomial Regression Analysis of Neighborhood Characteristics Associated with Caregiver Burden, 2010, SC

Variable	Severe Neuropsychiatric Symptoms (n=112)[c]		Non-severe Neuropsychiatric Symptoms (n=100)[c]	
	Unadjusted RR (95% CI)	Adjusted[d] RR (95% CI)	Unadjusted RR (95% CI)	Adjusted[d] RR (95% CI)
Rurality[a]				
Rural	0.87 (0.67-1.12)	0.87 (0.65-1.18)	0.89 (0.30-1.32)	0.99 (0.66-1.51)
Small urban	0.93 (0.69-1.25)	1.02 (0.74-1.40)	0.86 (0.56-1.37)	0.94 (0.59-1.50)
Large urban	1.00[e]	1.00[e]	1.00[e]	1.00[e]
Percent moved 1 year ago	1.02 (0.96-1.08)	1.02 (0.94-1.12)	1.00 (0.92-1.10)	0.95 (0.83-1.07)
Median household income[b]				
Low	0.91 (0.70-1.19)	1.05 (0.77-1.43)	0.88 (0.59-1.33)	0.90 (0.57-1.44)
Medium	0.94 (0.72-1.21)	1.01 (0.77-1.33)	0.65 (0.42-0.99)	0.74 (0.47-1.17)
High	1.00[e]	1.00[e]	1.00[e]	1.00[e]

[a]Rurality was measured based on the RUCA (Rural Urban Commuting Area codes). Large urban area was defined as metropolitan area; small urban area was defined as metropolitan area high commuting and metropolitan area low commuting; and rural area was defined as micropolitan area core, micropolitan high commuting, micropolitan low commuting, small town core, small town high commuting, small town low commuting, and rural areas.
[b]Median household income categories based on tertiles where low was (<$31,000), medium ($31-40,758), and high (>$40,758).
[c]Severe neuropsychiatric symptoms among those with AD defined as >median.

[d]Model adjusted for caregiver age, sex, race/ethnicity, employment, relationship to care recipient and sandwich caregiver status.
[e]Reference category.

Table 5.5. Unadjusted and Adjusted Multivariable Negative Binomial Regression Analysis of Neighborhood Characteristics Associated with Caregiver Distress, 2010, SC

Variable	Severe Neuropsychiatric Symptoms (n=112)[c]		Non-severe Neuropsychiatric Symptoms (n=100)[c]	
	Unadjusted RR (95% CI)	Adjusted[d] RR (95% CI)	Unadjusted RR (95% CI)	Adjusted[d] RR (95% CI)
Rurality[a]				
Rural	0.93 (0.75-1.15)	0.76 (0.61-0.95)	0.66 (0.39-1.13)	0.53 (0.28-1.01)
Small urban	0.95 (0.74-1.23)	0.90 (0.70-1.15)	0.66 (0.36-1.22)	0.63 (0.31-1.27)
Large urban	1.00[e]	1.00[e]	1.00[e]	1.00[e]
Percent moved 1 year ago	1.00 (0.95-1.06)	0.99 (0.92-1.06)	1.02 (0.90-1.16)	0.93 (0.78-1.12)
Median household income[b]				
Low	1.28 (1.02-1.59)	1.61 (1.26-2.04)	1.13 (0.64-2.00)	1.50 (0.73-3.08)
Medium	1.25 (1.00-1.55)	1.45 (1.17-1.78)	0.86 (0.48-1.56)	1.20 (0.63-2.28)
High	1.00[e]	1.00[e]	1.00[e]	1.00[e]

[a]Rurality was measured based on the RUCA (Rural Urban Commuting Area codes). Large urban area was defined as metropolitan area; small urban area was defined as metropolitan area high commuting and metropolitan area low commuting; and rural area was defined as micropolitan area core, micropolitan high commuting, micropolitan low commuting, small town core, small town high commuting, small town low commuting, and rural areas.
[b]Median household income categories based on tertiles where low was (<$31,000), medium ($31-40,758), and high (>$40,758).
[c]Severe neuropsychiatric symptoms among those with AD defined as >median.

[d]Model adjusted for caregiver age, sex, race/ethnicity, employment, relationship to care recipient and sandwich caregiver status.
[e]Reference category.

caregivers for recipients with non-severe NPS, we observed a pattern that caregivers living in small urban and rural neighborhoods have 37% (RR=0.63; 95% CI = 0.31-1.27) and 47% (RR=0.53; 95% CI= 0.28-1.01) lower distress scores, respectively, compared to those who live in urban neighborhoods, in the adjusted models, but this failed to reach statistical significance. No significant measures of association were observed between neighborhood characteristics and caregiver burden.

DISCUSSION

This study examined the impact of neighborhood characteristics on caregiver mental health among those co-habited with care recipients experiencing Alzheimer's disease, specifically examining the caregivers' levels of depression, burden, and distress. Key study findings include evidence to support the hypothesis that caregivers co-habited with care recipients experiencing severe NPS residing in low income neighborhoods experienced greater levels of mental health outcomes-- in particular, distress – compared to caregivers residing in high income neighborhoods. These findings were strongest for the level of caregiver distress score; the association between neighborhood income and caregiver distress was stronger among caregivers living in low income neighborhoods, compared to medium income neighborhoods and high income neighborhoods. We did not find statistically significant associations between neighborhood income and depressive symptoms or burden scores. Although, the rate ratios estimates suggested that caregivers living in lower income neighborhoods had greater average depressive symptoms, similar to findings for caregiver distress and consistent with previous literature elucidating pathways between disadvantaged neighborhoods and greater depressive symptoms among adults (19). Notably, among caregivers co-habited with non-severe NPS, the

results suggest that those living in lower income neighborhoods experienced lower depressive symptoms and burden scores. This may suggest the moderating role of neighborhood characteristics on caregiver outcomes among those living with a recipient of severe NPS status.

Few studies have sought to understand the association between neighborhood characteristics and caregiver mental health (3). The current study contributes to the caregiver literature on mental health by showing the differences in the association between neighborhood income and caregiver mental health related to the NPS severity of the care recipient. As previously noted, caregivers co-habited with recipients of severe NPS status experienced greater distress when living in low income, compared to those living in high income neighborhoods. Among caregivers of recipients with non-severe NPS status, we observed rate ratios suggesting that those living in lower income neighborhoods experienced lower levels of mental health outcomes. The reasons for these differences are unclear. It may be that low-income neighborhoods are associated with greater caregiver distress because they lack available resources, such as respite care, specialty clinics, or caregiver support groups, to help caregivers manage symptoms of their recipients. In this case, the association between low income neighborhoods and poor mental health would be expected to be greatest among caregivers of recipients with severe NPS, as found in the present study. On the other hand, previous research suggests that neighborhood disadvantage does not necessarily translate into poor caregiver mental health outcomes. In fact, a study by Beach et al., (10) reported that neighborhood disadvantage was associated with lower caregiver depression and associated with more positive aspects of caregiving (e.g., feeling confident about ability to care take),

suggesting that neighborhood characteristics play a moderating role on the impact of individual-level risk factors on caregiver outcomes (10). Most literature, however, demonstrates a relationship between disadvantaged neighborhoods and greater depressive symptoms (19,203), specifically among older adults (106,216,217), similar to our findings. Therefore, it is important to examine this relationship further among dementia caregivers in order to guide policies that better address needs of caregivers (e.g., formal services like educational workshops).

