MILD COGNITIVE IMPAIRMENT IN OLDER, RURAL-DWELLING ADULTS

by

Meghan K. Mattos

B.A. in History and Religious Studies, University of Virginia, 2006

M.S.N., University of Virginia, 2009

Submitted to the Graduate Faculty of

Nursing in partial fulfillment

of the requirements for the degree of

Doctor of Philosophy in Nursing

University of Pittsburgh

2016

UNIVERSITY OF PITTSBURGH

NURSING

This dissertation was presented

by

Meghan K. Mattos

It was defended on

September 22, 2016

and approved by

Susan M. Sereika, PhD, Professor, Health and Community Systems

Beth E. Snitz, PhD, Assistant Professor, Neurology

Lorraine M. Novosel, PhD, Assistant Professor, Health Promotion and Development

Dissertation Co-Chair: Lora E. Burke, PhD MPH, Professor, Health and Community Systems

Dissertation Co-Chair: Jennifer H. Lingler, PhD, Associate Professor, Health and Community

Systems

MILD COGNITIVE IMPAIRMENT IN OLDER, RURAL-DWELLING ADULTS

Meghan K. Mattos, MSN

University of Pittsburgh, 2016

Introduction: Rural-dwelling adults are particularly vulnerable to cognitive problems given known higher rates of associated risk factors and limited resources and access to care. Early cognitive changes remain understudied in this population.

Objective: To determine if and how rural residence is a unique risk factor for delayed detection of early-stage cognitive impairment.

Methods: Studies 1 and 2 involved secondary data analyses of the National Alzheimer's Coordinating Center Uniform Data Set and compared older rural- and urban-dwelling adults on key characteristics and cognitive symptom severity. *Study 1* used a cross-sectional design to examine sociodemographic factors, comorbid conditions and cognitive symptom severity between groups. *Study 2* used the same variables from Study 1, to examine possible differences in results using two geographic classification schemes. Studies 3 and 4 used qualitative methods including semi-structured, in-home interviews with participants with early cognitive changes and care partners. *Study 3* explored perceived determinants of health in these rural-dwelling dyads using thematic content analysis. *Study 4* described their subjective experiences at three time periods around a specialty research center visit.

Results: *Study 1*. Rural and urban groups differed significantly in mean (±SD) years since onset of cognitive symptoms (2.98±1.91 in rural and 3.89±2.70 in urban adults, t[260]= -2.23, *P* = .03), but they did not differ across sociodemographic features, comorbid conditions, or cognitive symptom severity. *Study 2*. Results varied both in magnitude and direction of odds ratio

differences between two geographic classification schemes for outcome variables. *Study 3.* Six

themes emerged about perceived determinants of health: 1) Staying active, 2) Eating well, 3)

Living with cognitive changes, 4) Living rural, 5) Connecting with neighbors and community,

and 6) Relying on children. *Study 4.* Dyad experiences varied across the three time periods.

Dyads sought to learn more about cognitive symptoms and described the impact of cognitive

changes on everyday life.

Conclusions: There were no significant differences in cognitive symptom severity between

rural- and urban-dwelling participants. Qualitative findings highlight critical aspects of rural

adults' perceived determinants of health and reactions to cognitive symptoms and diagnosis,

which may be used to help target earlier diagnosis and improve long-term disease management.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

PREFACE

There are not enough words to thank all of the individuals who have provided support, guidance, and patience during my PhD journey. Firstly, I would like to thank my dissertation committee. Thank you, Dr. Lora Burke, for sticking with me since our first meeting the summer before I began my doctoral work. You taught me what it means to do research in an academic setting, always leading by example and drawing upon your research expertise. You are a devoted and incredible mentor, making sure every anticipated or unanticipated need is met, and I am so very thankful. Dr. Jennifer Lingler, I don't know what I would have done without your guidance through the development of my dissertation research and beyond. You have offered me endless opportunities and direction which have led me to where I am today. Your love for research, nursing, and teaching is apparent in all that you do, and I am lucky to call you a mentor. Dr. Susan Sereika, thank you for your mentorship since before I knew how to do logistic regression. Your countless hours of teaching have provided me with the tools for my dissertation research, other research endeavors, and future research. Dr. Beth Snitz, thank you for offering your expertise and recommendations on a topic that was once new to me and helping me look beyond the obvious. Dr. Lorraine Novosel, thank you for supporting me during my doctoral program, beginning with your mentorship on my first doctoral publication to sharing your analytical skills and keen attention to detail. Thank you, Dr. Marianne Baernholdt. You single-handedly introduced me to the world of research and rural health, which led me to pursue my PhD and this research trajectory. Thank you, Dr. Judith Erlen, for believing in me and supporting me. Your kindness, honesty, and guidance has been unconditional and invaluable.

1.0   PROPOSAL

1.1   SPECIFIC AIMS

Although more than 20% of the United States (US) population live in rural areas (US Department of Agriculture Economic Research Service, 2013a), those residing in such areas constitute an underserved and understudied population. Healthy People 2020 calls for the elimination of disparities, and rural-dwelling persons are recognized as a population that health equity efforts should target (*The Vision, Mission, and Goals of Healthy People 2020*, 2011). Rural adults suffer disproportionately poorer health and worse health outcomes compared with the rest of the nation (Behringer & Friedell, 2006; Borak, Salipante-Zaidel, Slade, & Fields, 2012; Eberhardt & Pamuk, 2004), with rural-dwelling adults having higher rates of cardiovascular disease (CVD) and cerebrovascular disease than their urban counterparts (Halverson, Ma, & Harner, 2004). Considerably less research has focused on cognitive health and the risk factors associated with poor cognitive health among older, rural-dwelling adults. Chief among these poor cognitive health outcomes are late life cognitive disorders like mild cognitive impairment (MCI). MCI is a clinical syndrome that is widely recognized as a risk state for Alzheimer's disease (AD) and other dementias, and therefore, represents a key target for interventions aimed at the secondary prevention of dementia.

The prevalence of MCI is estimated to be as high as 19% among US older adults (Gauthier et al., 2006). MCI 1) involves decline in at least one cognitive domain, 2) requires maintenance of near normal functional activities, and 3) requires that the degree of cognitive impairment is not sufficient to warrant a diagnosis of AD or related dementia (Gauthier et al., 2006; Petersen et al., 2001). Subtle changes in cognition may not initially appear to directly affect daily living, but often significantly worsen over time. We believe that older, rural adults are especially vulnerable to MCI based on known higher rates of factors associated with the syndrome (e.g. diabetes and cerebrovascular disease (Gamm, Hutchison, Dabney, & Dorsey, 2003; Keppel, Pearcy, & Klein, 2004). Complicating matters, limited resources and access to care may lead to delayed detection of cognitive changes, making rural adults an especially vulnerable group that is possibly deprived of future opportunities for screening and early intervention in the disease process. Based on known rural health disparities, especially later diagnosis of chronic diseases, we believed it reasonable to hypothesize that MCI may present later in its course in rural adults; however, studies describing older, rural-dwelling adults with MCI had not been documented. This research addressed this void and examined rural adults with MCI and, as such, was innovative in its focus and multi-pronged approach.

We used both quantitative and qualitative methods to examine and gain insight into rural cognitive health. The primary purpose of this study was to determine if rural residence was a unique risk factor for delayed detection of MCI and to identify perceived social determinants of health in this population using the National Alzheimer's Coordinating Center (NACC) Uniform Data Set and qualitative interviews, both recruiting from older adults dwelling in the Appalachian region of the US. Within Appalachia, 42% of residents live in rural areas ("The Appalachian

Region," 2013), making this an ideal sample to address the research question. We proposed a two-phase study, using both quantitative and qualitative methods: (1) use a secondary data analysis approach to describe older Appalachian adults' MCI symptom severity and (2) use qualitative methods to conduct in-depth interviews to explore perceived social determinants of health and experiences surrounding cognitive diagnosis of older, rural-dwelling adults with early-stage cognitive impairment. The Social Determinants of Health and Environmental Health Promotion Model (Schulz & Northridge, 2004) places health outcomes in the greater context of complex systems that impact and promote health, and guided the research.

<u>Aim 1</u>: Compare MCI symptom severity between older rural and non-rural Appalachian adults. Using participant evaluation data from the NACC Uniform Data Set in the Appalachian region, we performed a descriptive study of older adults living in rural and non-rural areas within Appalachia. MCI symptom severity upon initial presentation for a cognitive evaluation was measured across four cognitive domains (memory, language, attention/ psychomotor speed, and executive function) and Clinical Dementia Rating-Sum of Boxes.

Hypothesis 1: Older, rural-dwelling Appalachian adults would present later in the course of MCI symptom progression compared to older, urban-dwelling Appalachian adults.

<u>Exploratory Aim</u>: Using data from Aim 1, we examined the effect of two geographic classification schemes, Rural-Urban Commuting Area Codes (RUCAs) and Rural-Urban Continuum Codes (RUCCs), on descriptive characteristics and variables describing impairment.

<u>Aim 2</u>: From the perspective of older, rural-dwelling Appalachian adults with a diagnosis of early-stage cognitive impairment and their care partners, we:

    a) **explored perceived social determinants of cognitive health** and

b) described experiences of Study 3 dyads at three time periods: pre-Alzheimer Disease Research Center (ADRC) visit, ADRC visit, and post-ADRC visit

Subjects were recruited through the University of Pittsburgh Alzheimer Disease Research Center (ADRC; PI: Lopez, P50AG005133), which included older Appalachian adults and contributes to the NACC UDS. We conducted nine interviews in participant homes to gain insight using a qualitative descriptive methodology until saturation was reached (Sandelowski, 2000, 2010). Ultimately, information from this aim helped identify experiences and perceptions surrounding both MCI and dementia diagnoses that could impact screening, course progression, and management.

Examination of disparities using a large data set and adding a qualitative study exploring needs of those with early-stage cognitive impairment provided the foundation to take the next step in this line of inquiry and focus on preventive or therapeutic interventions for older, rural-dwelling adults with early-stage cognitive impairment. The broad, long-term objectives of this program of research continues to be the reduction in rural health disparities and prevention of further disabilities in this underserved population.

1.2   BACKGROUND AND SIGNIFICANCE

1.2.1 Background

Although more than 20% of the US population live in rural areas (US Department of Agriculture

Economic Research Service, 2013a), rural-residing individuals constitute a clinically underserved and understudied population. Healthy People 2020 calls for the elimination of disparities, and rural-dwelling persons are recognized as a population that health equity efforts should target (*The Vision, Mission, and Goals of Healthy People 2020*, 2011). Rural adults suffer worse overall health and health outcomes when compared with the rest of the nation (Behringer & Friedell, 2006; Borak et al., 2012; Eberhardt & Pamuk, 2004). Specifically, breast, prostate, and colorectal cancers as well as cerebrovascular disease and stroke have greater prevalence and age-adjusted death rates and are diagnosed at later stages than their urban counterparts (Campo et al., 2008; Casey, Thiede Call, & Klingner, 2001; Gamm, Hutchison, Bellamy, & Dabney, 2010; Halverson et al., 2004).

This study focused on the Appalachian region of the US, spanning from southern New York to northern Alabama, Mississippi, and Georgia, and includes both rural and non-rural areas, making it an ideal setting for comparisons of rural and non-rural persons (Appendix 1). The Appalachian region as a whole suffers from inequalities in socioeconomic conditions (*Health, United States, 2012: With Special Feature on Emergency Care*, 2013), behavioral risk factors, and mortality rates compared to the nation as a whole (Halverson et al., 2004). For example, greater rates of behavioral risk factors such as smoking and a sedentary lifestyle (Bennett, Olatosi, & Probst, 2008; Larry Gamm et al., 2010) place rural Appalachian adults at greater risk for CVD and cerebrovascular disease. These disparities mirror those observed in other rural areas. Appalachia has a total population of almost 23 million inhabitants in over 400 counties and 13 states (Halverson et al., 2004). With over double the national percent of rural-dwelling adults within the Appalachian region and a greater proportion of older adults, older rural Appalachian adults are an important, understudied population. Poorer health outcomes in rural Appalachia continue to be

addressed in the literature (Casey et al., 2001; Gamm et al., 2010; Halverson et al., 2004; "The Appalachian Region," 2013), but one condition that is rapidly increasing among older adults is mild cognitive impairment. ("Latest Facts & Figures Report," 2013) which has not yet been examined extensively in this population.

Based on known health disparities and higher rates of risk factors in rural Appalachia, rural-dwelling Appalachian adults may be especially vulnerable to cognitive impairment. Established sociodemographic risk factors for cognitive impairment include older age (Ganguli, Snitz, Hughes, & Chang, 2013; Kryscio, Schmitt, Salazar, Mendiondo, & Markesbery, 2006; Petersen, 2010 Sachdev et al., 2012), lower education (Kryscio et al., 2006; Petersen, 2010), and male gender (Kryscio et al., 2006; Petersen, 2010). Medical conditions associated with cognitive impairment include hypertension (Chen et al., 2012; Ettorre et al., 2012; Sachdev et al., 2012), heart disease (Chen et al., 2012; Ettorre et al., 2012; Sachdev et al., 2012), diabetes (Cheng, Huang, Deng, & Wang, 2012; Crane et al., 2013; Gamm et al., 2003; Keppel et al., 2004), depression (Johnson et al., 2013; Rodríguez-Sánchez et al., 2011; Sachdev et al., 2012; Spira, Rebok, Stone, Kramer, & Yaffe, 2012), and genetic factors (Kryscio et al., 2006; Sachdev et al., 2012). Among these known risk factors, rural Appalachian residents have known lower levels of education (Billings & Blee, 2000; Gillum & Mussolino, 2003) as well as higher rates of hypertension (Eberhardt & Pamuk, 2004), heart disease (Pearson & Lewis, 1998), and diabetes (Pearson & Lewis, 1998).

Rural-dwelling adults face additional barriers to undergoing timely cognitive evaluations and accessing care delivery and have been shown to under-utilize both medical and social services compared to their urban counterparts (Bradford et al., 2009). In a systematic review examining factors contributing to missed and delayed diagnosis of dementias in primary settings, Bradford et

6

al (2009) included 18 original studies (three were solely rural participants) and identified five patient factors contributing to missed or delayed diagnosis of dementia. "Patient characteristics" was one of the factors identified and included descriptions of rural residence (Incalzi, Marra, Gemma, Capparella, & Carbonin, 1992), lower level of education (Ross et al., 1997), older age (Ross et al., 1997; Sternberg, Wolfson, & Baumgarten, 2000), lower severity of dementia (Sternberg et al., 2000), and single marital status (Sternberg et al., 2000). The second factor was "awareness/education about dementia" and included the assumption that cognitive changes were a part of normal aging. "Attitudes", "communication, and "access" were also identified as factors contributing to missed or delayed detection of dementia in the review. In addition to patient-related factors, the authors identified "resources" and "financial" factors are system-related factors contributing to missed and delayed diagnosis. Identified "resources" included "limited time with patients", "insufficient community services available", and "lack of specialists"; "financial factors" included "low financial incentives/reimbursement for dementia care", "limitations on diagnostic tests", and that dementia was not considered a priority in public health planning (Bradford et al., 2009). These factors may also contribute to misdiagnosis or under diagnosis by health care providers and systems.

According to state and national health leaders, access to quality health services remains the most often-cited rural health priority (Gamm & Hutchison, 2003; Gamm et al., 2010). Currently, only 10% of physicians practice in rural areas, while over 20% of Americans currently live in these underserved rural areas (Barley, Reeves, O'Brien-Gonzales, & Westfall, 2001). Average per capita income is also $7,000 lower than in urban areas, and even though 23% of American live in rural areas, over 30% of food stamp beneficiaries live in rural areas (Gamm et al., 2003). The

combination of higher prevalence of risk factors and limited access to care emphasizes the importance of early detection of MCI. Older adults with MCI should be clinically followed as many progress to later develop AD or other forms of dementia ("Latest Facts & Figures Report," 2013). According to the NIH National Institute of Aging (NIA) ("About Alzheimer's Disease: Treatment | National Institute on Aging," n.d.), current approaches in treatment focus on maintenance of mental function, management of behavioral symptoms, and slowing or delaying the symptoms of disease. Some interventions include treating depression and increasing physical activity. There are four primary subtypes of MCI: MCI Amnestic, MCI Non-Amnestic, MCI Multi-Domain, and MCI Single Non-Memory Domain. Although different subtypes of MCI are recognized in the literature, there is mixed evidence for how strongly each subtype of MCI predicts or precedes specific forms of dementia, such as AD (Abner et al., 2012; Busse, Hensel, Gühne, Angermeyer, & Riedel-Heller, 2006; Ganguli, Dodge, Shen, & DeKosky, 2004; Lopez et al., 2003; Ritchie, Artero, & Touchon, 2001). Since MCI is a recognized target for the secondary prevention of dementia, the time of MCI diagnosis may present a critical opportunity for interventions that help reduce health disparities in rural Appalachian adults.

Delayed detection of dementias may lead to increased patient and care partner burden in the long run and a lost opportunity to seek treatment for modifiable risk factors or treatable conditions. Compounding missed or delayed detection, it can be difficult to identify or diagnose cognitive impairment, especially at early stages or for less severe types of dementia (Borson, Scanlan, Watanabe, Tu, & Lessig, 2006). Teel (2004) found in his study examining dementia diagnosis in a rural setting that family recognition and acknowledgement of cognitive changes was largely responsible for a shorter time from symptom onset to time of clinician diagnosis. Findings

8

also supported previously identified limitations to diagnosis, including access to consultants and lack of community support systems (Teel, 2004). A study conducted by DiNapoli, Wu, and Scogin (2013) among Appalachian older adults found that social isolation, social disconnectedness, and perceived isolation predicted worse cognitive functioning and neuropsychological testing (DiNapoli, Wu, & Scogin, 2013). These predictors were based on previous studies that used each of these predictors as a measure of "social isolation," such that persons that are more disconnected report feeling lonelier (Cornwell & Waite, 2009). Health equity research also presents concerns in the definition of certain predictors or risk factors for cognitive impairment, such as race and education. Rural-dwelling residents are known to have overall lower levels of educational attainment, and the measurement of education is crucial to determining the role education plays in cognitive impairment. Education is typically measured as interval data as years of education completed, but current literature suggests that quality of education or literacy may be better predictors of cognitive decline (Ardila et al., 2010; Manly, Jacobs, Touradji, Small, & Stern, 2002; Manly, Schupf, Tang, & Stern, 2005). Additionally, there is conflicting evidence showing an association between educational attainment and dementia (Ardila et al., 2010), which may further support educational attainment as years completed as an inappropriate proxy for education. Finally, the observed higher rates of dementia among persons with low literacy could reflect overdiagnoses or misdiagnoses related to other, unidentified external factors.