Our findings suggest that residing in rural neighborhoods is associated with better caregiver mental health irrespective of care recipient NPS status. Particularly, we observed that caregivers living in rural areas had lower distress scores on average compared to those living in urban areas, although this difference was not statistically significant. This is consistent with previous findings that report greater depressive symptoms among older adults living in urban compared to rural areas (211). Other studies also show dementia caregivers living in rural areas experienced less caregiving difficulties compared to those in urban areas, despite having an annual household income <$25,000 or being unable to visit a doctor due to financial cost (210). While NPS severity among recipients is a known risk factor for depressive symptoms among caregivers (5), previous results suggest neighborhood characteristics buffer the impact of NPS on caregiver mental health (27). The present findings suggest that rural and small urban areas may fulfill a similar function of providing a buffer for the effects of NPS, with one potential buffer being greater social support and stronger community ties. This hypothesis is supported by previous research which reported fairly high levels of social support (e.g. having available tangible material assistance, someone to discuss problems with, or

positive regard and self-esteem from others) among dementia caregivers living in rural Alabama (218). Previous studies have also identified availability of someone with whom to talk (218) and ability to utilize places of worship (e.g. church) as sources for respite (209), as potential features of rural communities that may help rural caregivers better manage the challenges of dementia care, counteracting limited availability of caregiving resources in these communities (218). On the other hand, we did not observe significant differences in caregiver mental health outcomes by residential instability (e.g. a component of weak social cohesion), suggesting that social cohesion and support are not the only explanation for rural/urban differences. Another potential explanation for observing lower caregiver distress among those living in rural areas is the availability of more greenspace. In support of this hypothesis, previous research suggests that greenspace may help caregivers recover from stress, as well as stimulate physical activity and facilitate social contacts (117,219,220). As such, it is possible that the more greenery and natural aesthetics in rural compared to urban areas, may protect against depressive symptoms among caregivers (179). Yet, nature and use of greenspace differs between urban and rural areas with green urban areas typically being more accessible and managed (179). Hence, future studies can focus on measuring both quality and quantity of greenspace to further examine this relationship.

A strength of this study includes the use of validated and reliable questionnaires to capture depressive symptoms, caregiver burden, and distress score (213,215,221). The availability of the Registry subsample data (28) used for our study allowed the examination of neighborhood characteristics and caregiver mental health outcomes among a heterogenous, racially diverse population (30% live in rural areas and 55% are

non-Hispanic black). While the neighborhood was defined at a small scale, a limitation includes the assumption of uniformity across census tracts in order to use weighted administrative data. Another limitation includes the small sample size, which may explain the non-significant findings. Additionally, the cross-sectional study design and inability to assess changes in variables over time do not allow us to make causal conclusions about the associations between neighborhood characteristics and caregiver mental health. Longitudinal research will be helpful in identifying how change in residence, neighborhood composition, or resources are related to changes in caregiver mental health. Also, longitudinal investigations of AD care recipients may be particularly informative for caregiver mental health when change is examined during critical, transition periods (e.g., recipient behavioral changes or institutionalization). The cross-sectional design also does not take neighborhood selection effects (i.e. selective sorting into neighborhoods) into account. Although adjustment for individual-level data (e.g., caregiver employment) attempts to account for this, we cannot be sure that some of our findings are not simply the result of where caregivers have chosen to live. Another limitation worthy of note is potential selection bias regarding which caregivers chose to participate in the study; specifically, caregivers with a recipient with greater NPS severity might be less likely to respond given that they are providing care and do not have time for an hour-long phone interview. However, we did observe more caregivers (n=112) of recipients presenting severe NPS compared to non-severe NPS (n=100). Yet, we are unable to assess the potential direction of impact of this limitation, but that it may limit the representativeness of the sample population (28).

Implications and Future Research

The current research adds knowledge regarding the role between lower income neighborhoods and greater caregiver distress as related to the care recipients' NPS severity status. Because we observed greater caregiver distress among those living in low income compared to high income neighborhoods, future research can assess if this relationship is specifically due to lower access to care, less opportunities for caregivers' support group, or other potential mechanisms. By examining the role of additional neighborhood characteristics, especially caregiver support groups, future research could focus on the explicit pathways between neighborhood environments and caregiver mental health. Additionally, because the role of low-income neighborhoods was greater among caregivers living with a recipient with severe NPS, mitigation of NPS may help improve caregiver health. Similarly, perceived caregiver distress from NPS may be another potential mediator for the observed relationships between neighborhood characteristics and caregiver mental health. Thus, interventions can be specifically tailored to these caregivers who may be at higher risk for distress.

CONCLUSION

Our study concerns an important area of research, considering the anticipated growing burden on caregivers and lack of effective treatments for AD. Caregiver mental health is greatly associated with care recipients' NPS and disease progression; in cases where NPS persist, they increase burden on the caregiver indirectly by increasing risk for institutionalization, comorbidities, and mortality (175). Overall, we observed that caregivers co-habited of care recipients with AD presenting severe NPS living in low income neighborhoods experienced greater caregiver distress. These results suggest that,

neighborhood characteristics may serve to magnify other naturally occurring social stressors experienced by caregivers. This study supports an approach to identify neighborhood environment characteristics that influence caregiver mental health (e.g. stressors, like unemployment, in low income neighborhoods) in order to offer community-level interventions that can alleviate caregiver burden.

CHAPTER 6:

CONCLUSION

This dissertation examined associations between neighborhood characteristics and Alzheimer's disease and related dementias (ADRD) incidence for Aim 1, neuropsychiatric symptoms (NPS) among people with Alzheimer's disease (AD) for Aim 2, and mental health among AD caregivers for Aim 3. The purpose of this concluding chapter is to synthesize the dissertation findings as well as discuss areas that remain to be understood. I will discuss strengths and limitations of the dissertation as a whole as well as implications for practice and research that may prove useful to the field.

REVIEW OF MAIN FINDINGS

Overall, we observed that those living in disadvantaged neighborhoods, operationalized using high poverty and low-income, experienced greater ADRD incidence, NPS and poor caregiver mental health compared to those living in advantaged neighborhoods. These findings are similar to previous literature examining the association between disadvantaged neighborhoods and greater ADRD incidence (11), poor cognition among older adults (29,82), and depressive symptoms among adults (19). To our knowledge, there are no studies in the literature examining the relationship between the neighborhood environment and NPS among those with AD. Likewise, few studies have examined the relationship between the neighborhood environment and mental health outcomes among AD caregivers (27,204); previous literature focused on

aspects of social cohesion related to the neighborhood environment (27) or were conducted internationally (204) and thus are not comparable to our Aim 3 study. Our findings, however, are not consistent with a recent study conducted in Philadelphia, PA that concluded socioeconomic disadvantaged areas were associated with less depressive symptoms among ADRD caregivers (10).

We also observed lower ADRD incidence and average NPS among those living in rural compared to those living in urban areas. Although we did not observe significant associations between rurality and mental health, our results suggested that caregivers living in rural areas experienced on average lower depressive symptoms compared to caregivers living in urban areas. Our findings, however, contradict the literature where studies report greater ADRD incidence and prevalence in rural areas (13). Again, to our knowledge, we did not find any studies exploring the relationship between rurality and NPS. Meanwhile, the relationship between rurality and depressive symptoms remains unclear. A recent review among older adults reported greater depressive symptoms among those living in urban compared to rural areas (211). Conversely, research reports greater depressive symptoms globally among those living in rural compared to urban areas (222). Similarly, suicide rates are markedly higher in rural areas compared with major cities as documented in the U.S., United Kingdom, and Australia (223). Few studies have examined the relationship between rurality and mental health among AD caregivers. While some studies have reported high rates of depressive symptoms among AD caregivers living in rural areas (224), these rates were not compared to those living in urban areas.