1.2.2 Theoretical Model
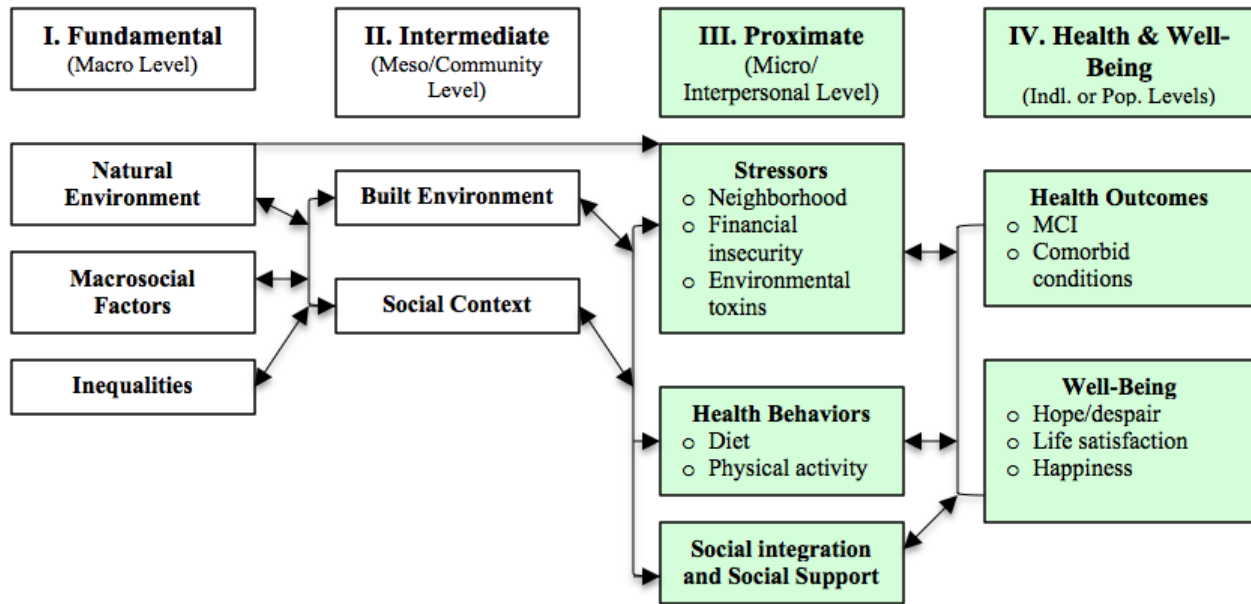
Figure 1. Social Determinants of Health and Environmental Health Promotion Model, adapted from Schulz and Northridge, 2004

The Social Determinants of Health and Environmental Health Promotion Model (SDH) guided the research conducted (see Figure 1, Schulz & Northridge, 2004). The model was adapted to present determinants of health hypothesized to impact older, rural-dwelling adults' health. The SDH Model places health outcomes in the greater context of the complex systems that may promote population health. The study 1) examined symptom severity of older, rural and non-rural Appalachian adults and 2) explored perceived determinants of health and experiences of older, rural-dwelling Appalachian adults with early-stage cognitive impairment. The health outcomes related to cognitive impairment fall within the larger theoretical model presented. Thus, it is important to note that the model's proposed relationships are not isolated from other variables

represented in the larger model. There are four levels described in the SDH Model: the fundamental or macro level, intermediate or meso-community level, proximate or micro/interpersonal level, and health and well-being at the population level. Across and within the immediately-connected levels, there are bidirectional relationships. These help demonstrate the complex nature of health and health promotion that we hoped to capture in the qualitative description of older, rural Appalachian adults by providing a more in-depth understanding of the social determinants and impact of early-stage cognitive impairment. The model provided the theoretical framework for Aim 2 (qualitative descriptive studies) and helped guide some interview questions and participant observations to better understand the social determinants of health in older, rural-dwelling Appalachian adults with early-stage cognitive impairment. As described in the background, there are a variety of social determinants that influence the individual or interpersonal levels in health promotion, such as the built environment and social context. By exploring self-perceived stressors, health behaviors, social support, and well-being through qualitative descriptive interviewing, we hoped to elucidate some of these social determinants unique and specific to this population.

1.2.3 Significance and Innovation

The study was significant because it described cognitive decline in older rural adults using a national dataset that required a comprehensive exam and consensus amongst clinicians to diagnose cognitive status. There is currently limited research examining older, rural-dwelling adults with early-stage cognitive impairment and overall cognitive decline, and this study proposed to help fill this gap. Findings from the quantitative study hoped to provide further support of health disparities

for older, rural-dwelling adults for cognitive decline, specifically MCI. The quantitative descriptive interviews helped describe rural-dwelling Appalachians across four states and will inform the development of future work, and possibly interventions, to promote cognitive health and subsequently reduce dementia incidence in this population.

The study was highly innovative because it provided a quantitative description of an understudied and difficult to recruit population sub-group and also provided further insight into the perceptions and experiences through in-depth interviews conducted during a participant home visit. Patient perceptions surrounding cognitive decline were described with the purpose of informing future research. The Social Determinants of Health and Environmental Health Promotion Model proposed by Schulz and Northridge (Schulz & Northridge, 2004b) provided the guiding framework for descriptive work on the dynamic relationships among variables that impacted health outcomes and well-being in this population, and presented an innovative approach to exploring health disparities.

1.3   RESEARCH DESIGN AND METHODS

Quantitative and qualitative methods were used to examine and gain insight into rural health disparities, particularly focusing on the needs of older, rural-dwelling Appalachian adults with early-stage cognitive impairment. The primary purpose was to determine if and how rural residence was a unique risk factor for delayed detection of early-stage cognitive impairment and to identify determinants of health impacting cognitive impairment progression and experiences of

participant-care partner dyads surrounding cognitive diagnosis. Access to the sample and data was granted by both NACC UDS and the University of Pittsburgh Alzheimer Disease Research Center (ADRC).

1.3.1 Quantitative Components

1.3.1.1 Aim 1/ Manuscript 1

Objective

Compare MCI symptom severity among older rural and non-rural Appalachian adults using the NACC UDS.

Study design

A cross-sectional, descriptive study of symptom severity among older Appalachian adults with MCI was performed. We took advantage of a unique, publically-available national database drawing on over 30 federally funded Alzheimer Disease Centers (ADCs). As with all secondary analyses, there were limitations. Chief among such limitations was that ADCs employ various recruitment strategies and the sample was not equivalent to one in a study using an epidemiological database. Nevertheless, NACC UDS provided the unique opportunity to use national multi-center data with detailed standardized neuropsychological assessments in a vulnerable, understudied population. This analysis was the first step to describe MCI in rural Appalachia.

Sample

We used data from the NACC UDS, a repository for data collected at approximately 30 ADCs throughout the US. The ADCs conduct clinical and biomedical research on AD and related disorders. Centers enroll their study subjects in various ways, including referral from clinicians, self-referral by patients or concerned family members, active recruitment through community organizations, and volunteers who wish to contribute to research. Most centers also enroll volunteer control subjects. The data were collected at the initial visit by clinicians, neuropsychologists, and other ADC research personnel, using up to 18 standardized forms at each visit. For our study, the NACC UDS drew upon participants with reported home addresses located in the Appalachian region, based on ZIP code. The parent study sample included adults who completed a memory evaluation at one of the ADC sites that serve Appalachian residents. ADC sites that contribute data to the larger UDS include Pittsburgh, PA; Lexington, KY; Atlanta, GA; as well as ADC ancillary sites. These centers capture most of the geographical area of the Appalachian region, including northern, central, and southern Appalachian regions (Borak et al., 2012). There were two cohorts that are targeted by the ADCs: "normal" controls and participants with symptoms associated with dementia. Self-referrals, referrals from community organizations, and referrals solicited from physicians from the respective ADC's partnering universities and surrounding regions contribute reflect examples of recruitment at ADCs. The normal control cohort is comprised of participants without subjective deficits. It is possible for "normal" controls to be diagnosed with memory problems at first evaluation or over time. The patient populations were not randomly selected, but each center continuously monitors cohorts to try and match overall

characteristics and include rural county inhabitants and minorities (Lingler, personal communication, May 7, 2014).

Inclusion criteria for the parent study were: >30 years of age, English speaker at an early age, >7 years of education, adequate visual and auditory acuity to complete neuropsychological testing, and a reliable care partner who was capable of providing correct information about the patient's clinical symptoms. *Additional inclusion criteria for Aim 1* are: ≥65 years of age, MCI diagnosis, and reside within the Appalachian region (rural or non-rural). *Exclusion criteria for the parent study were:* a lifetime history of schizophrenia, bipolar disorder, or schizoaffective disorder; recent history of electroconvulsive therapy; current alcohol or drug abuse/dependence within two years of onset of the symptoms of dementia; history of cancer other than skin cancer; or any significant disease or unstable medical condition that could affect neuropsychological testing such as severe pulmonary disease. *There were no additional exclusion criteria for Aim 1.*

Each ADC has a Data Management Core that stores and manages data for each site, and each is responsible for providing "error free data" UDS forms with assessment and evaluation data from each site to contribute to the greater national UDS. University of Pittsburgh IRB approval was obtained prior to data acquisition. De-identification of ZIP codes was performed to ensure patient confidentiality, since some participants lived in small, close-knit communities that may have made them vulnerable to identification by ZIP code. ZIP codes were collected based on the most recent ZIP code provided by ADCs. This decision was supported by evidence that older adults are less likely to change their residence than younger adults as evidenced by only 4% of older adults changing residence when compared to 13% of the under 65 population

(Administration on Aging, 2011). To make sure the data were de-identified before investigator analysis, Sarah Monsell, MS at NACC served as an honest broker.

Appalachia classification. Using the combined datasets from the three ADCs in Appalachia, Appalachia/non-Appalachia residence was determined for each participant using county of residence. The Appalachian Regional Commission (ARC) was created by the US government in 1965 to serve the Appalachian population's interests and currently provides classification of the counties within the Appalachian region ("The Appalachian Region," 2013).

Rural classification. Once Appalachian residence was determined, those participants identified as Appalachian were further classified according to United States Department of Agriculture Rural-Urban Commuting Areas Codes (RUCAs) using a scale from 1.0-10.6, providing a total of 33 codes. These codes were developed by both the US Department of Agriculture's Economic Research Service and the US Department of Health and Human Services RUCA codes were classified as non-rural and rural where non-rural was "urban" (Codes 1-3) and rural was "large rural city/town," "small rural town," and "isolated small rural town" (Codes 4-10, "Rural Urban Commuting Area Codes Data," n.d.-a).

MCI classification. We used the MCI criteria accepted by NACC and the following descriptive sub-types: 1) predominant focal amnestic disorder, 2) amnestic disorder plus changes in other cognitive domains not meeting the level of dementia, 3) impaired focal non-amnestic domain, and 4) non-amnestic disorder plus changes in other non-memory cognitive domains not meeting the level of dementia. For purposes of this study, all subtypes of MCI were accepted for a diagnosis of MCI and we accepted the definition for "clinical consensus-based MCI" as

presented at the Second International Working Group on MCI (Winblad, Palmer, Kivipelto, Jelic, & Fratiglioni, 2004).

Measures

To examine MCI symptom severity among older Appalachian adults, we used neuropsychological measures across four cognitive domains (see Table 1) and the Clinical Dementia Rating- Sum of Boxes (CDR-SOB) score. A cross-sectional analysis of older Appalachian adults with MCI was performed using diagnoses and neuropsychological assessment measurements as of a September 2014 data freeze.

Table 1: Neuropsychological Measures and Cognitive Domains

	Memory	**Language**	**Attention/ Psychomotor Speed**	**Executive Functioning**
Neuropsychological Measures	Logical Memory Immediate Recall	Boston Naming Test	Trailmaking A	Trailmaking B
	Logical Memory Delayed Recall	Category Fluency	Digit Symbol Substitution Task	Digit Span Backwards
			Digit Span Forwards	

Memory. Wechsler Memory Scale-R Logical Memory IA- Immediate is a measure of memory in which a brief story is read to the subject, who is asked to recall it immediately. Logical Memory IIA is a measure of delayed recall, whereby the subject recalls the same story after 30 minutes. The primary performance measure is number of story units recalled (Wechsler, 1987),

scored 0-25, with a higher score indicating better performance (Emilien, Durlach, Antoiniadis, VanderLinden, & Maloteaux, 2003).

Language. The Boston Naming Test measures ability to name line drawings of objects, for a total possible score of 60 (Wechsler, 1987). For the NACC UDS, only the score of the odd-numbered items are presented (scored 0-30). Category Fluency is a measure of semantic memory (verbal fluency, language) where the subject is asked to name different exemplars of a given semantic category. For the NACC UDS, the total number of animals or vegetables named in 60 seconds are scored from 0-77, respectively (Benton, 1968).

Attention/Psychomotor speed. Attention and psychomotor speed will be measured by three assessments: Trailmaking A (Reitan, 1958), Wechsler Adult Intelligence Scale-Revised (WAIS-R) Digit Symbol Substitution Task (DSST) (Wechsler, 1997), and Digit Span Forward (Wechsler, 1981). The Trailmaking Test A requires the subject to connect randomly placed encircled numbers that are strewn across a sheet of normal sized paper. The subject is asked to connect all numbers with a pen/pencil, in order beginning with 1, as fast as possible, for a maximum of 150 seconds (Reitan, 1958). Scores include seconds to complete (0-150), number of errors (0-48), and number of correct lines drawn (0-24). WAIS-R DSST asks subjects to take digit-symbol pairs and write the corresponding symbol for a list of digits in 90 seconds with a maximum of 93 items (0-93, total number of items correctly completed). Digit Span Forward is when the subject is asked to read number sequences of increasing length and asked to repeat them. Measures of performance include: the number of digit sequences recalled correctly, up to two consecutive errors (0-12) and the length of the highest digit sequences the subject is able to repeat correctly (0-8).

Executive Functioning. Trailmaking Test B requires the subject to connect both numbers and letters in order in an alternating pattern (e.g. 1-A-2-B) in a maximum of 300 seconds (Borkowski, Benton, & Spreen, 1967). Scores include seconds to complete (0-300), number of commission errors (0-48), and number of correct lines drawn (0-24). Digit Spans Backward is used to measure working memory. The subject is read number sequences of increasing length and then asked to repeat each sequence backward (Wechsler, 1981). The primary measure of performance is the number of digit sequences correctly reversed with up to two consecutive errors at the same digit length (0-12). The digit span backward length is also measured and is the length of the highest digit sequences the subject is able to reverse (0-7).

CDR-SOB. The CDR-SOB is commonly used to stage dementia severity (Hughes, Berg, Daziger, Coben, & Martin, 1982) and provides subjective information from the subject and care partner including memory, orientation, judgment/problem solving, community affairs, home/hobbies, and personal care, that may not be captured in the more objective neuropsychological measures included. Each of these six measures are given a score between 0-3 for a total range of 0-18 (Petersen et al., 1999).

Sample Size Estimation

It is important to note that NACC subjects with cognitive impairment are not a population-based sample and should be regarded as a referral-based or volunteer case series. Therefore, NACC data cannot be used for estimates of the occurrence of MCI in the general US population. Thus, this study provided preliminary findings that may be used to begin to describe this underrepresented, vulnerable population. As a secondary analysis, the number of participants was

also non-modifiable. A systematic review examining memory training in adults calculated effect sizes for neuropsychological assessments spanning three of the four domains included in the proposed research (Gates, Sachdev, Fiatarone Singh, & Valenzuela, 2011). Effect sizes for memory, language, and attention domains ranged from 0.10-1.21, with .99 as the greatest effect size with a 95% confidence interval that did not cross zero. An a priori power analysis using G*Power (Buchner, Erdfelder, Faul, & Lang, 2009) indicated that we would need 42 subjects in each group (rural and non-rural, respectively) to have 95% power for detecting a large-sized effect (0.8) when employing the traditional .05 criterion of statistical significance.

Sample Size Estimation

It is important to note that NACC subjects with cognitive impairment do not comprise a population-based sample and should be regarded as a referral-based or volunteer case series. Therefore, NACC data cannot be used for estimates of the occurrence of MCI in the general US population. Thus, this study provided preliminary findings that may be used to begin to describe this underrepresented, vulnerable population. As a secondary analysis, the number of participants was also non-modifiable. A systematic review examining memory training in adults calculated effect sizes for neuropsychological assessments spanning three of the four domains included in the proposed research (Gates et al., 2011). Effect sizes for memory, language, and attention domains ranged from 0.10-1.21, with .99 as the greatest effect size with a 95% confidence interval that did not cross zero. An a priori power analysis using G*Power (Buchner et al., 2009) indicated that we would need 42 subjects in each group (rural and non-rural, respectively) to have 95% power for

detecting a large-sized effect (0.8) when employing the traditional .05 criterion of statistical significance.

Data analysis

Data were analyzed using SPSS (version 23, IBM Statistics, NY). Initially data were screened using descriptive and exploratory data analysis methods to characterize the sample overall and by rurality status and to identify any data anomalies (e.g., missing data, outliers, multicollinearity, confounders, covariates). Possible confounders, identified from the literature and through data screening (e.g., gender, race, age, education, time since MCI diagnosis), were also explored.

MCI symptom severity was measured using a set of nine objective neuropsychological tests spanning four cognitive domains (memory, language, attention/ psychomotor speed, and executive functioning) and individually for CDR-SOB. To limit the inflation of type 1 error when testing hypotheses, data reduction methods were applied to decrease the dimensionality of the data yet retain much of the information contained in individual test scores. Exploratory factor analysis was also used to reveal factor structure mapping of individual neurocognitive tests to the latent cognitive domains. Because the scaling and directionality of individual tests varied, raw test scores were transformed into age-, sex-, and education-adjusted z-scores, if not already provided by NACC UDS. We then averaged the z-scores for each cognitive domain composite, where scores were measured in the same direction to ensure directionality. Four conceptually-based composites were computed from the averaged z-scores.

Using multivariate analysis of covariance, we examined the set of four domain composites simultaneously to examine symptom severity between rural and non-rural groups using the multivariate F-test, where the level of significance was set at .05 for two-sided hypothesis testing. We also explored domains individually using analysis of covariance (ANCOVA) to identify differences for each domain.

1.3.1.2 Exploratory Aim/ Brief Report

Objective

Using quantitative data acquired for Aim 1/ Manuscript 1, examine rural and urban differences in the same variables from Manuscript 1 to examine possible differences in results using two geographic classification schemes.

Design and Sample

A cross-sectional, descriptive study of older, Appalachian adults with MCI was conducted using NACC UDS data from Aim 1/ Manuscript 1. The sample for this secondary analysis included adults who were ≥65 years of age; with any MCI diagnosis; of Appalachian residence, based on county of residence; and having a designated informant/care partner at an Alzheimer's Disease Center (ADC) visit. Using data from NACC UDS, subjects who met inclusion criteria were classified as either rural- or urban-dwelling according to ZIP code (RUCA codes) or county (RUCC codes). Appalachian residence and MCI classification used to determine inclusion were described previously as well as details of the sample and data collection methods at ADCs, who provide data for the NACC UDS in Aim 1/Manuscript 1.

Measures

Descriptions of individual sociodemographic measures, comorbid conditions, medications measures, and outcome variables were presented in Aim 1/ Manuscript 1 measure descriptions. There were two classification schemes compared: Rural-Urban Commuting Area Codes (RUCAs) and Rural-Urban Continuum Codes (RUCCs). RUCAs use a numbered coding scheme from 1-10, where urban ("metropolitan") includes primary RUCA codes 1-3 and rural ("micropolitan," "small town," and "rural areas") includes codes 4-10 (US Department of Agriculture Economic Research Service, 2013a). RUCCs use a similar numbered coding scheme from 1-9, where RUCC codes 1-3 are urban ("metro") and codes 4-9 are rural ("nonmetro").