POTENTIAL EXPLANATION FOR FINDINGS

While overall findings demonstrated greater ADRD incidence, NPS and caregiver mental health among those living in disadvantaged neighborhoods (e.g., low-income neighborhoods), the exact mechanisms are still unknown. Disadvantaged neighborhoods are hypothesized to influence ADRD incidence, NPS and caregiver mental health via different mechanisms. Disadvantaged neighborhoods are clustered with other factors (e.g., high levels of environmental pollutants, overcrowding, or violence) thereby increasing exposure to multiple stressors (20) that may increase risk for ADRD, NPS, and poor mental health. High levels of exposure to psychosocial stress can lower the brain's threshold for neurotoxicity and thus increases risk for neurodegeneration and impacts cognitive function (113). In fact, long-term activation of the physiological stress response can lead to temporary or permanent physiological changes potentially influencing risk of ADRD (114). Similarly, disadvantaged neighborhoods are also characterized by lower access to healthcare services and resources, which may also play a role in influencing ADRD incidence, NPS, and caregiver mental health. Absence and lack of social and improved infrastructures in neighborhoods may lead residents to adopt behaviors and practices harmful to health. Constraints imposed by the environment (e.g., crime, fear of crime, drug use, incivility, or social disorder) may be causing residents to adopt unhealthy behaviors as a means of coping with the harsh and stressful environment. Finally, disadvantaged neighborhoods may reflect the composition of residents such that unhealthy people cluster in disadvantaged neighborhoods whose individual-level behaviors may then contribute to higher rates of ADRD, NPS, and poor mental health. Longitudinal, etiologic studies to test hypotheses about specific pathways by which

disadvantaged neighborhoods structure population risk of ADRD may help elucidate these mechanisms.

Overall findings regarding lower ADRD incidence, NPS and poor mental health among those living in rural compared to urban areas were inconsistent with the literature. It is likely that these results may have been influenced by bias and are not necessarily causally related. Possible explanations for these findings include migration, detection bias, reverse causation, or reporting bias. First, those living in rural areas may be moving to urban areas to seek care and other resources. This likely occurred among older adults diagnosed with other comorbid health conditions in Aim 1. Likewise, migration likely occurred among the care recipient-caregiver dyad used for Aim 2 & 3. Second, rural areas tend to have less healthcare resources and thus people living in these areas may have been less likely to have an ADRD detection and diagnosis. As such, these lack of diagnoses would be absent from our area-level analysis in Aim 1. Third, reverse causation may also be a likely scenario explaining our inconsistent findings. All three studies were conducted at a single point in time where temporality cannot be established. Although Aim 1 utilized ADRD incident cases, people are often diagnosed long after disease onset (151). Fourth and finally, reporting bias may potentially explain our inconsistent findings. Specifically, for Aim 2 & 3, caregivers answered questions about their care recipients' NPS as well as their own mental health via phone. It is possible that caregivers reported experiencing less mental health outcomes as their role as a caregiver in order to avoid judgment (e.g., social desirability bias). In addition, mental health has been stigmatized about non-Hispanic black adults (NHB) (225), a racial group that makes up more than half of the caregivers, which may in turn influence how caregivers answer.

In addition to stigmatization, general mental health may have been viewed differently by race/ethnicity. Typically, literature reports lower depressive symptoms and mental health outcomes among NHB compared to non-Hispanic white (NHW) adults (226). Nonetheless, the instrument used to measure depressive symptoms in Aim 3 (the Center for Epidemiologic Studies Depression Scale, CESD), had been validated among NHB older adults (227), NHB AD caregivers (228), and NHB caregivers in Missouri, where half of the sample consisted of those living in rural areas (229). Despite the validation of CESD by race, the role of caregiving may also be viewed differently by racial/ethnic groups. Specifically, NHB caregivers may have different expectations and perceptions on caregiving compared to NHW caregivers (230,231). This may have not only influenced how caregivers report distress and other mental health outcomes but also how caregivers report NPS among their care recipients. While there is limited information in the literature regarding NPS differences by race, one study found that NHB caregivers may be more likely to underreport NPS (232).

OVERALL STRENGTHS

This dissertation is one of the first to explore associations between neighborhood characteristics and ADRD incidence, NPS among those experiencing AD, and mental health among AD caregivers. Specifically, we did not find any studies exploring associations between neighborhood environments and NPS. Identifying factors to mitigate or intervene on NPS is especially important as these could benefit both those experiencing AD and their caregivers. Another strength included the use of a population-based registry for Aim 1 that allowed us to identify socioeconomic inequalities across the state of SC. These results are important for determining resource allocation and future

public policy. Furthermore, the use of a population-based registry allowed our results to be generalizable to older adults in SC across a range of demographic characteristics and neighborhoods.

DISSERTATION LIMITATIONS

Two major limitations for this dissertation, as is common with neighborhood health research, were neighborhood selection bias and reverse causation. If people with unhealthy behaviors select into disadvantaged neighborhoods, this could have influenced our results. Declining cognitive function may have also increased the likelihood of moving residences to access care and/or live with adult children. Although Aim 1 utilized incident cases, this bias is still present since ADRD diagnosis could occur decades after disease onset (151). This is especially important for Aim 2 because care recipients experiencing AD may have moved to another neighborhood to live with their caregivers. It is similarly likely that caregivers moved to another area to seek care or be closer to relatives for additional help in caregiving. Because we lacked geographic information on residential mobility, we were unable to assess this limitation. Likewise, we were unable to assess the cumulative effect of lifetime exposures to neighborhoods on health. Another primary concern was that we could not rule out detection bias occurring, such that ADRD may be more frequently diagnosed when in contact with the healthcare system (e.g., live close proximity to healthcare resources).

Another limitation for this dissertation, as similar with current neighborhood health research (61), is residual confounding. For Aim 1, only individual age and sex were taken into account as no other individual-level information was available, except for race. For Aim 2 & 3, we attempted to minimize confounding by controlling for

demographics, such as caregiver education (Aim 2) or caregiver employment (Aim 3); however, we were missing other potentially important confounders, such as caregiver income, which may have been important in the relationship between neighborhood environments and health outcomes (20,82).

Measurement error may be another limitation. This is especially true of neighborhood variables obtained from the American Community Survey (ACS), such as median household income, which were based on probability samples. To mitigate this problem, five-year data estimates were used for all three studies. Further, this dissertation did not include neighborhood built environment variables related to infrastructure, such as traffic, noise or walkability (e.g., high land use mix), which may play a role in influencing this dissertation's outcomes (29). Although sensitivity analyses with 1-mile and 3-miles buffers were used for Aim 2 & 3 respectively, the use of ½-mile and 1-mile buffers for these studies may have led to misspecification of the relevant geographic areas, particularly for those living in rural neighborhoods. Similarly, census tracts used for Aim 1 may not reflect meaningful neighborhood boundaries. Residents' exposures to area characteristics likely extend beyond the boundary lines of administrative units. A person's health may be affected not only by their local neighborhood but also by features of a wider surrounding area. Surrounding area deprivation, in particular, may magnify the local poverty health effect because of spatial isolation from resources associated with wealthy areas. Nevertheless, census tracts are geographical units employed to guide policy decisions and allocation of resources where individuals usually are unaware of which census tract they reside in.

Moreover, small sample sizes for Aim 2 & 3 may result in low power to examine the associations, particularly for Aim 3 that used a stratified analysis. Finally, generalizability of results from Aim 2 & 3 are limited to those with low incomes as the Registry subsample consisted of those eligible for a Medicaid waiver program.

IMPLICATIONS FOR PRACTICE

As determined by this dissertation, appropriate, prevention-focused, community-based approaches aimed at promoting opportunities for social and cognitive stimulation may delay the onset of ADRD. Given that results showed high poverty and low-income neighborhoods to have greater ADRD incidence and NPS severity, these areas should be targets for interventions and provision of greater resources. This information gained can be used to inform policymaking to both reduce ADRD risk and improve ADRD management. To better guide policymaking organizations in recommending public policy, dissemination products including a one-page sheet regarding main conclusions of this dissertation and impacts of high poverty and low-income neighborhoods on ADRD and NPS severity may be useful. Two organizations that serve to provide this type of information to policymakers are the Arnold School of Public Health Office for the Study of Aging (OSA) at the University of South Carolina and the SC Department of Aging Alzheimer's Resource Coordination Center. More so, the Alzheimer's Resource Coordination Center aims to expand resources to enhance statewide services, which may include healthcare resources in high poverty and low-income neighborhoods.

Another policy takeaway is that targeting areas with high concentrations of older adults with services and initiatives may help manage ADRD or slow disease progression, which may allow those with ADRD to live more independently. This may also indirectly

relieve caregivers. Services and initiatives may include senior centers, activities offered by local organizations, access to affordable meal programs, accessible health services including home care, and a befriending service. A befriending service may help people with ADRD to participate in community life and receive emotional support.

With regards to how the insights from this dissertation can inform actual ADRD patient care, the aforementioned organizations and other advocates may push local governments to plan and implement housing, transportation, public spaces and emergency response that enable people with ADRD and care partners to thrive. OSA also focuses on providing education on ADRD for professional caregivers and family members. As such, results focusing on areas to target for respite care may be disseminated to the OSA for such planning purposes. Similarly, the Alzheimer's Resource Coordination Center also serves information and education to assist persons with ADRD and their families. One method of this service includes the announcement of grant funding availability for the upcoming state fiscal year every February. Grant funds are allocated towards respite care programs and educational programs for families and caregivers of those with ADRD. Awarded grants assist local communities in developing programs to serve persons with ADRD and their caregivers. For example, if areas with more parks and recreational facilities are associated with lower risk of ADRD, then public health practitioners would have additional information through which to support investment of parks by cities and local municipalities. Likewise, if areas with more supermarkets and grocery stores are associated with lower risk of ADRD, then public health initiatives may work to increase access to grocery stores through new locations or expansion incentives.

This dissertation may also be useful for campaigning for public awareness and supporting future research. The foci of campaigns and future research in ADRD should deal with both environmental drivers of ADRD and community-based approaches to promote dementia-friendly neighborhoods – incorporating primary, secondary, and tertiary prevention. For example, the Alzheimer's Association relentlessly advocates for public policies that increase critical research funding and support all those affected. The Alzheimer's Association recently advocated in favor of a law introduced in Congress in 2017: S. 2076/H.R. 4256, or the "Building Our Largest Dementia Infrastructure for Alzheimer's Act." This law creates an AD public health infrastructure by establishing regional centers that address ADRD through public awareness campaigns; supports data collection on the incidence and prevalence of ADRD; and awards cooperative agreements to health departments for purpose of addressing ADRD. The law aims to improve quality of life with those with ADRD and their caregivers as well as reduce associated costs for individuals and the government, and thanks to the work of the Alzheimer's Association, the healthcare community, and Congress, was signed into law in 2019.

The Alzheimer's Association also has an advocacy group called AIM, or the Alzheimer's Impact Movement. The primary goal of AIM is to advocate for Alzheimer's Disease, and it seeks to recruit members of the public who can stay informed about legislative and policy priorities. Members of the AIM action network are alerted of simple ways to communicate with elected officials via petitions, phone calls, and other calls-to-action, and are invited to participate in advocacy and policy-related events. A second goal of AIM is to explore new treatments strategies by funding research. Drugs

that seem promising in early-stage studies may not work as hoped in large-scale trials, so it is critical that ADRD research continues to accelerate.

To date, a few initiatives exist to promote dementia-friendly societies. One major existing initiative is the Dementia Friendly America (DFA), a national network of communities, organizations, and individuals seeking to ensure that communities across the U.S. are equipped to support people with ADRD and their caregivers. Dementia friendly communities foster the ability of people living with ADRD to remain in community and engage in day to day living. The DFA also endorses a dementia-friendly communities local government toolkit developed by the Alzheimer's Society of British Columbia. This toolkit explains steps local governments can take to ensure communities are safe and welcoming to people with ADRD. For example, as the toolkit explains, a dementia-friendly community can include a physical environment that is easy to navigate with a variety of landmarks to aid wayfinding. Having small blocks and short streets that are well-connected allows for people with ADRD to more easily navigate their community. Furthermore, local governments can push for community-based supports and services to help people with ADRD maximize independent living. For example, wellness programs help people with ADRD, reduce severity of symptoms and thus necessary treatment. Dementia-focused programs, such as Dementia Friends, and community trainings, can leverage the broader community in providing a support network. Also, employers' policies that can better accommodate caregivers' responsibilities can help alleviate the burden experienced by caregivers. Likewise, education, counseling, and support for caregivers and their families allows them to continue their critical role in supporting people with ADRD. Further information regarding this local government

toolkit is found here: https://alzheimer.ca/sites/default/files/files/bc/advocacy-and-education/dfc/dfc_toolkit_v.jan2016.pdf.

Neighborhood environments are important for public health. Recently, neighborhoods have received more attention for aging in place initiatives by organizations such as the Alzheimer's Association and the U.S. Centers for Disease Control and Prevention. Greater knowledge of how neighborhood environment impacts ADRD may allow cities to design communities with the needs of the ADRD community in mind, moving towards the establishment of dementia-friendly communities. This way, policy can support dementia-friendly neighborhoods that help people with ADRD to continue to engage in everyday activities (186). By promoting access to outdoor spaces and designing safe and comfortable environments, decisionmakers can help people with ADRD remain in their neighborhoods independently for a longer time, maintaining a high quality of life, and stronger sense of independence. Thus, improved environments for older adults could help address the national public health challenge presented by ADRD, by delaying or preventing use of assisted living facilities. This would reduce the cost of ADRD on society, as well as the burden imposed on the patient and their family (233).

IMPLICATIONS FOR RESEARCH

Future work of this dissertation could include an examination of economic inequalities of ADRD incidence by race across SC. In Aim 1 of the present dissertation, we observed that higher proportion of NHB residents and high poverty rates were associated with greater ADRD incidence, compared to lower proportion of NHB residents and low poverty rates. Given these concurrent findings and knowledge that

differences in health outcomes and behaviors do not cluster along racial biological dimensions, but instead are reinforced under conditions of inequity and differential sociocultural contexts, a thorough examination by race is warranted. Previous studies demonstrated that greater racialized economic segregation was associated with other health outcomes (67), such as cancer (130). Future research could assess if a similar pattern for ADRD exists in SC by race. Such studies may help in understanding the mechanisms by which neighborhood environments influence ADRD risk. Understanding the specific pathways by which disadvantaged neighborhoods contribute to population risk of ADRD may be useful for identifying modifiable neighborhood characteristics to target for primary prevention of racial disparities.

Future work could also include examining additional important neighborhood variables that may play a role in influencing ADRD incidence, NPS, and caregiver mental health, such as green space (e.g. parks or recreational facilities), traffic, air pollution, and the food environment (e.g. presence of grocery stores). While Aim 1 considered air pollution and the food environment, these measures were not considered for Aim 2 & 3. Similarly, Aim 1 assessed both of these variables at a large geographic scale (i.e., county level). In future studies, these variables can be assessed at smaller, potentially more meaningful scales (e.g., census tracts or spatial buffers). Exploring the use of additional measures to capture other neighborhood dimensions may also be useful for both primary and secondary forms of prevention. Measuring specific neighborhood characteristics (e.g., local access to businesses and services), exposures (e.g. crimes), and social processes (e.g., social cohesion) may help us better understand the underlying

mechanism by which high poverty is associated with adverse health outcomes, including ADRD incidence.