The majority of sociodemographic measures were binary variables (e.g., male/female or yes/no); however, the following variables were measured as continuous variables: age (years), education (years), body mass index (kg/m^2), Geriatric Depression Score (total score), medications (total number), time since onset of symptoms (years), distance from ADC (miles), Mini Mental Status Examination (score), and all MCI symptom severity variables (adjusted z-scores for neuropsychological measures; raw score for Clinical Dementia Rating-Sum of Boxes [CDR-SOB]). All measurements have been described in previous work in greater detail (Mattos et al., 2016).

Analysis

Data were analyzed using IBM® SPSS® Statistics (version 23, IBM SPSS, Inc., Armonk, NY). Data were first screened using descriptive and exploratory data analyses to portray the sample in total and by coding scheme and to reveal any data anomalies. After applying each rural/urban

23

classification scheme, odds ratios (ORs) were calculated for each measure, where the rural classification served as the reference group. Next, the percent difference between ORs based on RUCA and RUCC schemes relative to the OR, based on RUCA, was calculated for each measure. To explore differences in precision between the classification systems, those measures with a percent OR difference >40% were further examined by calculating standard errors (SEs) for the ORs based on each classification scheme, and then percent difference in SEs for the ORs relative to the SE based on RUCA was calculated.

1.3.2 Qualitative Components

1.3.2.1 Aim 2a/ Manuscript 2

Objective

Explore perceived social determinants of health from the perspective of older, rural-dwelling Appalachian adults with MCI and their care partner.

Study design

Qualitative description (Sandelowski, 2000, 2010) was used to explore perceived social determinants of older, rural-dwelling adults with early-stage cognitive impairment. The purpose of this qualitative approach was to learn more about the beliefs and behaviors of individuals belonging to this culture-sharing group of older, rural-dwelling Appalachian adults, and identify social determinants of health related to early-stage cognitive impairment. Due to geographic distance between possible participants and vulnerability of participants, we conducted semi-

structured interviews in participants' home environment with the participant's care partner present and participating in the interview.

Sample, recruitment, and rationale

The sample was from the University of Pittsburgh ADRC. Inclusion and exclusion criteria were the same as for the parent study. Purposive sampling was used to promote heterogeneity. Specifically, participant characteristics such as sex, degree of rurality, and relative degree of cognitive impairment were considered during recruitment to maximize diversity within the sample (Glaser & Strauss, 1967). The ADRC had secured informed consent from all participants for communication between annual visits, including permission to contact individuals via telephone about other ancillary studies. Once possible participants were identified, the investigator introduced the study to participants and care partners over the phone in an IRB-approved and HIPAA-compliant manner. Those who expressed interest in the study were scheduled for a home visit where the study was presented in detail and written informed consent obtained. Capacity to consent was assessed using questions from the University of California, San Diego Brief Assessment of Capacity to Consent (UBACC, Jeste et al., 2007).

Data collection

Multiple data collection methods were used to provide a description of the social determinants of older, rural-dwelling Appalachian adults with early-stage cognitive impairment to gain insight into cultural and social nuances that may not be captured in dialogue alone. ***Participant observation*** was used and allowed for contact in or around the social setting of the participant for the purpose of making a qualitative assessment of the setting (Lofland, 1971). Through participant

observation the researcher could see "firsthand what occurs" (Altheide & Johnson, 1998) by observing what went on, who or what was involved, when and where things happened, how they occurred, and why things happened as they did in particular situations (Jorgensen, 1989; Malinowski, 1978). Events surrounding the interview, such as introductions, and other observations were made of the participant, care partner, and home, as captured by investigator home visit notes during and after the interview. Visit notes were reviewed and expanded to enhance recall (Pelto & Pelto, 1978).

Semi-structured interviews. Participant in-home interviews were conducted and continued until saturation (no new concepts or themes emerged) and rare cases were examined to ensure a comprehensive approach to sampling (Creswell, 2007). The investigator prepared for home visits by developing a few semi-structured interview questions, but also allowing for open dialogue among the participant, care partner, and investigator. Care partners were encouraged to participate in the interviews based on findings that their contributions help convey participants' stories (Holstein & Gubrium, 1995). Visits to the participant's home environment as well as extended interview length were used to cultivate a trusting relationship and meaningful data collection. Previous participation in Pittsburgh ADRC activities also helped to promote trust in this sample. Interviews were anticipated to last 60-90 minutes, to ensure there was adequate time to build rapport (see Appendix 3 for "Qualitative Interview Guide," Long & Weinert, 1999; Manusov, 2009; Winters & Lee, 2010,). It was imperative to have scheduled the meeting in advance with the participants and to allow 60-90 minutes for each visit. Interviews were audio recorded and transcribed. To ensure credibility (Beck, 1993), home visit notes from these

interactions, relationships developed, and the investigator's own actions, interactions, and behaviors were documented.

Data analysis

All transcribed data were transferred from a word processing program to Atlas.ti©, a computer program used to organize and manage qualitative data and chosen because the program is affordable and relatively easy for first-time users. Data analysis used a variety of techniques, including: 1) *Data reduction* - the process of selecting, focusing, simplifying, and abstracting data (Huberman & Miles, 1998). As data collection proceeded, further data reduction occurs in the form of coding, clustering, and identifying themes. 2) *Data display* - the process of organizing compressed information into an immediately accessible form (Miles & Huberman, 1994). Reduced data were displayed so that the research team may examine potential patterns, regularities, or irregularities that point toward possible components and relationships (Eisenhardt, 1989). 3) *Conclusion drawing/verification* - drawing meaning from the displayed data, requiring researchers to make interpretations by employing a variety of tactics including comparing and contrasting, looking for negative cases, examining the literature, and verifying possible conclusions among researchers and consultants (Morse, 1989). These analytic methods were selected because they: 1) permitted large amounts of data from a variety of sources to be condensed, clustered, sorted, and linked over time (Huberman & Miles, 1998) and 2) facilitated examination of components and relationships revealed in the data (Miles & Huberman, 1994). Using these methods, we gained further insight into possible stressors, health behaviors, support, and well-being needs of older, rural-dwelling adults with early-stage cognitive impairment.

27

1.3.2.2 Aim 2b/ Manuscript 3

Design

This study used qualitative description, as presented by Sandelowski (2000, 2010), to describe experiences of older, rural-dwelling adults with early cognitive changes and their care partners at three time periods: pre-Alzheimer Disease Research Center (ADRC) visit, ADRC visit, and post-ADRC visit. The methodological approach of qualitative description provided the opportunity to characterize the events and experiences across these periods of time as recalled in "the everyday terms of those events" (Sandelowski, 2000).

Semi-structured interviews are described in greater detail in Aim 2a/ Manuscript 2 proposal documents. A 14-question interview guide was used to promote open dialogue about dyad experiences living with early cognitive changes and the role of social determinants of health on cognitive health (Schulz and Northridge, 2004). There was one question that directly asked about a certain period of time or event; the question asked members of the dyad about their last visit to the ADRC, and contained follow-up probes inquiring about descriptions of feelings and events during the visit. Although not a direct focus of the interview, pre-ADRC and post-ADRC visit experiences were described, often spontaneously. Previous participation with the ADRC and prolonged in-home engagement promoted trust in this sample at first contact with the investigator. All interviews were audio recorded and later transcribed verbatim. The principal investigator compared each transcribed interview to the original audio recording to ensure accuracy of transcription. University of Pittsburgh Institutional Review Board approved all procedures prior to study recruitment.

Sample

Details about the sample description and recruitment are described in greater detail in Aim 2a/ Manuscript 2 proposal documents.

Measures

In addition to interview data, there was one quantitative variable computed: distance from participant home to ADRC. Home-ADRC distance was calculated between participant home address and ADRC address using Google Maps and measured in miles, rounded to the nearest whole number. A review of research data from the ADRC participant charts was also performed to confirm current medication list and collect comprehensive descriptive characteristics of the sample, both already collected by the ADRC.

Analysis

Transcribed data were entered into Atlas.ti© for organizational and analysis purposes. Qualitative content analyses were performed by three independent investigators beginning with line-by-line coding. Findings were organized by time period and categories of shared or similar experience. Category similarities, differences, and counter examples were then discussed among investigators until findings were verified by consensus and convergence. These analytic methods were selected because they: 1) permit large amounts of data to be condensed, clustered, sorted, and linked over time (Huberman & Miles, 1998) and 2) facilitate examination of components and relationships revealed in the data (Miles & Huberman, 1994).

1.3.2.3 Trustworthiness and Rigor

Several strategies were used to enhance confidence in the truth-value of the findings. Purposive sampling was used to ensure heterogeneity with regard to participant characteristics that may have affected descriptions (Glaser & Strauss, 1967). The researchers acquired data systematically from a variety of sources and through a variety of methods (Beck, 1993). Interviews were audiotaped and transcribed verbatim. The investigator kept a reflexive journal to document decisions, processes, and reflections over the course of the study (Erlandson, 1993). Bracketing was also acknowledged by the investigator from the beginning of study development through dissemination to separate individual biases or opinion from that which is actually observed (Sandelowski, 1986). Dr. Jennifer Lingler provided consultation during all stages of the study.

1.4   POTENTIAL LIMITATIONS OF THE PROPOSED PROCEDURES & ALTERNATIVES APPROACHES

There were potential limitations to using the NACC UDS. Most importantly, NACC subjects with cognitive impairment were not a population-based sample and should thus be regarded as a referral-based or volunteer case series. Therefore, NACC data could not be used for estimates of the occurrence of MCI in the general US population, but could be used for purposes of this study to begin to describe underrepresented, vulnerable populations. Subjects were also recruited in a variety of ways, based on each ADC's custom protocol, and tended to be more educated than a representative sample. Many ADCs also required that all participants agree to an autopsy before

being accepted for UDS participation, and this may impose further selection bias. These limitations were and will be acknowledged in publications resulting from this study. For the qualitative pieces, it could be said that the data collected was one-dimensional since it was conducted during one visit. This concern was addressed by descriptions observed in personal home settings and in-depth interviews with participants and care partners. By collecting data in the participant's unique environment, there were additional opportunities to capture rich, meaningful data that could not be collected in a generic location over a longer period of time.

There were multiple alternative approaches that may have been used for Aim 2 of the research study. Ethnography was not used due to the variability in participant locations, issues with diagnosis confidentiality or disclosure with others, and participant burden with repeated visits. Phenomenology was considered based on the shared experience of an ADC visit, but the aims of this study were to gain insight into the culture-sharing group rather than describing the "essence of the experience" (Creswell, 2007). Although the sample for Aim 2 only resided in a specific area of Northern Appalachia, findings help describe the perceived social determinants of health and diagnostic experiences in a difficult-to-study, vulnerable population. Qualitative findings are not generalizable to all of Appalachia; however, this study was significant and innovative as it can be used to guide future research in this field.

1.5 RESEARCH PARTICIPANT RISKS AND PROTECTION

1.5.1 Detailed Description of Human Subjects Involved

The secondary analysis used de-identified data from the National Alzheimer's Coordinating Center (NACC) Uniform Data Set (UDS), a repository for data collected at approximately 30 Alzheimer's Disease Centers (ADCs) throughout the US, to describe symptom severity in older rural-dwelling adults living within the Appalachian region. Centers enroll their study subjects in various ways, including referral from clinicians, self-referral by patients or concerned family members, active recruitment through community organizations, and volunteers who wish to contribute to research. There are two cohorts that are targeted by the ADCs: normal controls and subjects with cognitive impairment. Recruitment of ADC subjects with cognitive impairment is typically from referrals that are solicited from physicians from the respective ADC's partnering universities and surrounding regions. The normal control cohort is comprised of subjects without subjective cognitive deficits. It is possible for normal controls to be diagnosed with memory problems at the first evaluation or over time. The patient populations are not randomly selected, but each center continuously monitors cohorts to ensure representativeness to the greatest extent possible, with particular regard to rural county inhabitants and minorities. Specifically, NIA funds ADC satellites, such as the University of Virginia satellite in Charlottesville, Virginia, to increase representation of minorities, including rural residents.

1.5.1.1 Secondary Analysis Subjects from NACC UDS

Inclusion criteria for the parent study using the NACC UDS were: >30 years of age, English speaker at an early age, >7 years of education, adequate visual and auditory acuity to complete neuropsychological testing, and a reliable care partner who was capable of providing correct information about the patient's clinical symptoms. *Additional inclusion criteria for proposed secondary analysis are*: ≥65 years of age, MCI diagnosis, and reside within the Appalachian region (whether rural or non-rural)*. Exclusion criteria for the parent study* were: a lifetime history of schizophrenia, bipolar disorder, or schizoaffective disorder; recent history of electroconvulsive therapy; current alcohol or drug abuse/dependence within two years of onset of the symptoms of dementia; history of cancer other than skin cancer; or any significant disease or unstable medical condition that could affect neuropsychological testing such as severe pulmonary disease.

1.5.1.2 Qualitative Study Subjects from Pittsburgh ADRC

The same inclusions and exclusion criteria as the parent study using NACC UDS data were used for the older rural adults with MCI. Purposive sampling, based on multiple descriptive characteristics, was performed to include the most representative sample as possible. Inclusion criteria for care partners are: >18 years of age and identified as a close family member or kin-like friend by the subject.

1.5.2   Inclusion of Women

Based on the National Alzheimer's Coordinating Center (NACC) Uniform Data Set (UDS), we expected that 50% of our sample will be women. We purposively recruited 50% women from the Pittsburgh Alzheimer Disease Research Center (ADRC) sample for participation in the qualitative component of the research project. Women typically provide about 75% of caregiving support, and we expected similar representation for the number of female care partners for older rural adults with MCI.

1.5.3   Inclusion of Minorities

The study population was older, rural-dwelling adults, who comprise an underserved, underrepresented population. For inclusion of minorities in this population, we based our projections on demographic data from the NACC UDS and Pittsburgh ADRC. While both dataset subjects are primarily Caucasian, the racial and ethnic distribution of NACC UDS and Pittsburgh ADRC did reflect the older adult population nationally and Greater Pittsburgh. Almost 15% of NACC UDS and 12% of Pittsburgh ADRC subject's self-report belonging to an ethnic/racial minority group. Projections for the NACC UDS minority distribution for this proposed research were based on the minority distribution rates of Appalachia, as this is the specific population of interest. Within Appalachia, 8% self-report as Black or African American, 2% Hispanic, 2% Asian, and 2% more than one race. These percentages were used to calculate targeted enrollment for Aim 2.

For the Pittsburgh ADRC sample, there were a very small number of subjects involved. The primary racial/minority group in this region was African American with individuals of Hispanic, Asian, or other ethnicities representing a negligible proportion of rural older adults. Pennsylvania also has a lower estimated minority population, only 9% statewide compared to the national averages of 15% or more. Care partners are typically family members and were expected to share similar ethnic/racial background as the subject, which was expected to limit minority inclusion of care partners. Finally, preliminary estimates showed a limited number of rural adults with early-stage cognitive impairment from which to recruit (n=12), further limiting possible minority inclusion. No one was excluded based on gender, race, or ethnicity. Inclusion of one minority in a sample size of 19 was attempted, however was not successful.

1.5.4 Inclusion of Children

Children under the age of 18 years were not recruited for participation in this research. The rationale for excluding those under the age of 18 years was that the objective of this research was to describe cognitive impairment in older adults, and mild cognitive impairment is specifically seen in aging adults that do not affect persons in early adulthood. While it was conceivable that persons under 18 years may participate in an older relative's caregiving or medical decision-making, care partners under the age of 18 years were not included as developmental considerations in adolescence suggest that caregiving at that age is a fundamentally different process from that which this study was designed to examine. Therefore, this study was not intended for children under 18 years, and they would not have expected to benefit from it.

1.5.5 Sources of Materials

The sources of materials for the proposed study were abstracted data from existing research databases (NACC UDS and Pittsburgh ADRC), interview-based self-reports, interview-based care partner reports, audio recordings of interviews, investigator handwritten field notes, and electronically-entered transcribed interviews and field notes. Permission to extract data from existing databases was explicitly requested of subjects during the informed consent process from the Pittsburgh ADRC, and additional consent from both subjects and their care partner(s) was obtained to conduct the interviews in subject or care partner homes. Both the NACC UDS and Pittsburgh ADRC provided documentation of sample access prior to receiving funding.

1.5.6 Recruitment and Retention of Participants

One of the ADC sites, the Pittsburgh Alzheimer's Disease Research Center (ADRC), served as the source in recruiting older, rural-dwelling adults and their care partners for the qualitative component of the proposed research. To enroll in the parent study, subjects underwent a phone screening followed by the consent process and interviews of both the subject and care partner by a social worker. Most times the subjects present to the ADRC with their primary care partner as a dyad. Upon enrollment, Pittsburgh ADRC subjects provided consent to be contacted for other studies for which they may be eligible. For the qualitative aims, preliminary phone calls to purposively selected subjects were conducted. Those subjects who expressed interest in the study had a home visit. At the time of the visit, if a care partner was present and expressed interest in the

qualitative interview, both the subject and care partner underwent a detailed explanation of its purpose, risks, and potential benefits and were invited to provide written informed consent to participate in the qualitative study.

Determinations of capacity to consent to the proposed research study were based on a subject's ability to express an understanding the study's purpose, procedures, risks, and benefits during a one on one discussion with a member of the research team. Persons with cognitive impairment, by definition, have impaired memory and had varying abilities to understand elements of the consent process. The investigator received training to enhance subjects' ability to achieve decisional capacity during the consent process through formal training directed by Dr. Jennifer Lingler. For example, a one-page overview of key aspects of the study was provided to supplement the lengthier informed consent document. Those who did fulfill the criteria of being able to verbally express an understanding the study's purpose, consent procedures, risks, and benefits, either during the preliminary phone contact or in-person, would have been thanked for their interest in the study, but interviews or audio recordings were not performed.

Recruitment of rural-dwelling adults is difficult for a variety of reasons and include, but are not limited to, diverse geographic areas and transportation issues and distrust of "outsiders". Access to this population through the NACC US and Pittsburgh ADRC provided a unique opportunity to learn more about this population.

1.5.7 Potential Risks for Proposed Secondary Analysis and Qualitative Component

The NACC UDS data remained de-identified for the proposed secondary analysis, so as to limit potential risks to subjects, since some subjects live in small, close-knit communities that may make them vulnerable. For the Pittsburgh ADRC participants and care partners in the qualitative study, potential risks included breach of confidentiality and the possibility that discussing perceptions of determinants of health and experiences related to early-stage cognitive impairment may have evoked feelings of sadness or despair related to diagnosis.