Moreover, future work should assess the relationship between neighborhood environments and ADRD incidence, NPS, and caregiver mental health outcomes longitudinally. Longitudinal studies could, for example, establish temporality as well as account for individuals' residential mobility. Longitudinal studies may limit reverse causation and test etiologic hypotheses to disentangle the effects of the living environment on health from the influence of individual risk factors (82). Because ADRD does not have a cure, and the social, emotional, economic, and physical costs of these conditions remain significant, research must work to elucidate environmental drivers for ADRD and test macro-level changes to promote improved quality of life and better health outcomes in this population. These changes may take the form of additional neighborhood features to allow those with ADRD to live safely and independently in their community or to aid caregivers through supportive neighborhood environments that buffer impacts of caregiving.

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APPENDIX A:

MAPS OF SOUTH CAROLINA AND TABLES OF DATA SOURCES

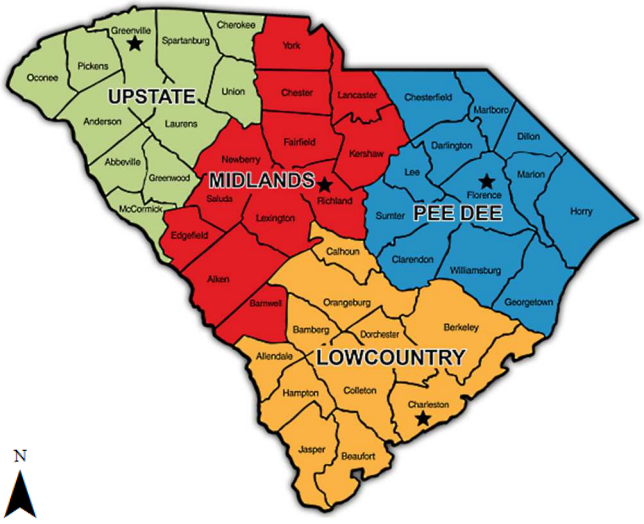

Figure A.1. South Carolina Department of Health and Environmental Control Public Health Regions

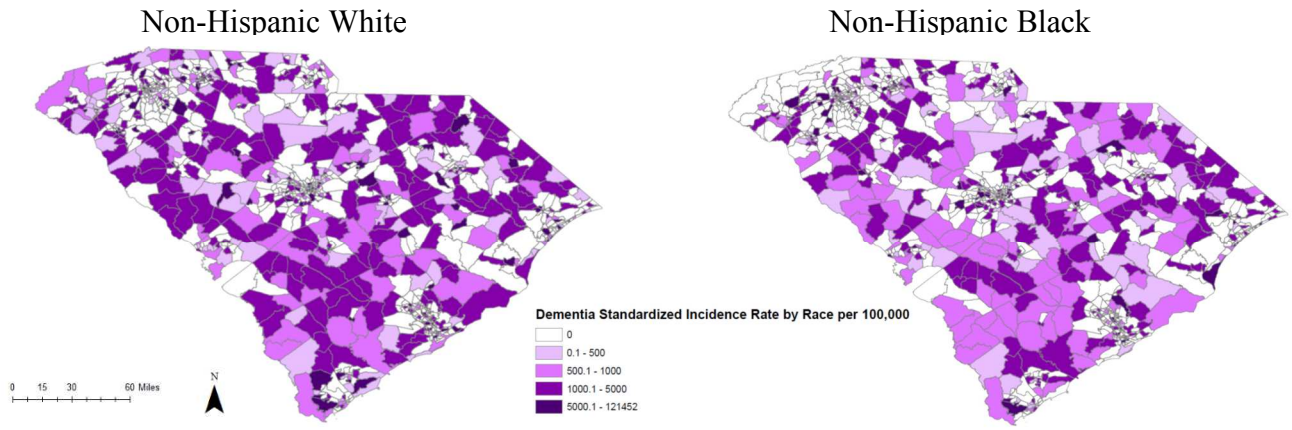

Figure A.2. Alzheimer's Disease and Related Dementia Standardized Incidence Rate by Census Tract among Non-Hispanic white and black, separately (n=1089), 2010-2014, SC

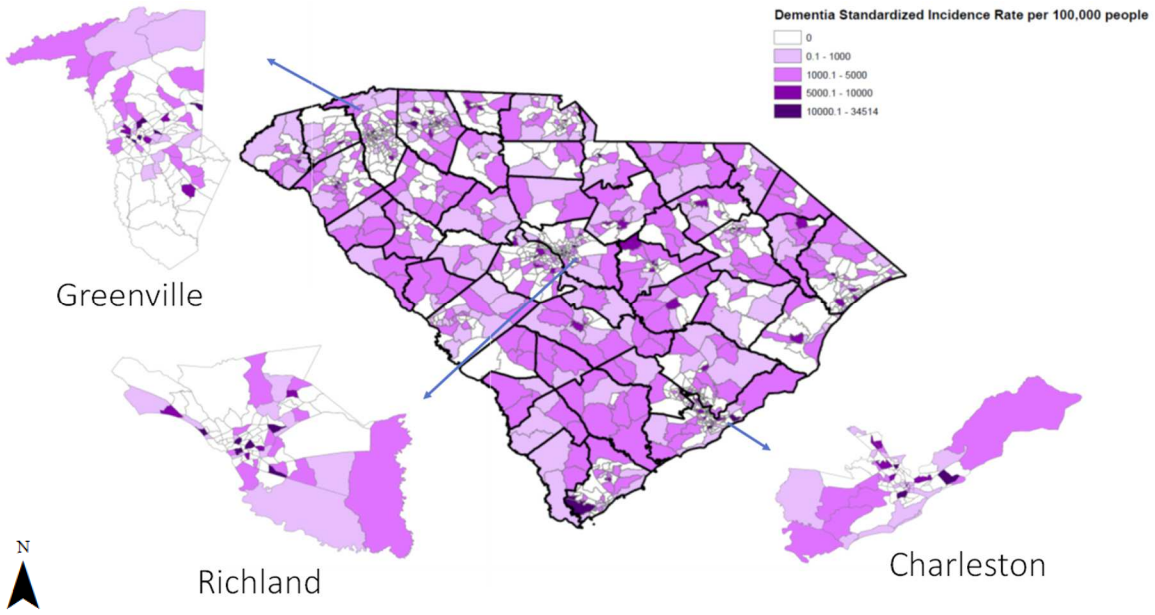

Figure A.3. Alzheimer's Disease and Related Dementia Standardized Incidence Rate by Census Tract and Enlarged for Greenville, Richland, and Charleston Counties (n=1089), 2010-2014, SC

Table A.1. Study Variables' Data Sources

Variables	Definition	Source
Proportion ≥50 years old	Percent of both sexes of total population ≥50 years	Decennial Census Summary File 1 (QTP1)
Proportion NHB	Percent of total population non-Hispanic black or African American	Decennial Census Summary File 1 (QTP3)
Poverty	Percent of families below federal poverty line	American Community Survey 2010-2014 (S1702)
Rurality	Large urban (metropolitan area core); Small Urban (metropolitan area high commuting and metropolitan area low commuting); Rural (micropolitan area core, micropolitan high commuting, micropolitan low commuting, small town core, small town high commuting, small town low commuting, and rural areas)	Rural Urban Commuting Area Code
Quality Care Rank	Preventable hospital stays rate per 1,000 Medicare enrollees; Percent of diabetics that receive HbA1c Screening; Percent of females that receive mammography screening	County Health Rankings (Dartmouth Atlas of Health Care); 2010
Air Pollution Z-score	Daily fine particulate matter (average daily measure in micrograms per cubic meter)	County Health Rankings (Centers for Disease Control and Prevention Wonder); 2008
Limited Access to Healthy Food Environment Z-score	Percent of population who live in poverty and more than 1 or 10 miles from a grocery store	County Health Rankings (United States Department of Agriculture Food Environment Atlas); 2912

Table A.2. Distribution of ADRD Incident Cases in SC, 2010-2014

Variable	**Percent (N)**
Age, mean (S.D.)	79.38 (10.53)
50-74 years	32.86 (20227)
≥75 years	67.14 (41337)
Sex	
Male	39.78 (24488)
Female	60.22 (37076)
Race/ethnicity	
Non-Hispanic White	67.69 (41671)
Non-Hispanic Black	23.30 (14343)
Hispanic	0.27 (166)
Asian	0.10 (63)
Native American	3.32 (2042)
Other	0.39 (239)
Unknown	4.94 (3040)

APPENDIX B:

RATE RATIOS OF NEUROPSYCHIATRIC SYMPTOMS BY NEIGHBORHOOD CHARACTERISTICS

Table B.1. Comparing Community-Dwelling Older Adults with Alzheimer's Disease Living with a Caregiver Demographics Among Those in Study Sample vs Full Sample, 2010, SC

Care Recipient Demographics	**Co-Habited AD Patients from Study Sample (n=212)**	**All Co-Habited AD Patients from Registry Subsample (n=283)**
	Percentage (N)	**Percentage (N)**
NPI total score, mean (S.D.)	26.33 (22.35)	27.10 (22.59)
Age, mean (S.D.)	82.42 (8.72)	82.72 (8.57)
Sex		
Male	27.36 (58)	27.21 (77)
Female	72.64 (154)	72.79 (206)
Race		
Non-Hispanic black	58.49 (124)	55.83 (158)
Other[a]	41.51 (88)	44.17 (125)
Caregiver Education		
<8th grade	35.38 (75)	38.52 (109)
8th – 12th grade	25.00 (53)	22.61 (64)
≥High School[b]	31.33 (66)	28.98 (82)
Unknown/Refused	8.49 (18)	9.89 (28)

[a]Other race included non-Hispanic white (n=87), Hispanic (n=1), and Asian (n=1).
[b]Caregiver education high school and more included those who completed the GED (n=46), some college (n=15), and graduated college (n=5).

Table B.2. Unadjusted and Adjusted Multivariable Negative Binomial Regression Analysis of Neighborhood Characteristics Associated with Apathy, 2010, SC (n=212)

Variable	Unadjusted RR (95% CI)	Adjusted[c] RR (95% CI)
Rurality[a]		
Rural	0.79 (0.46-1.36)	0.69 (0.36 - 1.30)
Small Urban	0.55 (0.29-1.05)	0.47 (0.23 – 0.94)*
Large Urban	1.00[d]	1.00[d]
Median household income		
Low (<$30,500)	0.92 (0.51-1.64)	1.25 (0.63 – 2.50)
Medium ($30,500-40)	0.72 (0.40-1.28)	0.87 (0.46 - 1.65)
High (>$40,000)	1.00[d]	1.00[d]
Residential Instability[b]	0.95 (0.85-1.06)	0.93 (0.82 - 1.05)

[a]Rurality was measured based on the RUCA (Rural Urban Commuting Area codes) where large urban was defined as metropolitan area care; small urban was defined as metropolitan area high commuting and metropolitan area low commuting; and rural was defined as micropolitan area core, micropolitan high commuting, micropolitan low commuting, small town core, small town high commuting, small town low commuting, and rural areas.
[b]Residential instability was defined as the percent who moved the past year.
[c]Model was adjusted for individual AD patient age, sex, race, and caregiver education.
[d]Reference category.
*p<.05

Table B.3. Unadjusted and Adjusted Multivariable Negative Binomial Regression Analysis of Neighborhood Characteristics Associated with Agitation, 2010, SC (n=212)

Variable	Unadjusted RR (95% CI)	Adjusted[c] RR (95% CI)
Rurality[a]		
Rural	0.75 (0.49-1.14)	0.62 (0.38 – 1.01)*
Small Urban	0.62 (0.38-1.03)	0.60 (0.36 - 1.02)*
Large Urban	1.00[d]	1.00[d]
Median household income		
Low (<$30,500)	1.12 (0.71-1.76)	1.53 (0.92 - 2.56)
Medium ($30,500-40)	0.88 (0.56-1.38)	1.20 (0.73 – 1.97)
High (>$40,000)	1.00[d]	1.00[d]
Residential Instability[b]	0.84 (0.85-1.03)	0.92 (0.83 - 1.01)

[a]Rurality was measured based on the RUCA (Rural Urban Commuting Area codes) where large urban was defined as metropolitan area care; small urban was defined as metropolitan area high commuting and metropolitan area low commuting; and rural was defined as micropolitan area core, micropolitan high commuting, micropolitan low commuting, small town core, small town high commuting, small town low commuting, and rural areas.
[b]Residential instability was defined as the percent who moved the past year.
[c]Model was adjusted for individual AD patient age, sex, race, and caregiver education.
[d]Reference category.
*p<.05

Table B.4. Unadjusted and Adjusted Multivariable Negative Binomial Regression Analysis of Neighborhood Characteristics Associated with Irritability, 2010, SC (n=212)

Variable	Unadjusted RR (95% CI)	Adjusted[c] RR (95% CI)
Rurality[a]		
Rural	0.88 (0.54-1.44)	0.51 (0.29 - 0.89)**
Small Urban	0.40 (0.22-0.74)	0.29 (0.15 - 0.55)**
Large Urban	1.00[d]	1.00[d]
Median household income		
Low (<$30,500)	1.56 (0.91-2.30)	2.37 (1.30 - 4.33)**
Medium ($30,500-40)	1.05 (0.61-1.80)	1.57 (0.89 – 2.77)
High (>$40,000)	1.00[d]	1.00[d]
Residential Instability[b]	0.98 (0.88-1.10)	0.94 (0.83 - 1.04)

[a]Rurality was measured based on the RUCA (Rural Urban Commuting Area codes) where large urban was defined as metropolitan area care; small urban was defined as metropolitan area high commuting and metropolitan area low commuting; and rural was defined as micropolitan area core, micropolitan high commuting, micropolitan low commuting, small town core, small town high commuting, small town low commuting, and rural areas.
[b]Residential instability was defined as the percent who moved the past year.
[c]Model was adjusted for individual AD patient age, sex, race, and caregiver education.
[d]Reference category.
**p<.01

APPENDIX C:

RATE RATIOS OF CAREGIVER MENTAL HEALTH OUTCOMES BY NEIGHBORHOOD CHARACTERISTICS

Table C.1. Comparing Caregiver Demographics Among Those in Study Sample vs Full Sample, 2010, SC

Caregiver Demographics	**Co-Habited Caregivers from Study Sample (n=212)**	**All Co-Habited Caregivers from Registry subsample (n=224)**
	Percentage (N)	**Percentage (N)**
CESD score, mean (S.D.)	10.27 (6.31)	10.25 (6.42)
ZBI score, mean (S.D.)	5.91 (3.95)	5.87 (3.94)
NPI-Q-CESD, mean (S.D.)	12.17 (10.42)	12.38 (10.66)
Age, mean (S.D.)	58.96 (11.09)	58.80 (10.19)
Sex		
Male	14.62 (31)	14.8 (33)
Female	85.38 (181)	85.2 (191)
Race/Ethnicity		
Non-Hispanic black	55.19 (117)	55.16 (124)
Other	44.81 (95)	44.84 (100)
Employment		
Employed	33.02 (70)	32.29 (72)
Retired/Unemployed	53.3 (113)	32.29 (72)
Other	13.68 (29)	13.90 (32)