1.5.8 Procedures for Protection against Risk

We stressed to all subjects and care partners that participation in the study was voluntary and would not affect clinical care at Pittsburgh ADRC, UPMC or involvement with the University of Pittsburgh. Assessments took place only with subjects' expressed permission. Study subjects were first contacted by phone to be given the opportunity to: 1) participate in the interview, 2) ask specific questions and receive answers, and 3) have their interview audio recorded. To minimize the risk of breach of confidentiality, unique numeric identifiers were used to link all study data to each subject and care partner(s). All other identifiers such as name, gender, and date of birth are maintained only in the subject file to enable follow-up. Every attempt was made to protect human subjects in this study. For one, all subjects and care partners were made aware of the research purpose and informed that IRB approval was necessary to participate. Subjects and care partners were also explicitly told that they can decide not to participate and can stop the interview, or refuse

individual questions, at any time. All interviews were tape recorded by the investigator. Sensitive information such as subject and care partner(s) names, subject demographic information, IRB consents, digital audio files, and field notes were and are kept in a secure location. Data were recorded and are identified by subject code numbers only. These materials file are kept under lock and key, accessed only by the investigator and the data analysis team. Identities of subjects are and will not be revealed in publications or presentations derived from this project.

1.5.9   Potential Benefits of Proposed Research

There was no direct benefit to either group for the research study. The interviews with subjects for the qualitative component of this study provided an opportunity for older, rural- dwelling adults with early-stage cognitive impairment and their care partner(s) to discuss their perceptions and experiences surrounding cognitive diagnosis and share their opinions and beliefs on health care access, barriers, and overall impact of cognitive changes on their life. The proposed study was beneficial for developing future interventions targeting specific determinants of health in this underserved and underrepresented population.

The knowledge derived from this study provides a description of older, rural-dwelling Appalachian adults with early-stage cognitive impairment, both through quantitative and qualitative data. Findings from this study help to inform the future development of interventions to provide earlier diagnosis of cognitive impairment and possibly delay progression to Alzheimer's disease or other dementias.

2.0   MANUSCRIPT 1, DATA-BASED: OLDER RURAL- AND URBAN-DWELLING APPALACHIAN ADULTS WITH MILD COGNITIVE IMPAIRMENT

2.1   ABSTRACT

Purpose: Mild cognitive impairment (MCI) is a well-recognized risk state for Alzheimer's disease and other dementias. MCI is rapidly increasing among older adults in general and has not yet been examined in older adults within the Appalachian region. Our objective was to compare MCI symptom severity among older rural and urban Appalachian adults with MCI at an initial neuropsychological testing visit.

Methods: A cross-sectional, descriptive study of older Appalachian adults with MCI was conducted using data from the National Alzheimer's Coordinating Center Uniform Data Set. Symptom severity was conceptualized as neuropsychological composite scores across 4 cognitive domains and Clinical Dementia Rating-Sum of Boxes (CDR-SOB) score. For group comparisons, MANCOVA was used for cognitive domains and ANCOVA for CDR-SOB.

Results: The sample (N = 289) was about half male (54.3%), predominantly white (91.7%), and living with others (83.5%), with a mean (±SD) 74.6 ± 6.2 years of age and 15.4 ± 3.0 years of education. Rural and urban groups differed significantly in years since onset of cognitive symptoms (2.98 ± 1.91 in rural and 3.89 ± 2.70 in urban adults, $t[260] = -2.23$, $P = .03$), but they did not differ across sociodemographic features or comorbid conditions. Rural and urban participants were similar across the 4 cognitive domains and CDR-SOB (P & .05).

40

Discussion: No differences were found between rural and urban Appalachian residents on MCI symptom severity. However, urban residents reported a longer time lapse from symptom identification to diagnosis than their rural counterparts. Future studies using more representative population samples of Appalachian and non-Appalachian adults will provide an important next step to identifying disparate cognitive health outcomes in this traditionally under- served region.

2.2   INTRODUCTION

The Appalachian region of the United States, which spans from southern New York to northern Alabama, Mississippi, and Georgia, has a total population of almost 23 million inhabitants in over 400 counties and 13 states (*Health, United States, 2012: With Special Feature on Emergency Care*, 2013). The Appalachian region suffers from inequalities in socioeconomic conditions, [2] behavioral risk factors for poor health outcomes, and higher mortality rates compared to the nation as a whole (Halverson et al., 2004). With over double the national percent of rural-dwelling adults within the Appalachian region ("The Appalachian Region," 2013; US Department of Agriculture Economic Research Service, 2013b) and a greater proportion of older adults ("The Appalachian Region," 2013), older rural Appalachian adults are an important, understudied population. Appalachian rural adults have worse overall health and health outcomes when compared with the rest of the nation (Behringer & Friedell, 2006; Casey et al., 2001; Eberhardt & Pamuk, 2004; Gamm, Hutchison, Bellamy, & Dabney, 2002; Halverson et al., 2004). Additionally, behavioral risk factors such as smoking and a sedentary lifestyle

41

(Bennett et al., 2008; Gamm et al., 2010) place rural Appalachian adults at greater risk for cardiovascular (CVD) and cerebrovascular disease. Poorer health outcomes in rural Appalachia continue to be addressed in the literature (Casey et al., 2001; Gamm et al., 2010; Halverson et al., 2004; "The Appalachian Region," 2013). However, one condition that is rapidly increasing among older adults in general ("Latest Facts & Figures Report," 2013) and has not yet been examined in this population is the clinical syndrome, mild cognitive impairment (MCI), which is a well-recognized risk state for Alzheimer's disease (AD) and other dementias.

Rural-dwelling Appalachian adults are especially vulnerable to late-life cognitive impairment based on known health disparities and higher rates of risk factors among those living in rural Appalachia. Established risk factors for cognitive impairment include older age (Ganguli et al., 2013; Kryscio et al., 2006; Petersen, 2010; Sachdev et al., 2012) less education (Kryscio et al., 2006; Petersen, 2010), and female gender (Kryscio et al., 2006; Petersen, 2010), as well as hypertension (Chen et al., 2012; Ettorre et al., 2012; Sachdev et al., 2012), heart disease (Chen et al., 2012; Ettorre et al., 2012; Sachdev et al., 2012), diabetes (Cheng et al., 2012; Crane et al., 2013), depression (Johnson et al., 2013; Sachdev et al., 2012; Spira et al., 2012), and genetic factors (Kryscio et al., 2006; Sachdev et al., 2012). Among these known risk factors for cognitive impairment, rural Appalachian residents have demonstrated lower levels of education (Billings & Blee, 2000; Gillum & Mussolino, 2003) and higher rates of hypertension (Eberhardt & Pamuk, 2004), heart disease (Pearson & Lewis, 1998), and diabetes (Pearson & Lewis, 1998). Moreover, delayed detection of cognitive changes, possibly attributed to fewer rural-dwelling health care providers (Barley et al., 2001; Gamm et al., 2010) and limited health services (Gamm et al., 2010), make rural Appalachian adults an especially vulnerable group. Since MCI is a recognized target

for the secondary prevention of dementia, the time of MCI diagnosis may present a critical opportunity for interventions that help reduce health disparities.

The prevalence of MCI is estimated to be as high as 19% among older US adults (Gauthier et al., 2006). An MCI diagnosis 1) involves decline in at least one cognitive domain (e.g., memory), 2) requires maintenance of near normal functional activities, and 3) requires that the degree of cognitive impairment is not sufficient to warrant a diagnosis of AD or related dementia (Gauthier et al., 2006; Petersen et al., 2001). Subtle changes in cognition may not initially appear to directly affect daily living, but they often significantly worsen over time and can impact day-to-day activities. Based on known rural health disparities, especially later diagnosis of chronic diseases, it is reasonable to hypothesize that MCI may present later in its course in rural adults; however, studies describing older, rural-dwelling adults with MCI have not been documented. The purpose of this study was to compare MCI symptom severity among older rural and urban Appalachian adults with MCI at an initial neuropsychological testing visit. It was hypothesized that older, rural-dwelling Appalachian adults with MCI would present with worse symptom severity, as evidenced by neuropsychological test scores, compared to their urban counterparts.

2.3 METHODS

2.3.1 Design

A quantitative, cross-sectional, descriptive study of symptom severity data collected from older Appalachian adults with MCI was performed. De-identified data were obtained from the National Alzheimer's Coordinating Center (NACC) Uniform Data Set (UDS), a publicly available national database drawing on over 30 federally funded Alzheimer Disease Centers (ADCs).

2.3.2 Sample

The ADCs, which contribute to the NACC UDS repository, conduct clinical and biomedical research on AD and related cognitive disorders. Individuals who participate in ADCs are enrolled through a variety of methods that include referrals from clinicians, family, or self-referral, and targeted recruiting through community organizations. In addition to enrolling individuals with AD and related cognitive disorders, most centers also enroll healthy control participants. There are 2 cohorts that are targeted by the ADCs: cognitively normal controls and individuals with symptoms associated with dementia.

Data are collected at an initial visit and each annual follow-up visit by clinicians, neuropsychologists, and other ADC research personnel, using up to 18 standardized data collection forms at each visit. The parent study (NACC UDS) sample, from which the present study sample was selected, includes adults who completed a memory evaluation at one of the ADC sites that

may serve the Appalachia region from September 2005 through September 2014 data freeze. ADC sites located within or close to the Appalachian region that contribute data to the larger UDS include the University of Pittsburgh Alzheimer Disease Research Center, the University of Kentucky Alzheimer's Disease Center, and Emory University's Alzheimer's Disease Research Center, as well as ADC ancillary sites affiliated with these centers.

Inclusion criteria for the present study were ≥65 years of age; any MCI diagnosis; Appalachian residence, based on county of residence; and having a designated informant/care partner. There were no additional exclusion criteria. For the current study, individual ADCs were contacted and additional data were requested, including 5-digit ZIP codes for the purpose of rural classification. ZIP code data were provided by the individual ADCs for participants meeting the inclusion/exclusion criteria determined by and provided by NACC. ZIP codes reflect the most recent ZIP code data provided by the participant and/or care partner. The University of Pittsburgh Institutional Review Board approval was obtained prior to data acquisition.

After merging NACC UDS and ADC data, there were a total of 3,086 ADC visits for 936 participants with an MCI diagnosis across the 3 Centers. Applying the study's inclusion and exclusion criteria, only initial visit data were used, 135 participants were younger than 65 years of age, 446 were not living within Appalachia, and 66 were excluded for other reasons such as no ZIP code available for classification. Ultimately, 289 participants were available for analysis (urban n=231, rural n=58). Participants reported residence across 9 states within Appalachia including Georgia (n=32, 15.6% rural), Kentucky (n=18, 100% rural), Maryland (n=2, 100% rural), North Carolina (n=2, 100% rural), Ohio (n=3, 33.3% rural), Pennsylvania (n=228, 12.7% rural), and West Virginia (n=4, 25.0% rural). Overall, 50.0% of the rural, Appalachian sample

resided in Pennsylvania, and the University of Pittsburgh ADRC provided 86.1% of the urban sample.

2.3.3   Measures

Appalachia Classification

Appalachian residence was determined using the Appalachian Regional Commission classification of US counties located within the Appalachian region ("The Appalachian Region," 2013). Five-digit ZIP codes were converted to counties using the US Census Bureau's online resource, "Locate a county by place name" to classify residents as living within the Appalachia region (US Department of Commerce, 2013).

Rural Classification

Once participants were determined to be of Appalachian residence, they were further classified according to United States Department of Agriculture Rural-Urban Commuting Areas Codes (RUCAs) using codes from 1 to 10. This classification scheme was developed by the US Department of Agriculture's Economic Research Service and the US Department of Health and Human Services, where urban ("metropolitan") includes primary RUCA codes 1-3 and rural ("micropolitan," "small town," and "rural areas") includes codes 4-10 (US Department of Agriculture Economic Research Service, 2013a).

MCI Classification

We used the MCI criteria implemented by NACC: (1) cognition is determined to be not normal and (2) clinical dementia is not present (Winblad et al., 2004). We included all MCI sub-types, including (a) predominant focal amnestic disorder, (b) amnestic disorder plus changes in other cognitive domains, (c) focal non-amnestic disorder, and (d) non-amnestic disorder plus changes in other non-memory cognitive domains (Winblad et al., 2004).

Descriptive, Comorbid Conditions, and Medication Measures

Sociodemographic variables included age (measured in years) and education (measured in years) as continuous variables and sex (male/female), race (white/non-white), living situation (living with someone/not living with someone), and marital status (married/not married) as binary variables. Comorbid conditions and family of a first degree relative with dementia were coded as binary variables (recent/active and remote/inactive or absent/present), except for body mass index (BMI, kg/m^2) and Geriatric Depression Score (GDS) (Yesavage et al., 1983) that were measured as continuous variables and collected by clinician. Age of onset of cognitive decline was also measured as a continuous variable, as determined by the participant and family/informant self-report. Time since onset of symptoms was calculated by subtracting the age of onset of cognitive decline from the current participant age (in years). Total number of self-reported medications was reported as the sum of all prescription, nonprescription, and vitamins/supplements reported.

Distance to ADC

ArcMap (Esri, Redlands, California) was used for geocoding ZIP codes and ADCs into separate layers. The ArcGIS Network Analyst Origin-Destination (OD) function was used to compute driving distance between resident ZIP code and ADC address. The new OD cost matrix

extension calculated distance between the 2 locations with a gravity model for access, assigning the same weight for each participant.

2.3.4   Outcome Variables: Neuropsychological Measures

To examine MCI symptom severity, we clustered neuropsychological measures conceptually across 4 cognitive domains: Memory (Wechsler Memory Scale-R Logical Memory IA – Immediate and Delayed), Language (Boston Naming Test and Category Fluency – animals or vegetables), Attention/Psychomotor Speed (Trailmaking Test A, Wechsler Adult Intelligence Scale-Revised [WAIS-R] Digit Symbol Substitution Task [DSST], and Digit Span Forward), and Executive Functioning (Trailmaking Test B and Digit Span Backwards). Neuropsychological measures are described below.

Memory. Wechsler Memory Scale-R Logical Memory IA – Immediate is a measure of memory in which a brief story is read to the participant, who is asked to recall it immediately. Logical Memory IIA is a measure of delayed recall, where the participant recalls the same story after 30 minutes. The primary performance measure is number of story units recalled (Wechsler, 1987), scored 0-25, with a higher score indicating better performance (Emilien et al., 2003).

Language. The Boston Naming Test (Wechsler, 1987) measures ability to name line drawings of objects, for a total possible score of 60. For the NACC UDS, only the score of the odd-numbered items are presented (scored 0-30). Category Fluency is a measure of semantic memory (verbal fluency, language) where the participant is asked to

name different exemplars of a given semantic category. For the NACC UDS, the total number of animals or vegetables named in 60 seconds are scored from 0 to 77 (Benton, 1968).

Attention/Psychomotor Speed. Attention and psychomotor speed is measured by 3 assessments: Trailmaking A (Reitan, 1958), Wechsler Adult Intelligence Scale-Revised (WAIS-R) Digit Symbol Substitution Task (DSST) (Wechsler, 1997), and Digit Span Forward (Wechsler, 1981). The Trailmaking Test A requires the participant to connect randomly placed encircled numbers that are strewn across a sheet of normal-sized paper. The participant is asked to connect all numbers with a pen/pencil, in order beginning with 1, as fast as possible, for a maximum of 150 seconds (Reitan, 1958). Scores include seconds to complete (0-150), number of errors (0-48), and number of correct lines drawn (0-24). WAIS-R DSST asks participants to take digit-symbol pairs and write the corresponding symbol for a list of digits in 90 seconds with a maximum of 93 items (0-93, total number of items correctly completed). Digit Span Forward is when the participant is read number sequences of increasing length and asked to repeat them. Measures of performance include: the number of digit sequence recalled correctly, up to 2 consecutive errors (0-12), and the length of the highest digit sequences the participant is able to repeat correctly (0-8).

Executive Functioning. Trailmaking Test B requires the participant to connect both numbers and letters in order in an alternating pattern (eg, 1-A-2-B) in a maximum of 300 seconds (Borkowski et al., 1967). Scores include seconds to complete (0-300), number of errors (0-48), and number of correct lines drawn (0-24). Digit Spans Backward is used to measure working memory. The participant is read number sequences of increasing length

49

and then asked to repeat each sequence backward (Wechsler, 1981). The primary measure of performance is the number of digit sequences correctly reversed with up to 2 consecutive errors at the same digit length (0-12). The digit span backward length is the length of the highest digit sequences the participant is able to reverse (0-7).

The Clinical Dementia Rating-Sum of Boxes (CDR-SOB) score was also considered as an independent outcome. CDR-SOB is calculated by summing 6 domain box scores (memory, orientation, judgment and problem solving, community affairs, home and hobbies, and personal care) obtained from the Clinical Dementia Rating (range: 0-18) (Morris, 1993; O'Bryant et al., 2008). This is included as a measure of symptom severity based on clinician judgment and participant account of his/her ability to perform activities of daily living, rated independently of neuropsychological test performance.

MCI symptom severity was measured using these 9 objective neuropsychological tests spanning 4 cognitive domains and individually for CDR-SOB. Composite scores were derived based on this mapping of individual neuropsychological tests to conceptual domains to provide averaged adjusted z-scores for each cognitive domain composite. For all neuropsychological measurements, age-, sex-, and education-adjusted z-scores were used, as adjusted using the normative calculator for the UDS neuropsychological test battery (Shirk et al., 2011) and provided by the NACC UDS. The initial visit neuropsychological assessment measurements were used for analysis, and the time since onset of symptoms was considered as a covariate in the analysis of each outcome domain.

2.3.5   Analysis

Data were analyzed using IBM® SPSS® Statistics (v.23, IBM Corp., Armonk, New York). Initially data were screened for anomalies (eg, outliers, missing data, violations of statistical assumptions) using descriptive and exploratory data analysis methods to characterize the sample overall and by rural/urban classification. Group comparisons were conducted for all sociodemographic variables by rural/urban classification using 2-sample t-tests for continuous-type descriptors and chi-square or Fisher exact tests for categorical characteristics prior to proceeding with analysis of the neuropsychological outcome variables. All sociodemographic variables were examined as covariates for each outcome variable.

Mean adjusted z-scores for each cognitive domain composite were analyzed using multivariate analysis of covariance (MANCOVA) by examining the set of 4 cognitive domain composites simultaneously to compare MCI symptom severity between rural and urban groups using the multivariate F-test. Effect sizes were reported as partial eta-squared. Sociodemographic variables (eg, sex, education, age) were also examined for possible associations with cognitive outcome variables and, if significant associations were found, were controlled for in the analysis. Analysis of covariance (ANCOVA) was used to compare CDR-SOB scores between rural and urban samples while controlling for sociodemographics. For all analyses, the level of statistical significance was set at .05 for 2-sided hypothesis testing.

2.4   RESULTS

Our final sample (N=289; 231 urban, 58 rural) included participants who were, on average (± standard deviation [SD]), 74.6 ± 6.2 years of age, predominantly white (91.7%), male (54.3%), and with a reported mean 15.4 ± 3.0 years of education. Most reported living with at least one person (83.5%) and being married (77.5%). Of those participants living with someone, 93.7% were married; of those participants who were not married, 75.8% lived alone. Rural and urban groups did not differ significantly across any sociodemographic features. See Table 1 for more detailed sociodemographic information.

Gender and education had statistically significant associations across outcome variables. Male gender was associated with lower adjusted z-scores for memory, language, and attention/psychomotor speed domains as well as higher CDR-SOB scores. Fewer years of education was associated with lower language and attention/psychomotor speed domain scores as well as higher CDR-SOB scores. Age had no statistically significant associations across outcome variables. Race was also considered; however, the small number of nonwhite participants in both rural and urban groups did not provide sufficient variability to warrant inclusion as a confounder. The identified significant associations for each outcome variable were adjusted for, and similar results were obtained for each outcome variable.