Relationship to Care Recipient		
Spouse	16.51 (35)	16.14 (36)
Child	67.92 (144)	67.71 (152)
Other	15.57 (33)	16.14 (36)

Table C.2. Unadjusted and Adjusted Multivariable Negative Binomial Regression Analysis of Neighborhood Characteristics Defined at the 3-Mile Buffer Associated with Caregiver Depressive Symptoms, 2010, SC

Variable	Severe Neuropsychiatric Symptoms (n=112)[c]		Non-severe Neuropsychiatric Symptoms (n=100)[c]	
	Unadjusted RR (95% CI)	Adjusted[d] RR (95% CI)	Unadjusted RR (95% CI)	Adjusted[d] RR (95% CI)
Rurality[a]				
Rural	1.05 (0.83-1.35)	0.98 (0.75-1.27)	0.88 (0.65-1.22)	0.98 (0.69-1.39)
Small urban	0.89 (0.66-1.19)	0.96 (0.71-1.28)	0.89 (0.62-1.28)	1.02 (0.68-1.51)
Large urban	1.00[e]	1.00[e]	1.00[e]	1.00[e]
Percent moved 1 year ago	1.03 (0.95-1.12)	1.04 (0.95-1.12)	0.98 (0.89-1.09)	0.98 (0.89-1.09)
Median household income[b]				
Low	1.18 (0.91-1.53)	1.33 (1.00-1.78)	0.82 (0.59-1.14)	0.80 (0.56-1.17)
Medium	1.19 (0.93-1.54)	1.25 (0.97-1.61)	0.74 (0.53-1.05)	0.77 (0.53-1.12)
High	1.00[e]	1.00[e]	1.00[e]	1.00[e]

[a]Rurality was measured based on the RUCA (Rural Urban Commuting Area codes). Large urban area was defined as metropolitan area; small urban area was defined as metropolitan area high commuting and metropolitan area low commuting; and rural defined as micropolitan area core, micropolitan high commuting, micropolitan low commuting, small town core, small town high commuting, small town low commuting, and rural areas.
[b]Median household income categories based on tertiles where low was (<$34,352), medium ($34,352-41,927), and high (>$41,927).
[c]Severe neuropsychiatric symptoms among those with AD defined as >median.

[d]Model adjusted for caregiver age, sex, race/ethnicity, employment, relationship to care recipient and sandwich caregiver status.
[e]Reference category.

Table C.3. Unadjusted and Adjusted Multivariable Negative Binomial Regression Analysis of Neighborhood Characteristics Defined at the 3-Mile Buffer Associated with Caregiver Burden, 2010, SC (n=212)

Variable	Severe Neuropsychiatric Symptoms (n=112)[e]		Non-severe Neuropsychiatric Symptoms (n=100)[e]	
	Unadjusted RR (95% CI)	Adjusted[d] RR (95% CI)	Unadjusted RR (95% CI)	Adjusted[d] RR (95% CI)
Rurality[a]				
Rural	0.87 (0.67-1.12)	0.87-0.65-1.17)	0.89 (0.60-1.32)	0.99 (0.65-1.51)
Small urban	0.93 (0.68-1.25)	1.02 (0.74-1.40)	0.86 (0.55-1.36)	0.94 (0.59-1.50)
Large urban	1.00[e]	1.00[e]	1.00[e]	1.00[e]
Percent moved 1 year ago	1.03 (0.95-1.11)	1.02 (0.94-1.11)	0.96 (0.85-1.09)	0.95 (0.83-1.07)
Median household income[b]				
Low	0.91 (0.70-1.19)	1.05 (0.77-1.33)	0.88 (0.59-1.33)	0.90 (0.57-1.44)
Medium	0.94 (0.72-1.22)	1.01 (0.77-1.33)	0.65 (0.42-1.00)	0.74 (0.47-1.17)
High	1.00[e]	1.00[e]	1.00[e]	1.00[e]

[a]Rurality was measured based on the RUCA (Rural Urban Commuting Area codes). Large urban area was defined as metropolitan area; small urban area was defined as metropolitan area high commuting and metropolitan area low commuting; and rural defined as micropolitan area core, micropolitan high commuting, micropolitan low commuting, small town core, small town high commuting, small town low commuting, and rural areas.
[b]Median household income categories based on tertiles where low was (<$34,352), medium ($34,352-41,927), and high (>$41,927).
[c]Severe neuropsychiatric symptoms among those with AD defined as >median.

[d]Model adjusted for caregiver age, sex, race/ethnicity, employment, relationship to care recipient and sandwich caregiver status.
[e]Reference category.

Table C.4. Unadjusted and Adjusted Multivariable Negative Binomial Regression Analysis of Neighborhood Characteristics Defined at the 3-Mile Buffer Associated with Caregiver Distress, 2010, SC (n=212)

Variable	Severe Neuropsychiatric Symptoms (n=112)[e]		Non-severe Neuropsychiatric Symptoms (n=100)[e]	
	Unadjusted RR (95% CI)	Adjusted[d] RR (95% CI)	Unadjusted RR (95% CI)	Adjusted[d] RR (95% CI)
Rurality[a]				
Rural	0.87 (0.67-1.12)	0.76 (0.61-0.95)	0.89 (0.59-1.32)	0.53 (0.29-1.01)
Small urban	0.93 (0.68-1.25)	0.89 (0.70-1.15)	0.87 (0.55-1.36)	0.63 (0.31-1.27)
Large urban	1.00[e]	1.00[e]	1.00[e]	1.00[e]
Percent moved 1 year ago	1.02 (0.95-1.11)	0.99 (0.92-1.05)	0.96 (0.85-1.09)	0.93 (0.78-1.11)
Median household income[b]				
Low	0.91 (0.69-1.19)	1.61 (1.26-2.04)	0.88 (0.59-1.33)	1.50 (0.73-3.08)
Medium	0.94 (0.72-1.22)	1.45 (1.17-1.78)	0.65 (0.42-0.99)	1.20 (0.63-2.28)
High	1.00[e]	1.00[e]	1.00[e]	1.00[e]

[a]Rurality was measured based on the RUCA (Rural Urban Commuting Area codes). Large urban area was defined as metropolitan area; small urban area was defined as metropolitan area high commuting and metropolitan area low commuting; and rural defined as micropolitan area core, micropolitan high commuting, micropolitan low commuting, small town core, small town high commuting, small town low commuting, and rural areas.
[b]Median household income categories based on tertiles where low was (<$34,352), medium ($34,352-41,927), and high (>$41,927)
[c]Severe neuropsychiatric symptoms among those with AD defined as >median.

[d]Model adjusted for caregiver age, sex, race/ethnicity, employment, relationship to care recipient and sandwich caregiver status.
[e]Reference category.

Table C.5. Unadjusted and Adjusted Multivariable Negative Binomial Regression Analysis of Neighborhood Characteristics Defined at the 1-Mile Buffer Associated with Caregiver Depressive Symptoms, 2010, SC

Variable	Unadjusted RR (95% CI)	Adjusted[d] RR (95% CI)
Rurality[a]		
Rural	0.96 (0.78-1.17)	0.97 (0.77-1.21)
Small urban	0.86 (0.68-1.09)	0.91 (0.71-1.16)
Large urban	1.00[c]	1.00[c]
Percent moved 1 year ago	1.01 (0.94-1.08)	1.00 (0.94-1.07)
Median household income[b]		
Low	0.99 (0.80-1.23)	1.04 (0.83-1.32)
Medium	0.99 (0.79-1.23)	1.04 (0.83-1.30)
High	1.00[c]	1.00[c]

[a]Rurality was measured based on the RUCA (Rural Urban Commuting Area codes). Large urban area was defined as metropolitan area; small urban area was defined as metropolitan area high commuting and metropolitan area low commuting; and rural defined as micropolitan area core, micropolitan high commuting, micropolitan low commuting, small town core, small town high commuting, small town low commuting, and rural areas.
[b]Median household income categories based on tertiles where low was (<$31,000), medium ($31-40,758), and high (>$40,758).
[c]Reference category.
[d]Model adjusted for caregiver age, sex, race/ethnicity, employment, relationship to care recipient and sandwich caregiver status.

Table C.6. Unadjusted and Adjusted Multivariable Negative Binomial Regression Analysis of Neighborhood Characteristics Defined at the 1-Mile Buffer Associated with Caregiver Burden Score, 2010, SC

Variable	Unadjusted RR (95% CI)	Adjusted[d] RR (95% CI)
Rurality[a]		
Rural	0.84 (0.67-1.06)	0.89 (0.69-1.15)
Small urban	0.86 (0.65-1.13)	0.93 (0.70-1.22)
Large urban	1.00[c]	1.00[c]
Percent moved 1 year ago	1.00 (0.93-1.07)	0.98 (0.91-1.05)
Median household income[b]		
Low	0.88 (0.69-1.12)	1.00 (0.77-1.31)
Medium	0.82 (0.64-1.05)	0.94 (0.73-1.21)
High	1.00[c]	1.00[c]

[a]Rurality was measured based on the RUCA (Rural Urban Commuting Area codes). Large urban area was defined as metropolitan area; small urban area was defined as metropolitan area high commuting and metropolitan area low commuting; and rural defined as micropolitan area core, micropolitan high commuting, micropolitan low commuting, small town core, small town high commuting, small town low commuting, and rural areas.
[b]Median household income categories based on tertiles where low was (<$31,000), medium ($31-40,758), and high (>$40,758).
[c]Reference category.
[d]Model adjusted for caregiver age, sex, race/ethnicity, employment, relationship to care recipient and sandwich caregiver status.

Table C.7. Unadjusted and Adjusted Multivariable Negative Binomial Regression Analysis of Neighborhood Characteristics Defined at the 1-Mile Buffer Associated with Caregiver Distress Score, 2010, SC

Variable	Unadjusted RR (95% CI)	Adjusted[d] RR (95% CI)
Rurality[a]		
Rural	0.78 (0.57-1.07)	0.65 (0.45-0.94)
Small urban	0.78 (0.53-1.12)	0.71 (0.48-1.03)
Large urban	1.00[c]	1.00[c]
Percent moved 1 year ago	0.98 (0.88-1.09)	0.94 (0.84-1.04)
Median household income[b]		
Low	1.14 (0.81-1.60)	1.55 (1.05-2.28)
Medium	1.14 (0.81-1.59)	1.49 (1.05-2.11)
High	1.00[c]	1.00[c]

[a]Rurality was measured based on the RUCA (Rural Urban Commuting Area codes). Large urban area was defined as metropolitan area; small urban area was defined as metropolitan area high commuting and metropolitan area low commuting; and rural defined as micropolitan area core, micropolitan high commuting, micropolitan low commuting, small town core, small town high commuting, small town low commuting, and rural areas.
[b]Median household income categories based on tertiles where low was (<$31,000), medium ($31-40,758), and high (>$40,758).
[c]Reference category.
[d]Model adjusted for caregiver age, sex, race/ethnicity, employment, relationship to care recipient and sandwich caregiver status.

Table C.8. Unadjusted and Adjusted Multivariable Negative Binomial Regression Analysis of Neighborhood Characteristics Defined at the 3-Mile Buffer Associated with Caregiver Depressive Symptoms, 2010, SC

Variable	Unadjusted RR (95% CI)	Adjusted[d] RR (95% CI)
Rurality[a]		
Rural	0.96 (0.78-1.17)	0.97 (0.77-1.21)
Small urban	0.86 (0.68-1.09)	0.91 (0.71-1.16)
Large urban	1.00[c]	1.00[c]
Percent moved 1 year ago	1.01 (0.94-1.08)	1.00 (0.94-1.07)
Median household income[b]		
Low	0.99 (0.80-1.23)	1.05 (0.83-1.32)
Medium	0.99 (0.79-1.23)	1.04 (0.83-1.30)
High	1.00[c]	1.00[c]

[a]Rurality was measured based on the RUCA (Rural Urban Commuting Area codes). Large urban area was defined as metropolitan area; small urban area was defined as metropolitan area high commuting and metropolitan area low commuting; and rural defined as micropolitan area core, micropolitan high commuting, micropolitan low commuting, small town core, small town high commuting, small town low commuting, and rural areas.
[b]Median household income categories based on tertiles where low was (<$34,352), medium ($34,352-41,927), and high (>$41,927).
[c]Reference category.
[d]Model adjusted for caregiver age, sex, race/ethnicity, employment, relationship to care recipient and sandwich caregiver status.

Table C.9. Unadjusted and Adjusted Multivariable Negative Binomial Regression Analysis of Neighborhood Characteristics Defined at the 3-Mile Buffer Associated with Caregiver Burden Score, 2010, SC

Variable	Unadjusted RR (95% CI)	Adjusted[d] RR (95% CI)
Rurality[a]		
Rural	0.84 (0.67-1.06)	0.89 (0.69-1.15)
Small urban	0.86 (0.65-1.13)	0.93 (0.70-1.22)
Large urban	1.00[c]	1.00[c]
Percent moved 1 year ago	0.99 (0.93-1.08)	0.98 (0.91-1.05)
Median household income[b]		
Low	0.88 (0.69-1.12)	1.00 (0.77-1.31)
Medium	0.82 (0.64-1.05)	0.94 (0.73-1.21)
High	1.00[c]	1.00[c]

[a]Rurality was measured based on the RUCA (Rural Urban Commuting Area codes). Large urban area was defined as metropolitan area; small urban area was defined as metropolitan area high commuting and metropolitan area low commuting; and rural defined as micropolitan area core, micropolitan high commuting, micropolitan low commuting, small town core, small town high commuting, small town low commuting, and rural areas.
[b]Median household income categories based on tertiles where low was (<$34,352), medium ($34,352-41,927), and high (>$41,927).
[c]Reference category.
[d]Model adjusted for caregiver age, sex, race/ethnicity, employment, relationship to care recipient and sandwich caregiver status.

Table C.10. Unadjusted and Adjusted Multivariable Negative Binomial Regression Analysis of Neighborhood Characteristics Defined at the 3-Mile Buffer Associated with Caregiver Distress Score, 2010, SC

Variable	Unadjusted RR (95% CI)	Adjusted[d] RR (95% CI)
Rurality[a]		
Rural	0.77 (0.57-1.07)	0.65 (0.45-0.94)
Small urban	0.77 (0.53-1.12)	0.71 (0.48-1.03)
Large urban	1.00[c]	1.00[c]
Percent moved 1 year ago	0.98 (0.88-1.09)	0.94 (0.84-1.04)
Median household income[b]		
Low	1.14 (0.81-1.59)	1.55 (1.05-2.28)
Medium	1.14 (0.81-1.59)	1.49 (1.05-2.11)
High	1.00[c]	1.00[c]

[a]Rurality was measured based on the RUCA (Rural Urban Commuting Area codes). Large urban area was defined as metropolitan area; small urban area was defined as metropolitan area high commuting and metropolitan area low commuting; and rural defined as micropolitan area core, micropolitan high commuting, micropolitan low commuting, small town core, small town high commuting, small town low commuting, and rural areas.
[b]Median household income categories based on tertiles where low was (<$34,352), medium ($34,352-41,927), and high (>$41,927).
[c]Reference category.
[d]Model adjusted for caregiver age, sex, race/ethnicity, employment, relationship to care recipient and sandwich caregiver status.