Overall there were no statistically significant differences in most comorbid conditions between rural and urban participants ($P \geq .05$). However, there was a difference in the time since onset of cognitive symptoms between groups (2.98 ± 1.91 years in rural adults and 3.89 ± 2.70 in urban adults, t[260] = -2.23, $P = .03$). Table 2 presents prevalence of comorbid conditions and

distance traveled for the total sample as well as rural and urban samples. Rural- and urban-dwelling participants did, however, have significant differences in distance traveled to ADC. Rural participants traveled, on average, 65.03 ± 36.06 miles (range: 23.13-181.50) to ADC, compared to urban participants who traveled on average 17.20 ± 16.49 miles (range: 0.59-138.55) (t[287]=14.926, $P < .001$).

There were no significant differences between rural and urban participants across the 4 objective cognitive domains or CDR-SOB: Memory (F[1,287] = 1.35, $P = .25$, partial $\eta^2 < .01$); Language (F[1,287] = 0.12, $P = .73$, partial $\eta^2 = < .01$); Attention/Psychomotor Speed (F[1,287] = 0.07, $P = .79$, partial $\eta^2 < .01$); Executive Function (F[1,287] = 0.90, $P = .34$, partial $\eta^2 <. 01$); and CDR-SOB (t[287] = -0.15, $P = .88$). When looking at individual neuropsychological tests, there were also no differences between rural- and urban-dwelling adults, except for 2 tests within the Attention/Psychomotor Speed domain, Trailmaking A and Digit Span Forward. Older, rural adults with MCI scored significantly worse in the Trailmaking A test compared to urban adults (t[286] = -3.16, $P < .01$), while older, urban adults with MCI scored significantly worse in Digit Span Forward compared to rural adults (t[287]= 2.27, $P = .02$). Table 3 presents results for individual neuropsychological tests.

2.5   DISCUSSION

We hypothesized that older, rural-dwelling Appalachian adults would have worse cognitive symptom severity than their urban counterparts at an initial neuropsychological testing visit. This

hypothesis was not supported by our analyses. Across 4 cognitive domains and CDR-SOB, we found significant differences within the attention/psychomotor speed domain for 2 of the individual tests, Trailmaking A and Digit Span Forward tests. However, the differences for the 2 tests were in different directions, and thus we believe that these are isolated findings likely due to chance and should not be over-interpreted regarding their clinical significance. There was no evidence of rural/urban differences at the domain level.

Of note, our analysis revealed a significant difference in the length of time from onset of symptoms to MCI diagnosis between older rural and urban adults, where rural adults were presenting for diagnosis earlier than their urban counterparts. This was unexpected as breast, prostate, and colorectal cancers, as well as cardiovascular disease (CVD) have been found to be diagnosed at later stages for rural adults than their urban counterparts (Campo et al., 2008; Casey et al., 2001; Larry Gamm et al., 2010; Halverson et al., 2004). A recent systematic review examining barriers to cognitive screening in rural America found that lack of knowledge about cognitive changes, lack of knowledgeable providers to offer cognitive screening, and geographic distance are barriers to cognitive screening (Kirk Wiese, Williams, & Tappen, 2014). One reason for the shorter length of time from onset of symptoms to diagnosis for rural-dwelling adults compared to urban-dwelling adults may be that rural-dwelling adults are more likely to take the time to seek out and use specialty health care services if they have a first degree relative with dementia. Although over 50% of both rural and urban adults with MCI reported having at least one first degree relative with dementia, those living in rural areas may be more likely to be proactive in seeking out care and treatment at ADCs to try and prevent dementia symptoms or outcomes seen in their relatives. This may be explained by the significant difference in distance

traveled by rural participants to ADC site compared to urban participants, with consideration for the fact that most specialty health care services are located within urban centers. Additionally, symptom identification by family members' familiar with cognitive symptoms or knowledge of specialty health care centers may also play a role in bringing older, rural-dwelling adults to specialty centers earlier.

Historically, recruitment for research in rural America can be challenging (Cudney, Craig, Nichols, & Weinert, 2004; Dibartolo & McCrone, 2003), and recruitment for cognitive changes may be compounded because cognitive symptoms may be dismissed as normal aging (Kirk Wiese et al., 2014). However, once involved in memory research, Hunsaker at al (2011) found that both rural and urban research participants believed memory research benefited the participant, family, and society. For example, participation in memory research allowed them to understand age-related memory changes and provided family members with "an enhanced understanding of the disease process" (Hunsaker et al., 2011).

Interpretation of results is limited as the older adults living in rural areas who attended the ADCs may not be typical of most older, rural-dwelling adults in Appalachia, as seen in the sociodemographic characteristics presented. For example, only 20.1% of the total sample lived in rural areas compared to 42% of the Appalachian population living in rural areas ("The Appalachian Region," 2013). Within the Appalachian region, 55% are married, compared to 77.5% married in our total sample; 26% live alone in Appalachia compared to 16.5% of our total sample (Haaga, 2004). Our study participants also had a greater number of years of formal education (almost 3 years of college) compared to only 20.7% of adults over 25 years of age attaining a bachelor's degree or more residing in the Appalachian region (Pollard & Jacobsen, 2015).

ADCs also employ various recruitment strategies and patient populations were not randomly selected. However, each center continuously monitors cohorts to try and match overall characteristics and recruit to include rural county inhabitants and minorities. This is apparent in the similarities between the rural and urban samples. Both participant characteristics and recruitment strategies support selection bias (Barnhart et al., 1995; Kokmen, Ozsarfati, Beard, O'Brien, & Rocca, 1996), and generalizations to all older adults in Appalachia are not presumed. We also acknowledge that there are regions within Appalachia that are not well represented in this analysis, which could be attributed to location or recruitment strategies of ADCs within the region. However, we have included all participants living within Appalachia as it provides important new information about an underserved population receiving cognitive evaluations at a specialty research center. With consideration for the limitations of this study, NACC UDS provided the unique opportunity to use national multi-center data with detailed standardized neuropsychological testing to describe a region underrepresented in research settings.

2.6   CONCLUSION

This study can serve as an initial description of MCI in the underserved Appalachian region. Findings did not show differences in MCI symptom severity between older rural and urban residents within this region; this may be due to the lack of variability in the sample, as all participants lived within the Appalachian region, or because rural and urban Appalachian residents are more similar to each other than other rural/urban comparisons. Future studies of cognitive

impairment using more representative population samples of Appalachian and non-Appalachian older adults will provide an important next step to identifying disparate cognitive health outcomes among residents in this traditionally underserved region.

3.0   BRIEF REPORT: COMPARISON OF TWO GEOGRAPHIC CLASSIFICATION

SYSTEMS TO EXAMINE DIFFERENCES IN OLDER, RURAL- AND URBAN-

DWELLING ADULTS WITH MILD COGNITIVE IMPAIRMENT

3.1   INTRODUCTION

Currently there are multiple ways to classify residents in the US in terms of the degree of urbanization or rurality of their place of residence (Hall, Kaufman, & Ricketts, 2006). The classification of rural residence, sometimes referred to as micropolitan or frontier residence, is an important classification as different definitions of rural residence contribute to the variability in how resources are allocated and interventions tailored to reduce disparities for rural residents. Two of the most commonly used classification schemes used in research and policy include Rural-Urban Commuting Area Codes (RUCAs) and Rural-Urban Continuum Codes (RUCCs). US Postal Service Zone Improvement Plan (ZIP) codes serve as the basis for RUCA coding, and a scale of 1.0-10.6 is used, where lower numbers typically represent more "urban" areas with better accessibility to city centers and resources ("Rural Urban Commuting Area Codes Data," n.d.). Another rural-urban classification scheme uses RUCCs, which were developed by the Department of Agriculture using US Census coding criteria to determine urban and rural status by county and Office of Management and Budget (Hall et al., 2006). RUCCs classify degree of rurality, metro and nonmetro categories, on a scale of 0-9 and are used by the US government to designate Medically Underserved Areas (MUAs) to direct funding towards those with greatest health

58

disparities based on the Index of Medical Underservice ("Medically Underserved Areas/Populations," 1995). Both of these classification systems present US residence across a spectrum (1-10 and 1-9), and this continuum provides the opportunity for recognition of more narrowly defined communities or populations to receive targeted efforts or resource allocation. However, government and private organizations use different systems to determine residential needs and resources, and the diversity of different classification systems presents concern due to a lack of a uniform definition of rural/urban residence and therefore, inability to accurately compare across communities and populations. Dichotomizing residence as either urban or rural may not delineate smaller communities; however, broad rural/urban comparisons continue to be made in the literature. Thus, the effect of using different rural/urban classification approaches should be explored further. One way to explore this is to compare the different classification schemes across descriptive variables of rural and urban samples, such as sociodemographic characteristics. The National Alzheimer's Coordinating Center (NACC) Uniform Data Set (UDS) provides the unique opportunity to examine rurality classification scheme differences across a large sample of older adults with mild cognitive impairment (MCI), a primordial risk state for Alzheimer's disease. The purpose of this study was to examine the effect of two geographic classification schemes on descriptive characteristics and variables describing impairment.

3.1.1 Design and Sample

A cross-sectional, descriptive study of older, Appalachian adults with MCI was conducted using NACC UDS data. The sample for this secondary analysis included adults who were ≥65 years of

age; with any MCI diagnosis; of Appalachian residence, based on county of residence; and having a designated informant/care partner at an Alzheimer's Disease Center (ADC) visit. Using data from NACC UDS, subjects who met inclusion criteria were classified as either rural- or urban-dwelling according to ZIP code (RUCA codes) or county (RUCC codes). Appalachian residence and MCI classification used to determine inclusion were described previously as well as details of the sample and data collection methods at ADCs, who provide data for the NACC UDS (Mattos et al., 2016).

Measures

Descriptions of individual sociodemographic measures, comorbid conditions, medications measures, and outcome variables have been presented in previous work that examined rural/urban differences using the RUCA classification scheme (Mattos et al., 2016). RUCAs use a numbered coding scheme from 1-10, where urban ("metropolitan") includes primary RUCA codes 1-3 and rural ("micropolitan," "small town," and "rural areas") includes codes 4-10 (US Department of Agriculture Economic Research Service, 2013a). RUCCs use a similar numbered coding scheme from 1-9, where RUCC codes 1-3 are urban ("metro") and codes 4-9 are rural ("nonmetro").

The majority of sociodemographic measures were binary variables (e.g., male/female or yes/no); however, the following variables were measured as continuous variables: age (years), education (years), body mass index (kg/m^2), Geriatric Depression Score (total score), medications (total number), time since onset of symptoms (years), distance from ADC (miles), Mini Mental Status Examination (score), and all outcome variables (adjusted z-scores for neuropsychological measures; raw score for Clinical Dementia Rating-Sum of Boxes [CDR-SOB]). All measurements have been described in previous work in greater detail (Mattos et al., 2016).

3.1.2 Analysis

Data were analyzed using IBM® SPSS® Statistics (version 23, IBM SPSS, Inc., Armonk, NY). Data were first screened using descriptive and exploratory data analyses to portray the sample in total and by coding scheme and to reveal any data anomalies. After applying each rural/urban classification scheme, odds ratios (ORs) were calculated for each measure, where the rural classification served as the reference group. Next, the percent difference between ORs based on RUCA and RUCC schemes relative to the OR based on RUCA was calculated for each measure. To explore differences in precision between the classification systems, those measures with a percent OR difference >40% were further examined by calculating standard errors (SEs) for the ORs based on each classification scheme, and then percent difference in SEs for the ORs relative to the SE based on RUCA was calculated.

3.2   RESULTS

When RUCA and RUCC coding schemes were applied to the sample, each coding scheme showed different rural and urban sample sizes. When the sample was classified using RUCA codes, the sample was 58 rural-dwelling older adults and 231 urban-dwelling older adults (20% rural-dwelling). All participants were able to be classified using both approaches. When classified using RUCC codes, the sample was 38 rural-dwelling older adults and 251 urban-dwelling older adults (13% rural-dwelling).

Overall, there were no significant differences in mean ORs from the null value when comparing rural/urban group differences by RUCC or RUCA coding classifications for sociodemographic factors, comorbid conditions or cognitive symptom severity (see Tables 2, 3, and 4). Relative to ORs based on the RUCA classification, there was variability in the percent difference in the odds ratios between classification schemes across all measures. Percent OR difference ranged from -71.76% (history of psychiatric disorders) to +30.23% (first degree relative with dementia). For sociodemographic features, there was reduction in the OR in going from RUCA to RUCC for all measures except age, which yielded a +2.14% increase in OR (Table 1). There were two variables that had percent OR differences reduced by over 40% going from RUCA to RUCC coding: race, coded as either white or black (-70.50%) and living situation, coded as either living with someone or living alone (-46.73%). For comorbid conditions, there was variability in both magnitude and direction across measures, with the greatest percent OR difference reflecting a reduction in going from RUCA to RUCC coding for history of alcohol abuse (-71.76%), cigarette smoking, past 30 days (-64.57%), and psychiatric disorder (-71.76%). Across cognitive symptom severity measures, both neuropsychological measures and CDR-SOB, no consistent magnitude or direction change patterns in percent OR difference emerged. Percent OR differences ranged from -22.50% to 24.50% for individual measures and -20.47% to 10.39% by domain. As reported in Table 5 for five measures with greater than 40% OR difference (in magnitude), all measures showed a reduction in the percent SE difference, ranging from -0.46% (cigarette smoking, past 30 days) to -8.66% (living situation). There were only six instances where the calculated OR differences changed from being less than 1 to greater than 1: diabetes (RUCA OR, 1.19 and RUCC OR, 0.91), other psychiatric disorders (RUCA OR, 0.73 and RUCC OR,

1.26), number of total medications (RUCA OR, 0.99 and RUCC OR, 1.02), language domain (RUCA OR, 1.07 and RUCC OR, 0.95), attention/psychomotor speed domain (RUCA OR, 0.94 and RUCC OR, 1.14), and CDR-SOB (RUCA OR, 1.02 and RUCC OR, 0.94).

Table 2. Percent Difference in Odds Ratio by RUCA and RUCC classification for Socio-demographic Features of Older, Appalachian-dwelling

Adults with MCI, N=289

Variable	RUCA classification			RUCC classification			% OR difference
	Rural (n=58)	Urban (n=231)	RUCA OR	Rural (n=38)	Urban (n=251)	RUCC OR	
Age, mean years ± SD	74.10 ± 6.15	74.78 ± 6.18	0.98	73.39 ± 5.86	74.83 ± 6.20	0.96	2.14
Education, mean years ± SD	14.90 ± 3.18	15.52 ± 2.98	0.94	15.21 ± 3.14	15.42 ± 3.01	0.98	-4.60
Sex, % male	46.6	56.3	1.48	44.7	55.8	1.56	-5.41
Race, % white	96.6	90.5	0.34	94.7	91.2	0.58	-70.50
Marital Status, % married	81.0	76.6	1.30	81.6	76.9	1.33	-2.07
Living Situation, % live with someone (n=285)	87.9	82.4	0.64	84.2	83.4	0.94	-46.73

Note: OR is odds ratio; RUCA is Rural-Urban Commuting Area Codes; RUCC is Rural-Urban Continuum Codes; SD is standard deviation

Table 3. Percent Difference in Odds Ratio by RUCA and RUCC classification for Descriptive Characteristics of Older, Appalachian-dwelling Adults with MCI, N=289

Comorbid Condition[a]	RUCA classification			RUCC classification			% OR difference
	Rural (n=58)	Urban (n=231)	RUCA OR	Rural (n=58)	Urban (n=231)	RUCC OR	
Heart attack/arrest, % yes	17.2	10.0	1.88	15.8	10.8	1.56	17.41
Atrial Fibrillation, % yes	13.8	10.4	1.38	15.8	10.4	1.62	-17.61
Angioplasty/ Endarterectomy, % yes	19.0	10.4	2.02	21.1	10.8	2.21	-9.56
Cardiac bypass procedure, % yes	15.5	9.5	1.74	13.2	10.4	1.31	24.87
Pacemaker, % yes	3.4	7.4	0.45	2.6	7.2	0.35	22.22
Congestive HF,% yes	5.2	1.3	4.14	5.3	1.6	3.43	17.23
Stroke, % yes	3.4	9.6	0.34	0	9.6	0	100
Hypertension, % yes	48.3	57.1	0.70	50.0	56.2	0.78	-11.43
Hypercholesterolemia, % yes	65.5	60.6	1.23	63.2	61.4	1.08	12.55
Diabetes, % yes	19.0	16.5	1.19	15.8	17.1	0.91	23.72
Active depression, % yes	29.3	35.2	0.76	28.9	34.8	0.76	0
Alcohol abuse, % yes	5.2	2.6	2.04	7.9	2.4	3.50	-71.15
Cigarette smoking, past 30 days, % yes	1.8	3.1	0.56	2.6	2.9	0.91	-64.57
Cigarette smoking, > 100 in lifetime, % yes	50.9	48.0	1.12	50.0	48.4	1.07	4.81
Other psychiatric disorders, % yes	5.2	6.9	0.73	7.9	6.4	1.26	-71.76

Table 3 continued

Comorbid Condition[a]	RUCA classification			RUCC classification			% OR difference
	Rural (n=58)	Urban (n=231)	RUCA OR	Rural (n=58)	Urban (n=231)	RUCC OR	
First degree relative with dementia, % yes	52.4	54.4	0.92	43.2	54.2	0.64	30.23
Body Mass Index (kg/m^2), mean ± SD	27.33±5.51	27.85±4.94	0.98	26.86±5.11	27.88±5.04	0.96	2.04
Geriatric Depression Score, total score, mean ± SD	2.35±2.40 (n=57)	2.32±2.61 (n=225)	1.00	1.95±2.31 (n=37)	2.38±2.61 (n=245)	0.93	7.56
Number of total medications, mean ± SD	6.47±4.01 (n=57)	6.58±3.46 (n=231)	0.99	6.76±4.38 (n=37)	6.53±3.44 (n=251)	1.02	-2.62
Time since onset of symptoms (years), mean ± SD	**2.98±1.91* (n=49)**	**3.89±2.70* (n=213)**	0.85	**2.75±1.80* (n=32)**	**3.85±2.66* (n=230)**	0.80	5.43
Distance from Alzheimer's Disease Center (miles), mean ± SD	**65.03±36.06***	**17.20±16.49***	1.08	**69.21±35.60***	**20.37±21.64***	1.05	2.69
Age, sex, and education adjusted Mini-Mental Status Examination score	- 1.04±1.94	-1.08±1.73	1.01	-0.83±1.85	-1.11±1.76	1.10	-8.29
Note: OR is odds ratio; RUCA is Rural-Urban Commuting Area Codes; RUCC is Rural-Urban Continuum Codes; SD is standard deviation							

Table 4. Percent Difference in Odds Ratio by RUCA and RUCC Classification for Cognitive Function Variables of Older, Appalachian-Dwelling Adults with MCI, N=289

Variable	RUCA classification			RUCC classification			% OR difference
	Rural (n=58)	Urban (n=231)	RUCA OR	Rural (n=38)	Urban (n=251)	RUCC OR	
Memory	-0.99 ± 1.09	-0.82 ± 0.97	0.84	-0.94 ± 1.31	-0.84 ± 0.94	0.90	-7.14
Logical Memory 1A- Immediate	-0.89 ± 1.15	-0.72 ± 1.05	0.86	-0.87 ± 1.38	-0.74 ± 1.02	0.89	-3.71
Logical Memory 1A- Delayed	-1.09 ± 1.09	-0.92 ± 0.98	0.84	-1.02 ± 1.30	-0.94 ± 0.95	0.92	-10.14
Language	-0.31 ± 0.75	-0.35 ± 0.76	1.07	-0.36 ± 0.81	-0.33 ± 0.75	0.95	10.93
Boston Naming Test Score	-0.69 ± 1.12	-0.52 ± 0.97	0.85	**-0.87 ± 1.16***	**-0.51 ± 0.96***	0.72	15.29
Category Fluency, Animals	-0.52 ± 0.87	-0.57 ± 0.88	1.06	-0.53 ± 0.93	-0.56 ± 0.87	1.04	2.08
Category Fluency, Vegetables	0.29 ±1.05 (n=58)	0.06 ± 1.22 (n=230)	1.18	-0.32 ± 1.08	0.07 ± 1.20	1.19	-0.93
Attention/Psychomotor Speed	-0.25 ± 0.77	-0.23 ± 0.63	0.94	-0.18 ± 0.61	-0.24 ± 0.67	1.14	-20.47
Trailmaking A Score	**-0.58 ± 1.75* (n=58)**	**-0.06 ± 0.89* (n=230)**	0.71	-0.35 ± 1.32	-0.14 ± 1.10	0.87	-22.50
Wechsler Adult Intelligence Scale - R Digit Symbol Substitution	-0.35 ± 0.93 (n=58)	-0.19 ± 0.91 (n=230)	0.82	-0.28 ± 0.93	-0.21 ± 0.91	0.91	-11.72
Digit Span Forward	**-0.03 ± 0.86***	**-0.35 ± 0.98***	1.43	-0.11 ± 0.78	-0.32 ± 0.99	1.26	11.91
Digit Span Forward Length	-0.05 ± 0.87	-0.30 ± 0.97	1.34	0.00 ± 0.86	-0.29 ± 0.96	1.40	-4.39
Executive Functioning	-0.43 ± 0.82	-0.32 ± 0.78	0.84	-0.50 ± 0.77	-0.32 ± 0.79	0.75	10.39
Trailmaking B Score	-0.75 ± 1.36 (n=58)	-0.51 ± 1.24 (n=229)	0.87	-0.63 ± 1.28	-0.54 ± 1.27	0.95	-9.56
Digit Span Backward	-0.27 ± 0.96	-0.21 ± 0.90	0.93	-0.42 ± 0.87	-0.19 ± 0.92	0.75	19.42
Digit Span Backward Length	-0.27 ± 0.90	-0.25 ± 0.86	0.97	-0.44 ± 0.82	-0.22 ± 0.87	0.74	24.05
Clinical Dementia Rating Sum of Boxes (range 0-17)	1.57 ± 1.27	0.98	1.02	1.51 ± 1.27	1.60 ± 1.27	0.94	3.87

* Statistically significant within-group differences
Note: OR is odds ratio; RUCA is Rural-Urban Commuting Area Codes; RUCC is Rural-Urban Continuum Codes; SD is standard deviation

Table 5. Percent Difference in Standard Error by RUCA and RUCC Classification for Selected Variables with Percent Odds Ratio Differences

40%+ of Older, Appalachian-Dwelling Adults with MCI

	RUCA Standard Error	RUCC Standard Error	% Difference in Standard Error
Race, % white	.754	.760	-0.80
Living situation, % living with someone	.439	.477	-8.66
History of alcohol abuse, % yes	.723	.730	-0.97
History of cigarette smoking, past 30 days, % yes	1.079	1.084	-0.46
History of other psychiatric disorders, % yes	.647	.655	-1.24
Note: RUCA is Rural-Urban Commuting Area Codes and RUCC is Rural-Urban Continuum Codes			

3.3   DISCUSSION

For this study, the purpose was to understand how RUCA and RUCC classification schemes differ when examining differences between rural and urban samples with Mild Cognitive Impairment (MCI). The odds ratios (ORs) and the differences in ORs between classification schemes provide a type of effect size. Overall, results showed variability in both magnitude and direction of difference in the calculated ORs between the RUCA and RUCC classification schemes for sociodemographic factors, comorbid conditions and cognitive symptom severity measures. However, there were five measures that had large changes in the magnitude of the RUCA to RUCC schemes: race, living situation, history of alcohol abuse, history of cigarette smoking in the past 30 days, and history of psychiatric disorder. One reason for these observed percent differences in ORs may be attributed to the marked reduction in the number of participants classified as rural when applying the RUCC classification (n=58 to n=38, respectively), creating an even smaller rural sample size, in contrast with the urban sample size, and therefore a greater difference in the percent OR change. For example, for race, only two participants were non-white using *both* RUCA and RUCC classifications. However, rural/urban sample size changes for race between classifications schemes did present a large difference between the two schemes (>70% OR difference), where we would not assume there to be a clinically meaningful difference between the two classification schemes for black race. Additionally, there were small numbers of participants

within certain groups (e.g., black race and having a *positive* history of a health condition), and RUCA/RUCC differences may be more sensitive to a change in a few participant's rural/urban classification than those conditions presenting a greater number of participants that report a positive history of a certain condition (e.g., hypertension). There were six cases where the calculated OR differences changed from being less than 1 to greater than 1. Half of the cases changed from less than 1 to greater than 1 and vice versa, thus we believe these are isolated findings likely due to chance and should not be over-interpreted.

One limitation of this study is the small rural sample size, regardless of the rural/urban classification scheme applied. Although the sample was large overall (N=289), only 20% of the sample was classified as rural by RUCA codes and 13% of the sample classified as rural by RUCC codes. This marked difference in sample sizes as well as small number of "positive" cases for certain variables contributed to the variability in findings. In the future, more equally distributed rural/urban sample comparisons are recommended to provide further insight into differences in classification schemes, particularly for sociodemographic variables, that may play a larger role in policy decisions, resource allocation, and/or research.

Currently, the US federal government reports use of two rural classification schemes (US Department of Health & Human Services, 2015). One is based on US Census Bureau data and is determined solely by population size, where 19.3% of the US population is classified as rural. The second classification scheme is also based on US Census data but considers commuting distance, where only 15% of the total population is classified as rural. The second classification scheme is very similar to RUCCs; however, RUCCs are based on individual county classification, whereas multiple counties can be considered a "core-based statistical area" (CBSA), or smallest

70

geographical area in the second scheme used by the US government. This individual county classification used in RUCCs is important as it allows for delineation of geographical units, specifically smaller rural communities. The US Department of Health and Human Services also recognizes RUCA codes as an important way to examine rurality, both using Census data as well as considering distance to services (US Department of Health & Human Services, 2015). At present, there is limited research on differences in outcomes research between classification schemes, and use of new or modified classification schemes is common at the federal level, making standardization difficult for rural classification. As there are many different agencies and groups working to improve rural health disparities, use of rural classification schemes that help describe the population and identify disparate areas in the US is essential. Identification of a universal "rural" definition may not be appropriate at this time as different definitions are being used for a variety of different purposes, however the ability to compare differences between and among different rural-urban health indicators is crucial to identifying and targeting rural communities to improve health and quality of life.

4.0   MANUSCRIPT 2: PERCEIVED SOCIAL DETERMINANTS OF HEALTH IN OLDER, RURAL-DWELLING ADULTS WITH EARLY-STAGE COGNTIVE IMPAIRMENT

4.1   ABSTRACT

Background: Limited access to resources and delayed detection of subtle cognitive changes may negatively impact the long-term cognitive health of rural-dwelling adults. This study explored perceived social determinants of health within older, rural-dwelling adults with early-stage cognitive impairment.

Methods: Semi-structured interviews were conducted with older, rural-dwelling adults with early-stage cognitive impairment, and their care partners. Thematic content analysis was performed, supplemented by dyadic observations to provide a thicker characterization of social determinants of health.

Results: Participants (n=9) were 73.7±6.0 years of age with 14.2±3.1 years of education and care partners (n=10) were 70.9±7.4 years of age with 15.6±2.3 years of education. Data analysis revealed six themes: *Staying active*, *Eating well*, *Living with cognitive changes*, *Living rural, Connecting with neighbors and community*, and *Relying on children*.

Discussion: Dyads' depictions of perceived social determinants of health focused on the advantages of living in rural areas and the importance of social connectedness.

4.2   INTRODUCTION

Rural adults suffer disproportionately poorer health and worse health outcomes compared with urban-dwelling adults (Jaffe, 2015). Limited resources and access to care impact rural adults ability to receive timely management for both chronic and acute conditions (Gamm et al., 2010). Currently, only 10% of physicians practice in rural areas, while almost 20% of Americans live in these underserved rural areas (Barley, Reeves, O'Brien-Gonzales, & Westfall, 2001; US Census Bureau Geography, 2010). Additionally, lack of accessible specialists (Barley et al., 2001; Gamm et al., 2010) may lead to delayed detection of subtle health changes in rural older adults. The combination of higher prevalence of risk factors and limited access to care emphasizes the importance of early detection and diagnosis of specialist-managed health changes in this population.

Among older adults, changes in cognition represent a prime example of a health status alteration that may go undiagnosed or be diagnosed at later stages, particularly because late life cognitive changes may not initially appear to directly affect daily living. Specifically, early cognitive changes associated with Mild Cognitive Impairment (MCI) or early-stage Alzheimer's disease (AD) may ensue insidiously, worsen over time and, ultimately, have profound implications for affected individuals' ability to carry out daily activities. MCI is considered a likely prodromal state for dementia (e.g. AD, Petersen et al., 2001). A diagnosis of MCI is typically established in a specialty setting and 1) involves decline in at least one cognitive domain, 2) requires maintenance of near normal functional activities, and 3) requires that the degree of cognitive impairment is not sufficient to warrant a diagnosis of AD or related dementia

(Gauthier et al., 2006; Petersen et al., 2001). While older adults with MCI are at greater risk than those without MCI for developing dementia, it is not clear that everyone who develops dementia passes through a well demarcated clinical syndrome of MCI (Mitchell & Shiri-Feshki, 2008, 2009).

Both those with MCI and early stage AD may benefit from early detection of cognitive decline. In the case of MCI, early detection of symptoms may trigger referral to a specialist for further evaluation and monitoring for evidence of progression to dementia. In the case of early AD, early detection is needed to ensure prompt access to current approaches in treatment which focus on maintenance of mental function, management of behavioral symptoms, and slowing or delaying the symptoms of disease ("About Alzheimer's Disease: Treatment | National Institute on Aging," n.d.).

Health status, including cognitive functioning, is widely recognized to be influenced by a host of factors, including social determinants of health (*The Vision, Mission, and Goals of Healthy People 2020*, 2011). Such factors may be of particular importance to rural-dwelling persons affected by MCI and early stage dementia. A systematic review examining factors contributing to missed and delayed diagnosis of dementias in primary settings found that patient-related factors, as well as resource and financial system-related factors, contributed to missed and delayed diagnosis (Bradford et al., 2009). The identification of perceived determinants of health may help promote identification of early cognitive changes and facilitate lifestyle modifications in underserved populations such as rural communities. In rural communities, identification of specific social determinants that may contribute to cognitive health in rural-dwelling adults may provide critical information for improving the long-term cognitive health of this already underserved

group. The purpose of this study was to explore perceived social determinants of health within older, rural-dwelling adults with early-stage cognitive impairment.

4.3   METHODS

4.3.1   Participants

Participants were drawn from a longitudinally followed cohort at the University of Pittsburgh Alzheimer's Disease Research Center (ADRC, P50 AG005133 PI: O. Lopez, MD). Inclusion criteria for the ADRC study were: >30 years of age, English speaker, >7 years of education, adequate visual and auditory acuity to complete neuropsychological testing, and a reliable care partner who is capable of providing information about the participant's clinical symptoms. Additional inclusion criteria for the current study were ≥65 years of age and a current diagnosis of either 1) mild cognitive impairment (MCI) diagnosis based on Petersen et al. (2001) and Lopez et al. (2003) or 2) Probable Alzheimer's disease (AD) diagnosis based on McKhann et al. (1984) with a Mini Mental Status Exam score of 18 or higher. This approach helped minimize the possibility that participants may have advanced cognitive symptoms, which may have impeded their ability to share their perceptions of social determinants of cognitive health. Purposive sampling was used to promote heterogeneity. Specifically, participant characteristics such as sex, degree of rurality, and relative degree of cognitive impairment were considered during recruitment to maximize diversity within the sample (Glaser & Strauss, 1967). United States Department of

Agriculture Rural-Urban Commuting Areas Codes (RUCAs) were used to classify ZIP codes using codes from 1-10, where rural included primary RUCA codes 4-10 and included "micropolitan", "small town", and "rural areas" (US Department of Agriculture Economic Research Service, 2013a). A list of identified rural ZIP codes across four states was provided to the ADRC coordinator, who identified individuals meeting the study inclusion criteria and then called to ask if they would be interested in participating in the study. If they agreed to be contacted by the study, the participant was then called by the study PI to present the study in greater detail. Family care partners of the participants with MCI or early-stage AD were concurrently recruited and invited to consent to the study and participate in the interviews. There were no exclusion criteria for care partners. Previous participation in Pittsburgh ADRC activities helped promote trust in this sample beginning at first contact with the investigator.

The University of Pittsburgh ADRC secures written informed consent from all participants for communication between annual visits, including permission for the ADRC recruitment coordinator to contact individuals via telephone about other ancillary studies. Once the ADRC coordinator identified potential participants, the investigator introduced this ancillary study to eligible participants and their care partners over the phone. Those participants who expressed interest in the study were scheduled for a home visit where the study was presented in detail and written informed consent was obtained from both participants with cognitive impairment and their care partners. Capacity to consent was assessed using questions from the University of California, San Diego Brief Assessment of Capacity to Consent (UBACC, Jeste et al., 2007). There were no indications of a lack of decisional capacity based on the UBACC during the consent process. University of Pittsburgh Institutional Review Board approved all procedures.

4.3.2 Design & Data Collection

Qualitative description (Sandelowski, 2000, 2010) was used to explore social determinants of health within older, rural-dwelling adults with early-stage cognitive impairment. The purpose of this approach was to explore beliefs and behaviors of individuals belonging to this culture-sharing group, older, rural-dwelling adults, and identify perceived social determinants of health for this population. We conducted semi-structured interviews in each participant's home environment with the participant's care partner present and participating in the interview. Prolonged engagement through home visits and extended interview length were used to cultivate a trusting relationship and meaningful data collection. Care partners were encouraged to participate in the interviews. In one interview, two care partners, husband and daughter, participated in the interview. While data from both of those care partners were included in the analysis, data from the corresponding participant was excluded. During the first 30 minutes of the interview the participant appeared to be confused and displayed frustration and distress requiring the interviewer to stop directing questions to her.

The interview guide consisted of fourteen semi-structured interview questions and was designed to allow for open dialogue among participants, care partners, and the investigator. The Social Determinants of Health and Environmental Health Promotion (SDH) Model proposed by Schulz and Northridge (2004) provided the scaffolding framework to guide interviews and participant observations, with a particular focus on gaining participant perspectives on promoting health at the community, interpersonal, and individual levels (as depicted by shading in Figure 1). Within the model, there are key factors contributing to health promotion including:

environment, social context, health behaviors, social integration and support, and well-being. Four of the fourteen interview guide questions directly addressed concepts presented in the SDH model, and this was intentional as the guide wanted to refrain from leading participants to discuss the factors that may have been expected based on the model.

Recorded interviews lasted 80 ± 9 minutes and ranged from 66-95 minutes in length; length of the individual home visit lasted 110 ± 23 minutes and ranged from 84-160 minutes. Interviews continued until data saturation, which included a total of nine interviews with participant-care partner dyads. One investigator interviewed all dyads and made observations before, during, and following the interviews. The investigator kept a reflexive journal to document decisions, processes, and reflections over the course of the study (Erlandson, 1993). Bracketing was acknowledged by the investigator from the beginning of study development through dissemination to separate individual biases or opinion from that which is actually observed (Sandelowski, 1986).

In addition, multiple data collection methods were applied to gain insight into cultural and social nuances that may not be captured in dialogue alone. Observations of both participants and their surroundings were used for the purpose of making a qualitative assessment of the social setting of the participant's home and surrounding environment (Lofland, 1971). Through observation, the researcher observed what went on, who or what was involved, when and where things happened, how they occurred, and why things happened (Jorgensen, 1989; Malinowski, 1978). Events surrounding the interview, such as introductions and other observations, were captured by investigator home visit notes during and after the interview as described by (Pelto & Pelto, 1978). To ensure credibility (Beck, 1993), home visit notes from these interactions,

relationships were reviewed and expanded to enhance recall following the interviews. Interviews and visit notes were transcribed and transcripts verified by a different person than the transcriptionist. Furthermore, the primary investigator listened to every tape and read all transcripts to ensure accurate transcription and checking.

Between interviews, comparative analyses were performed. Analysis of participant responses led to changes in the order of interview questions and the approach to asking the questions. Additionally, the investigator's own actions, interactions, and behaviors were documented promptly following the interview, and reflexive journaling by the primary investigator was used to document these modified approaches to interviews and communication with participants.

4.3.3 Data Analysis

All transcribed data were transferred from a word processing program to Atlas.ti$^{©}$ (version 4.2, Scientific Software Development, Berlin). Data analysis used multiple techniques: line-by-line coding of transcriptions, data reduction (Huberman & Miles, 1998), data display (Miles & Huberman, 1994), emerging theme identification, and conclusion drawing/verification (Erlandson, 1993). First, the primary investigator (MM) line-by-line coded all interviews and three other independent researchers (JL, MN, & LH) line-by-line coded up to four interviews each. Consensus between investigators was reached for codes that emerged within each interview and among interviews. Following line-by-line coding consensus, categorized data were displayed in matrices so that the research team could examine potential patterns, regularities, or irregularities that point

toward possible themes and relationships (Miles & Huberman, 1994). After categories were reduced and displayed, a team of four interdisciplinary investigators (MM, JL, AH, & AD), three from nursing and one from social work, met in-person to discuss themes and sub-themes, verify findings, and draw conclusions. It is important to note that the SDH model was not used to guide coding or category identification, but was later used as a way of organizing the themes and conclusions.

4.4   RESULTS

Participants (n=9) with cognitive impairment were 73.7 ± 6.0 years of age with 14.2 ± 3.1 years of education; 44.4% were female, 100% white, 88.9% married, and 100% lived with someone. Care partners (n=10) were 70.9 ± 7.4 years of age with 15.6 ± 2.3 years of education; 70% were female, 100% white, 80% married, and 90% lived with someone, specifically their care partner. Eight of the ten care partners were spouses (80%), one was a daughter, and one was a friend of over 30 years of the participant. In-home interviews took place across four states with RUCA codes across "micropolitan", "small town", and "rural areas" (RUCA codes 4.0, 4.2, 5.2, 7.4, 8.0, & 10.0).

Six themes emerged from the semi-structured interviews with the dyads: *Staying active*, *Eating well*, *Living with cognitive changes*, *Living rural, Connecting with neighbors and community*, and *Relying on children*. Of the 9 dyads, 4-8 contributed to each theme, with at least one counter example noted for each theme. Before describing the six themes, it is important to

note that across eight of the nine interviews, conversation directing by members of the dyad was used to help guide conversation. Conversation directing refers to either 1) the participant or care partner's attempt to redirect conversation back to the interview questions or away from certain topics or 2) allowing the other member of the dyad to contribute to the interview. Examples of redirection back to interview questions include: "We better get back to the questions" and "Why don't we get back to what we're supposed to be doing?" Similarly, care partners would try and encourage the participant to talk or respond to prompts. For example, "What do you think? [The researcher] wants to know what you think." Redirection by loved ones contributed to maintaining an open interview environment, and provided a buffer by which the interview could remain focused on the topics of interest.

Staying Active

  Staying active emerged as a major theme across eight of the nine interviews, and the value participants and care partners placed on *staying active*, whether in the context of growing older or in light of their diagnosis, was striking. Within the theme, *Staying active*, there also were two subthemes identified: *staying physically active* and *staying mentally active*. One subtheme, *staying physically active*, focused on physical ability and desire to be active. For example, a 65-year-old female care partner said of her husband with MCI, "He's very – he's very physical. He's always doing something. He's not the one to sit around and not do anything…anything he can go to when he's home, he does..." Activities mentioned by participants ranged from taking walks alone to structured group classes at a local YMCA. On the other hand, a few care partners also shared concern that they believed either they or their loved one weren't being physically active: "Sometimes it's motivation or whatever and it's stickin' to it. And it's easier not to bother" (68-

year-old female care partner). Overall, a sense of personal responsibility and self-initiative came out through discussions of exercise by four of nine dyads.

There was also mention of *staying mentally active* to maintain brain and general health by six of the nine dyads. A 68-year-old female care partner said the dyad placed importance on "keeping interactive [with others]." Another example comes from a 69-year-old female with MCI who spoke about reading, "I read a lot in my book group… I do keep my brain, you know, as… active as I can." Other activities members of the dyads presented to help promote mental activity included involvement in weekly church activities, puzzles (e.g., word finding and Sudoku), and playing cards. In contrast to these examples, there was a care partner who said keeping the "brain active" was important, but her husband with MCI did not: "And for him to keep his brain active…it's a fight and I can't get him to do it." In the three cases that care partners spoke about lack of their loved one's or their own mental activity, there was also the direct and indirect acknowledgement that promotion of brain or mental activity is good for one's health.

Eating Well

Eating Well was identified as another major theme in interviews with two subthemes: 1) *making healthy food selections* and 2) *avoiding chemicals and preservatives*, which were typically presented during discussion of brain health. Seven of the nine dyads spoke about making, or trying to make, healthy food choices, and two dyads specifically mentioned how they make efforts to avoid chemicals and preservatives. Making healthy food selections, such as eating fruits and vegetables, was important to participants: "We're healthy eaters… We try to be healthy eaters…we eat a lot of salads and fruit" (81-year-old male with AD). For one family, they noted that food choices changed after receiving an AD diagnosis: "And since this has happened to us, I've gotten

82

into… it more." Eating habits ranged from making recent efforts to improve food choices to modifying healthy eating habits adopted in the past.

In addition to healthy food choices, the avoidance of chemicals and preservatives in food emerged. A 67-year-old female care partner spoke about how her own health promotion-seeking led her to this decision:

"I was reading about [Alzheimer's disease] and it said that sometimes it's the preservatives in your meat, and I thought well we're going to raise beef…That was just something that was very important to me. That way we know what's going into them and that they aren't being filled with preservatives and all the crap that they put in the meat."

Another female care partner spoke to the maintenance of the family garden, "… we have our own garden and eat stuff that way so I can't say that they're necessarily be chemicals…it's more natural or whatever, our own stuff." The dyad's choice to raise their own livestock or maintain a garden demonstrates the efforts undertaken to promote, what they consider to be, an important feature of healthy eating.

Participant's emphasized healthy daily health behaviors, including staying active and eating well, related to both general and cognitive health. The importance placed on eating well and staying active, both physically and mentally, was apparent throughout interviews and highlights efforts to promote healthy lifestyles.

Living with cognitive changes

The theme, *Living with cognitive changes*, emerged and is described through three subthemes: *loss/stressors, maintaining control,* and *symptom dismissal*. Eight of the 9 dyads

contributed to the theme, specifically 8/9 to *loss/stressors,* 6/9 to *maintaining control,* and 6/9 to *symptom dismissal*.

Dyads mentioned familial *loss/stressors* related to their well-being. One participant noted a current stressor: "My mother has nobody but me. Just me. There's nobody in the family. I can't imagine. Back then I didn't—it didn't register, what my mother was going through." A care partner tried to provide some background information on her husband and said, "He lost his daughter, his one daughter…he lost her to cancer in [year]. And he also lost a grandson in a snowmobile accident ..." Disclosure of life events and stressors throughout interviews was common and also illustrates the trusting relationship between the dyad and investigator.

Some participants and care partners described *maintaining control* when discussing their cognitive symptoms, while others reported feeling that their life course was out of their control. One participant presented feelings of control over current circumstances: "…anything I can do to prolong it or make it easier, that's what I'm trying to do right" (73-year-old male with MCI). On the other hand, a 73-year-old female with MCI shared feelings that the diagnosis was out of her control, "I mean if I got it, I got it, you know? I didn't ask for it; you know what I'm saying?" A 75-year-old male with AD, shared similar feelings, "We don't know what caused it, so how could we tell you what we could have done to avoid it now?" *Maintaining control* was a pervasive theme throughout interviews, as evidenced by the positive health behaviors discussed as well as feelings of control of one's life.

There also were forthcoming discussions of how to *maintain control* using available resources to minimize the impact of cognitive symptoms. However, there were two instances presenting concerns with quality and efficiency of medical care, specifically referring to

84

inefficiency and frustration with doctors. During a recent visit to her primary care provider a 69-year-old female with MCI said, "And it was… the care is very frustrating." On the other hand, resources included examples such as home health aides, family, friends, and adult day health centers.

The third subtheme, s*ymptom dismissal,* was highlighted through sarcasm and humor when participants discussed cognitive symptoms or events. For example, one participant made a joke about his memory concerns, and ended with "Well, I'm dying," followed by laughter. Conversation about cognitive symptoms varied across interviews, however the way in which participants, in particular, dismissed and downplayed their own symptoms or disease trajectory provides insight into possible coping mechanisms for this population. Comments about pending or inevitable death following symptom dismissal jokes point to a viewing death as an inevitability as a potential way to help cope with these cognitive changes. Although participant symptom dismissal was noted across six dyad interviews, there also were a number of counter examples demonstrating participant or care partner acceptance, as presented in *maintaining control.*

Living Rural

Living rural emerged as another major theme in interviews, with participants consistently emphasizing the advantages over disadvantages of living in a rural area. *Living rural* was divided into advantages and disadvantages with subthemes for each. Seven of the nine dyads spoke to advantages of living in a rural area, while only two dyads spoke to the disadvantages.

Advantages of living rural

Overall, the majority of dyads spoke about the reasons why living further from the city or in a rural area was advantageous, and there were two subthemes: *slower pace of life* and a *good*

85

place to raise children. Speaking to the rural lifestyle, a 67-year-old female care partner stated, "I'll be perfectly honest with you – you know – you look at the crime rate and the traffic, and we just decided we were much happier at a slower pace." Participants also spoke to problems with drugs "in town", which influenced their decision to raise their family outside the city, as well as simply being "a good place to raise my kids" at the time they were married (65-year-old female care partner). Although only mentioned by two dyads, the pride and responsibility of having animals on their land also emerged. Participants shared that they owned and cared for cows on their land or enjoyed preparing food for seasonal hummingbirds. During discussion of caring for animals on their land, three dyads spoke to the "advantage of living where we do" for the outdoor work, green space, and open space.

Disadvantages of living rural

There were two subthemes within disadvantages of living rural*: traveling longer distances by car* and *fracking. Traveling longer distances by car* was identified by two participants as a disadvantage of living further away from a city when talking about why their friends do not want to travel to or live in a rural area. One 73-year-old female with MCI said, "…they don't want to come…nothing going on [laughter], and, it's like, it's a wonderful place to live. Why wouldn't you want to come?" Another 73-year-old female care partner said,

> "…a lot of our peers, uhm, they think that [big city] is so far away and if they have to have something done, they would never go to [big city]. They're afraid of it. They're afraid of traffic."

When distance from a city was mentioned, it was during discussion about what "other people" thought about living or visiting rural areas, our participants did not share their own

86

stressors related to residence. There was also no mention by any dyad that traveling long distances in the car was a disadvantage to living in a rural area or a concern for accessing care. Only one dyad mentioned fracking, however the spontaneous mention of the impact of fracking on their immediate environment was notable. A 63-year-old female care partner said,

> "… you feel like something is majorly on fire, which is, I mean there is. It's glowing. You can see it for miles… and I talked to some people who are closer and they said they can actually hear this roaring rush when it's burning off and it burned for days, week—I don't know—it seemed forever that it burned. You know, it makes me uneasy…"

Not all dyads resided in areas that may be conducive to fracking, but for this one dyad, its impact was significant in that the care partner had conversations with other people that were also impacted or experienced the effects of fracking on nearby lands.

Relying on Children

The theme, *Relying on children*, emerged during discussion of daily or weekly activities, focusing on the supporting roles children play in their lives or their lack of involvement within the larger family. Some dyads (5/9) spoke about the reasons for and frequency of family-related events or visits with family. The majority of visits or attended events were with children or grandchildren, and for many dyads, family celebrations were mentioned as a source of joy. A 73-year-old female care partner spoke about her daughters as a resource for caring for her husband with early-stage AD when she had scheduled events to attend, "If I have to be somewhere overnight, one of the girls will come and stay overnight with them, with him [participant with early-stage AD]." Although most dyads with children had at least one child living nearby, one 81-year-old female with AD shared concerns that they did not have assistance from children because of distance: "We

87

don't have any kids around here to help us with. That's our problem, see?" Of the two dyads that did not explicitly speak about their children or grandchildren, one was never married nor disclosed she had children, and the other dyad included a child of the participant. For the dyad that included the child, the daughter's role in providing care to her mother and father was evidenced by the attendance and knowledge of her parent's doctor's appointments, coordination of care for her mother with early-stage AD, and concern for her parent's well-being.

Connecting with Neighbors and Community

The theme, *Connecting with neighbors and community,* arose through discussion about the role the participant and/or his/her care partner play(s) in the community and identification or use of community resources by four dyads. One of the most striking statements speaking to sense of community was repeated by both members of a married couple who stated, "We have our own community." Another 81-year-old female with AD spoke about the helpfulness and camaraderie of her neighbors, "all of us on this road are … real friendly and help each other." There was, however, one counter example of note, a 62-year-old care partner who reported feeling that her family did not have adequate social resources, which she perceived as a disadvantage to the family: "All these people [my parents] took care of for years and years and they're all gone and there isn't the resources of people that'll come." Three dyads spoke explicitly about relationships with their neighbors or larger community, and there was only one example of a lack of this connection. It was also notable that no participants were currently involved or participating in any AD support groups.

4.5   DISCUSSION

Semi-structured interviews with older, rural-dwelling adults with early cognitive changes and their care partners focused on adopting a healthy lifestyle, describing relationships with others, and living in rural areas. Correspondence was noted between many of the emergent themes in the study and those factors outlined in the Social Determinants of Health and Environmental Health Promotion Model (SDH, Schulz & Northridge, 2004), however there were also themes, such as *Living with cognitive changes,* that did not clearly correspond with determinants found in the SDH model.

Correspondence with the Social Determinants of Health and Environmental Health Promotion Model

Themes, *Staying active* and *Eating well,* that emerged from interviews with dyads highlight the importance of how health behaviors, such as physical/ mental activity and eating habits, are related to and promote health and well-being. Both *Staying active* and *Eating well* appear in the SDH model under health behaviors as "Dietary practices" and "Physical Activity," and classified under the interpersonal level or proximate level. Participants and care partners that attend the ADRC receive suggestions and information from the ADRC to promote health and try to reduce AD risk factors, hence, health behaviors mentioned in interviews may reflect information provided to participants during an ADRC visit or subsequent follow-up on their own. A previous study also noted these positive lifestyle changes in self-initiated health behaviors following a cognitive diagnosis (Morgan, Garand, & Lingler, 2012). Although our study did not probe for details about participant or care partner's nutrition and physical activity, these topics have been explored in the

89

literature. For example, a previous study in a rural and remote memory clinic found that of 260 adults with non-amnestic MCI or amnestic MCI, only about 4% reported exercising the recommended amount and frequency each week and less than a 20% reported meeting Canada's Food Guide recommendations (Bello-Haas, Connell, & Morgan, 2014). The same study showed that those with AD or other non-AD dementias had higher rates of recommended exercise and nutrition compared to those at earlier stages of cognitive impairment, despite the possibility that those in earlier stages may benefit even more from lifestyle interventions (Bello-Haas et al., 2014). It is encouraging that our participants voiced proactive efforts to improve nutrition and exercise frequency. Follow-up inquiry into quantifiable diet and nutritional intake as well as measured exercise could provide both further clarification as to what it means to "eat healthy" and "stay active." This is important for practitioners to both 1) know what people perceive as eating healthy and staying active and 2) be able to provide input or guidance for reaching or maintaining balanced energy intake/output.

The theme, *Living rural,* mirrored the SDH concept of "Built Environment," and emerged in discussions that emphasized the advantages and downplayed the disadvantages of living in a rural area. Within the SDH model, the built environment includes physical or material buildings or structures, as well as other aspects such as the presence or adoption of a slower or positive environment that were mentioned in the study. The "Built Environment" is considered a community level determinant of health and includes considerations such as land use or transportation systems, which may impact rural residents in particular. For example, the lack of public or private transportation systems needed access to health care providers and services may delay routine medical visits for rural residents, as well as cognitive screenings or follow-up

appointments by specialists typically working in city centers (Barley et al., 2001; US Census Bureau Geography, n.d.).

Themes, *Connecting with neighbors and community* and *Relying on children,* aligned conceptually with "Social Integration and Support" and highlight the importance of social connectedness. For example, family, community, and church events played a recurring role in weekly activities for most dyads. These interactions and planned events through spending time with friends or family promote feelings of connectedness with others and promote engagement in daily activities (Han, Radel, McDowd, & Sabata, 2015), which may promote cognitive and mental health. A study conducted by DiNapoli, Wu, and Scogin (2013) among older, Appalachian adults found that social isolation, social disconnectedness, and perceived isolation predicted worse cognitive functioning and neuropsychological testing. When distance, time, or circumstance may not permit in-person meetings or events, technology may be a potential accompanying tool to promote social connections in persons living with early cognitive and their care partners.

Stressors

A particularly interesting finding was that there was limited mention of stressors, another key concept in the SDH model, by participants or care partners. The absence of talk concerning stressors was noted to be in direct contrast to frequent and forthcoming discussions of resources and other factors that serve as buffers to the strain imposed by cognitive symptoms during interviews. Although interview questions did not ask explicitly about possible stressors, such as finances, this was something that investigators believed would emerge through prolonged engagement with participants and open discussion about a variety of topics. Instead dyads spoke to how they live with cognitive changes, such as through positive lifestyle changes or attitude.

91

Previous research has presented how certain traits in rural adults, such as stoicism and resilience, which may help explain the absence of mention of stressors and focus on what can be changed for this population (Ford, Wong, Jones, & Steel, 2016).

None of the care partners of family members with AD were attending a formal AD support group. There are several explanations as to why care partners were not currently involved. One reason may be because of the requirement to travel longer distances to meet with other care partners in a group setting, thus limiting face-to-face meetings. Traveling greater distances to access health care has been presented in the literature as an important determinant of health (AHRQ, 2005; Hunter & Wilson, 2012), however, travel was not mentioned as a stressor or limiting factor for receiving medical services or support networks, such as AD support groups, by any participants or care partners. Another reason may be that dyads prefer to retain their privacy within small communities and not share cognitive diagnosis or daily struggles with others who could then share this information within social circles in a small rural community. Finally, there may be a lack of resources to create and maintain formal in-person support groups in rural areas, particularly for individuals with MCI, which is a less commonly applied diagnosis than AD. Connecting with support groups via the Internet have been shown to reduce rural-dwelling caregiver's feelings of isolation (Blusi, Kristiansen, & Jong, 2015), and should be considered as an option to improve social connections and build support systems where in-person support groups may not be possible or desirable. The Alzheimer's Association also offers online message boards and chat rooms (Alzheimer's Association, 2016) that allows for anonymity and accessibility for those with privacy or travel concerns.

One limitation of the study is that there may be selection bias as dyads were recruited from a research center, possibly limiting true purposive sampling of this population and leading to a lack of heterogeneity in the sample. For example, dyads in this study were very highly educated and participants involved in research may be more information seeking than those who do not participate in research. There is likely also variability in the time since diagnosis, which may influence how participants identify their current health state and possibly how they do or do not modify their activities of daily living. However, this study provides unique insight into the perceived social determinants of health as presented by older, rural-dwelling adults with early cognitive impairment and their care partners that may be used to help focus interventions to improve cognitive and overall health in this underserved population.

4.6   CONCLUSION

Through interviews with older, rural-dwelling adults with early cognitive impairment, we identified themes corresponding to social determinants of health, descriptions of how dyads cope with illness, and minimal mention of stressors. Our findings help contribute to creating a better foundation to understand rural health disparities for this population, and further inquiry into rural cognitive health should be explored in greater detail in the future. Specially, future research should consider examining perceived determinants of health prior to cognitive impairment diagnosis, specifically focusing on health behaviors, social integration and support and how these may change after a cognitive impairment diagnosis. This may provide crucial information about where to focus

93

education and intervention work before or at the time of cognitive impairment diagnoses. The emergent themes, specifically those corresponding to established social determinants of health, may be used to promote the adoption of self-management and prevention behaviors, particularly lifestyle changes such as exercise and nutrition.

5.0   MANUSCRIPT 3: EXPERIENCES SURROUNDING EARLY-STAGE COGNITIVE DIAGNOSIS IN OLDER, RURAL-DWELLING ADULTS

5.1   INTRODUCTION

Misdiagnosis, lack of specialists, and patient dismissal of symptoms can contribute to delayed detection of early cognitive impairment. Compounding these factors, it can be difficult to identify or diagnose cognitive impairment, especially at early stages or for less severe types of dementia (Borson et al., 2006). Delayed detection of dementias may lead to increased participant and care partner burden over time and a lost opportunity to seek treatment for modifiable risk factors or treatable conditions contributing to cognitive health.

Mild cognitive impairment (MCI) and mild Alzheimer's disease (AD) are recognized as early stage cognitive disorders, a time when many patients are able to still perform instrumental activities of daily living (Petersen, 2004; Sperling et al., 2011). The early cognitive changes and symptoms associated with these disorders may also go unnoticed by patients, family, friends, and even healthcare professionals for a wide range of reasons including a patient's ability to compensate for the changes and the potential for the changes to be overlooked or viewed as a normal part of aging (Knopman, Donohue, & Gutterman, 2000; Teel & Carson, 2003). The recognition of worsening cognitive symptoms and heightened initiative to seek out specialty healthcare ultimately impacts overall health and disease management. However, there remains a gap in the literature exploring patients' and care partners' perspectives during and around the time

of cognitive diagnosis, especially in underrepresented populations.

Bradford et al (2009) examined factors contributing to missed and delayed cognitive diagnosis, and five patient characteristics were identified as likely causes: rural residence, age, lower severity of dementia, lower level of education, and single marital status. This study will focus on older, rural-dwelling adults with early-stage cognitive impairment. Rural-dwelling adults face additional barriers to undergoing timely cognitive evaluations and accessing care delivery, and have been shown to under-utilize both medical and social services, as compared to their urban counterparts (Bradford et al., 2009). There are also fewer rural-dwelling health care providers (Barley et al., 2001; Gamm et al., 2010) and limited resources in rural areas (Gamm et al., 2010), further emphasizing the importance of early detection of cognitive changes in this population.

There is a lack of research on the experiences surrounding early cognitive diagnoses, particularly in older, rural-dwelling adults. Patient and family member descriptions of experiences and feelings during this time may ultimately inform healthcare providers to provide targeted, population-specific care and services during critical times of cognitive change. Thus, the purpose of this study was to explore experiences of older, rural-dwelling adults with early cognitive changes and their family care partners (patient-care partner dyads) surrounding cognitive diagnostic evaluation. Patient and family experiences prior to, during, and after a diagnostic cognitive evaluation at a specialty research center are explored to understand and improve the recognition of cognitive symptoms, ways in which symptoms are addressed (or not addressed), and subsequent changes made following diagnosis.

5.2   METHODS

5.2.1   Approach

This study used qualitative description, as presented by Sandelowski (2000, 2010), to describe subjective experiences of older, rural-dwelling adults with early cognitive changes and their care partners at three time periods: pre-Alzheimer Disease Research Center (ADRC) visit, ADRC visit, and post-ADRC visit. The methodological approach of qualitative description provided the opportunity to characterize the events and experiences across these periods of time as recalled in "the everyday terms of those events" (Sandelowski, 2000).

Semi-structured interviews with participant-care partner dyads were conducted in the participant's home and lasted from 66-95 minutes; individual home visit length varied from 84-160 minutes. A 14-question interview guide was used to promote open dialogue about dyad experiences living with early cognitive changes and the role of Social Determinants of Health on cognitive health (Schulz and Northridge, 2004). There was one question that addressed a specific period of time or event. The question asked members of the dyad about their last visit to the ADRC, and contained follow-up probes that encouraged participants to describe feelings and events they experienced during the visit. Details of the interview approach and other interview questions have been described in previous work (Manuscript 2 citation). Although not a direct focus of the interview, pre-ADRC and post-ADRC visit experiences were described, often spontaneously, throughout the interview about social determinants of health (Schulz & Northridge, 2004c) as well as prolonged engagement with the dyad in their home. Previous participation with the ADRC and

prolonged in-home engagement promoted trust in this sample at first contact with the investigator. All interviews were audio recorded and later transcribed verbatim. The principal investigator compared each transcribed interview to the original audio recording to ensure accuracy of transcription. University of Pittsburgh Institutional Review Board approved all procedures prior to study recruitment.

5.2.2   Sample

The sample was recruited from University of Pittsburgh Alzheimer Disease Research Center (ADRC) that enrolls study participants in various ways, including referral from clinicians, self-referral by participants or concerned family members, active recruitment through community organizations, and volunteers who wish to contribute to research. Data are collected at the initial visit and each annual follow-up visit by clinicians, neuropsychologists, and other ADRC research personnel over the course of 2-4 hours, with at least 17 standardized tests administered at each visit. Participants are required to come with a care partner for visits, as care partners provide information about the participant's clinical symptoms; thus, care partners were concurrently recruited and invited to consent to the study to provide a thicker description of experiences and events. Care partners contributions to interviews have been found to help convey participants' stories (Holstein & Gubrium, 1995). Details about the sample description and recruitment have been described in greater detail in previous work (Manuscript 2 citation, Lopez et al., 2000). After a multidisciplinary evaluation and consensus conference with clinicians, a standardized diagnostic

feedback session is conducted by neurologist and social worker with the dyad to discuss findings from the evaluation (Lingler et al., 2006).

5.2.3 Measures

In addition to interview data, there was one quantitative variable computed: distance from participant home to ADRC. Home-ADRC distance was calculated between participant home address and ADRC address using Google Maps (Google Maps, 2016) and measured in miles, rounded to the nearest whole number. A review of research data from the ADRC participant charts was also performed to confirm current medication list and also obtain comprehensive descriptive characteristics of the sample, both already collected by the ADRC.

5.2.4 Analysis

Transcribed data were entered into Atlas.ti© (version 4.2, Scientific Software Development, Berlin) for organizational and analysis purposes. Qualitative content analyses were performed by three independent investigators beginning with line-by-line coding. Findings were organized by time period and categories of shared or similar experience. Category similarities, differences, and counter examples were then discussed among investigators until findings were verified by consensus and convergence. These analytic methods were selected because they: 1) permit large amounts of data to be condensed, clustered, sorted, and linked over time (Huberman & Miles,

1998) and 2) facilitate examination of components and relationships revealed in the data (Miles &
Huberman, 1994).

5.3   RESULTS

Participants (n=9) with cognitive impairment were 73.7 ± 6.0 years of age with 14.2 ± 3.1 years
of education; 44.4% were female, 100% white, 88.9% married, and 100% lived with someone.
Five of the nine participants (55.6%) had a diagnosis of mild cognitive impairment, four a
diagnosis of early-stage AD. Care partners (n=10) were 70.9 ± 7.4 years of age with 15.6 ± 2.3
years of education; 70% were female, 100% white, 80% married, and 90% lived with someone,
specifically their care partner. In-home interviews took place across four states with RUCA codes
across "micropolitan", "small town", and "rural areas" ("Rural Urban Commuting Area Codes
Data," n.d.).

Participant and care partner experiences were explored across three time periods: 1) pre-
ADRC visit, 2) ADRC visit, and 3) post-ADRC. Most pre-ADRC visit dyad experiences were
similar overall, while ADRC visit and post-ADRC visit experiences varied. Details about the
ADRC visit typically emerged when specifically asked about the visit; however, the events and
experiences before and after the ADRC visit emerged spontaneously during the interview process.

Pre-ADRC visit

There were four categories identified: 1) Description of cognitive symptoms, 2) Health care provider visits before ADRC visit, related to cognitive symptoms, 3) Reasons for making an ADRC appointment, and 4) Reactive to cognitive changes.

Description of Cognitive Symptoms

Both participants and care partners offered rich characterizations of symptoms and specific examples of the cognitive changes exhibited by participants prior to the ADRC visit. Most descriptions (5/9 dyads) pointed to cognitive changes occurring over a period of time; however, there were four care partners who described a sudden onset of participant symptoms. For those participants with cognitive changes occurring over time, there were a number of reported symptoms including: difficulty balancing the checkbook, getting lost while driving, "forgetting things," repeatedly asking questions, intermittent confusion, difficulty conjuring specific words, "losing words," difficulty concentrating, and discontinuing activities that previously made participants happy (e.g., journaling or reading). One 71-year-old female care partner said her husband repeatedly asked her the same questions, but thought "he was just not paying attention to me." It was not until a close work colleague told her "there was a definite problem," that she realized she was not the only one noticing her husband's memory changes.

Two care partners noticed a sudden onset of cognitive symptom(s) or decline in cognitive abilities. One 73-year-old female care partner noted it was, "His math is what triggered me, because he was always so quick with math… and then all of the sudden things were kind of messed up." Another care partner, a 62-year-old female, noticed sudden, more severe changes in her mother: "…she suddenly forgot how to stand up and forgot how to dress herself and was very

confused uhm and we ended up hospitalizing her." There were two dyads where the participant noted sudden changes and the care partner shared both specific event(s) and long-term cognitive changes. For example, one 65-year-old female care partner said her husband shared with her a specific incident where he became confused regarding his final destination while en route to his long-time friend's house. When probed further about the participant's symptoms, the care partner explained that her husband, a 71-year-old with MCI, has had trouble understanding and performing well in school since he was a child, and this was a possible reason as to why she had not noticed cognitive concerns earlier. Overall, both sudden and insidious cognitive symptoms were described by dyads.

Health Care Provider Visits Before ADRC Visit

Seven of the nine participants mentioned seeing another health care provider for cognitive concerns before attending a ADRC cognitive evaluation, while one participant did not see a health care provider with such concerns and the last participant did not share this information during the interview. Of the seven who saw another health care provider prior to their ADRC visit, five were seen by their primary care provider (PCP) and two sought out specialty care. Two participants were prescribed cognitive medications after seeing the health care provider, one saw his PCP and the other saw a specialist, and the immediate initiation of a cognitive medication with limited diagnostics was concerning to both dyads. The 67-year-old care partner quoted the PCP as saying, "We'll start you on Aricept^{TM} because it couldn't hurt." The other dyad's 65-year-old female care partner said that following her husband's visit to the specialist, her husband told her that he was prescribed a cognitive enhancing medication, and when she asked what tests the specialist ran, her husband answered, "Well he didn't."

At three of the seven visits, health care providers shared with participants that they did not have Alzheimer's disease, one 73-year-old male with MCI saying, "In fact I talked to my one doctor about [my cognitive symptoms], and he told me I didn't have Alzheimer's, I had CRS [Can't remember sh*t]." The majority of participants saw another health care provider prior to their ADRC-visit and current diagnosis, and there were inconsistencies in evaluation and treatment of cognitive concerns across interviews.

Reasons for Making ADRC Appointment

For most dyads, participation and evaluation at a specialty research center was related to, or in response to, previous diagnostic uncertainty, seeking additional information, and concern related to a family history of AD. One example of diagnostic uncertainty was related to being put on medication immediately following a visit (66-year-old male with MCI): "I had been recently diagnosed by my family doctor… with no testing, and I questioned, well, is there some testing that needs to be done…" Another care partner (62-year-old female) said that before their ADRC visit, "we were just trying to get some answers to have some sort of understanding of what was going on…" Those participants with a family history of AD spoke to wanting to know their current status, including diagnosis and any other available descriptive testing. A family history of AD was also included as a reason for ADRC participation and evaluation.

All participants attended ADRC evaluations on their own accord; however, the person who scheduled the ADRC appointment was not always the participant. Of the nine participants, only three participants scheduled their own ADRC evaluations, five care partners scheduled the evaluation, and one participant's sister scheduled the evaluation, as she was already enrolled at the

Center. Motivations or reasons for the decision as to who made the appointment were not captured in interviews.

Overall, dyads spoke about being reactive and seeking out medical care and information for participants or self with cognitive changes (9/9 dyads). Four participants clearly stated they sought out medical attention for cognitive concerns; the other five dyads discussed both personal and care partner concerns about cognitive changes, but it was uncertain whether the care partner or participant ultimately scheduled the medical care. A 62-year-old female care partner said that the process of exploring her mother's cognitive changes was because, "I pushed… because I wanted answers." Dyads wanting to "get answers" was offered as a reason for making the ADRC appointment, but it also showed the initiative and motivation of the dyads to seek out care. Dyads shared that at the time of cognitive symptom recognition, they also sought out information to describe or explain changes via internet websites (e.g., Mayo Clinic), primary care providers, specialists, or in two cases, they directly contacted the ADRC for an appointment.

There were no questions asked during the interview regarding family history of dementia or Alzheimer's disease; however, four participants spontaneously mentioned family history of dementia/AD, and this was also presented by participants as a precipitous for seeking information in response to their cognitive changes. For example, a 75-year-old male with AD stated "there's some pressure behind me [to look into cognitive changes]" due to his family history of AD. There was variation in how dyads were reactive in that some used internet health resources, others health care services, and others directly sought out an ADRC as a resource. However, all dyads spoke to being proactive or demonstrated proactive behaviors at the time of cognitive symptom recognition.

104

ADRC visit

There were three categories that emerged from interviews describing the ADRC visit: 1) ADRC evaluation, 2) information presented was helpful, and 3) distance traveled to ADRC.

ADRC Evaluation

Overall, dyads stated that the ADRC evaluation was thorough, "helpful and informative." The majority of dyads mentioned spontaneously that staff was "wonderful," "friendly", "kind", or helpful. There were two participants who did not remember the last evaluation with much or any detail and another participant that seemed confused as to the purpose of the visit. Of the two that did not seem to recall the visit well, one 71-year old male with MCI said, "I remember going down but I don't remember what I did." The other participant, a 69-year-old female with MCI said, "Honestly, I don't remember [the ADRC evaluation]." The participant who seemed confused was a 75-year-old male with AD, who said he "wonder[ed] what they're [ADRC staff] after…" during the ADRC visit. He shared concerns that he did not know what the purpose of his visit was at the time. As the sample was cognitively impaired, these findings are not surprising, but it is important to note that not all participants were able to recount the events of or their feelings regarding their ADRC visit.

Information Presented Was Helpful

Most participants or care partners (4/9) said the information provided by the ADRC staff was helpful, and two participants spoke to the amount of information provided. One participant, a 66-year-old male with MCI said the evaluation was "extremely comprehensive" and a 65-year-old female care partner reflected that ADRC staff provided "a lot of good information." For a 73-year-old female care partner, she spoke about how ADRC staff provided "suggestions that are…

105

helpful, and…we follow through on them… when we think we should." This highlights the idea that although there is "a lot of information" provided by ADRC staff, the dyads' ultimately chose what they hear and act upon.

There was limited discussion of events, such as specific testing, that occurred during the evaluation, but two participants spoke about the experience as being stressful. One 70-year-old participant with MCI focused on "how tough it is to go through that [testing].. I was just wiped out. It was the worst thing I have ever done going through that." Although this sentiment was not shared by most participants, it is important to acknowledge the commitment these individuals undertook to participate in ADRC-related activities, sometimes lasting as long as four hours a visit.

Distance Traveled to ADRC

Overall, eight of the nine dyads did not believe the distance traveled to the ADRC to be a concern or they did not discuss the distance or commute. To help describe the sample and possible burden of an in-facility ADRC evaluation, the average distance traveled from participant home to ADRC was calculated. On average, dyads traveled about 100 miles to reach the ADRC (99 ± 52 miles, Range: 40-182). This is around a two-hour commute each way, depending on traffic and road conditions. There was mention of the process of scheduling and traveling to the ADRC by one 73-year-old female with MCI who said that the "tough[est] thing is getting there." This quote was not surprising as the sample was rural-dwelling and the ADRC was located in a busy, large urban area; however, this was an isolated counter example, and the majority of dyads did not indicate that the commute was a concern.

Post-ADRC visit

There were two categories describing the post-ADRC visit experience for participants with cognitive impairment and their care partners: 1) emotion and psychological reaction to diagnosis, and 2) changes following ADRC diagnosis.

Emotional and Psychological Reaction to Diagnosis

Reactions to cognitive diagnoses were generally positive and dyads stated feelings of relief after learning the diagnosis. For example, 73-year-old female with MCI said, "Just psychologically, I feel so much better [since I've learned my diagnosis]." One care partner who learned her husband had no amyloid build up in his brain, a risk factor for AD, from an ADRC study, said that once they learned the encouraging results, "… it was like a weight lifted…off of both of us. And it made a big difference, I thought, in his behavior. Not just his outlook but his daily behavior" (67-year-old female care partner). Another care partner said that a follow-up brain scan showed improvement and "burst into tears." Dyad's emotional responses to the ADRC diagnoses and shared psychological effect on everyday life demonstrated the impact of learning of a cognitive impairment diagnosis for a loved one or self.

Changes Following ADRC diagnosis

Both participant and care partners shared examples of how things have changed since receiving the ADRC diagnosis, both by individual participants and by dyad. For example, three participants shared how they changed or made accommodations to certain activities in response to ADRC staff recommendations following diagnosis. One participant stopped driving voluntarily, another informed his employer of the diagnosis, but continued working, and the last began taking cognitive medication to treat cognitive symptoms.

Both members of the dyad also spoke to how they made changes in their lifestyle after diagnosis, ranging from improved eating/exercising habits to withdrawing from community involvement. Speaking to improving health behaviors, one 73-year-old female with MCI said that after her ADRC visit and diagnosis, "All of the sudden I don't know why; I decided to get healthy." Another participant, a 70-year-old male with AD, begun exercising six times a week, doing crossword puzzles and online brain stimulation games, and drinking green tea in response to the diagnosis. However, not all dyads spoke to perceived positive changes in response the ADRC visit and diagnosis. For example, a 73-year-old male with MCI who used to be actively involved in driving community members to doctor's appointments stopped driving shortly after the diagnosis and said, "I know there's a lot of things that I don't get into [anymore]. I used to, but I just kind of just pull back a little bit right now because I have a hard enough time trying [to] not make myself look silly without actually extending myself." A 62-year-old female care partner also noted that family members did not call as much since [the participant] got sick," and now she faces concerns as to how her mother is going to live in her current condition, dependent on around-the-clock aids to provide care. Overall, there were many reactions to ADRC diagnoses and subsequent changes, both positive and negative, made by participants and care partners during the post-ADRC visit period.

5.4   DISCUSSION

Rural-dwelling participants with cognitive impairment and their care partners' experiences varied across the three time periods explored. Although dyads presented similar experiences prior to the ADRC visit, experiences within categories varied, and ADRC visit and post-ADRC visit time period experiences further highlight differences in dyad reactions and subsequent life changes following ADRC visit. Overall, dyads presented their experiences leading up to the ADRC visit and reactions to cognitive changes in greatest detail and quantity. As participant diagnoses ranged from MCI to early-stage AD, there was variation in cognitive symptoms described; however, dyads consistently reported seeking to learn more about cognitive symptoms and they all spontaneously described the impact of cognitive changes on everyday life throughout the three time periods.

Rural-dwelling individuals' diagnostic uncertainty combined with participant's reactive approach to investigate cognitive changes are reflected in subthemes presented in a recent metasynthesis of qualitative research on adults with MCI by Gomersall et al. (2015). Participants and care partners present narratives about how they make sense of the cognitive diagnosis across a continuum in both our study and the studies presented in Gomersall et al. (2015). Similar to our selected time periods, Gomersall et al. (2015), presents cognitive changes across three time periods: past, present, and future. However, the "nostalgia for past relationships, roles and experiences" seen in the past period, which was found throughout the literature included in the metasynthesis, did not emerge in our interviews, but rather the reactive, or proactive, efforts undertaken by dyad's at the time of symptom recognition. Our study also captured care partner

109

experiences describing the uncertainty in their loved one's diagnosis and how they try to make sense of the diagnosis over time.

Our findings support and build on the work of Johansson, Marcusson, & Wressle (2015), that explored participants with cognitive impairment and care partners' experiences with cognitive impairment and its consequences in everyday life. Categories emerged in our work mirroring similar categories found in their interviews: recognition and burden of cognitive symptoms, uncertainty about the future, and changes patients made to their activity patterns. Johansson, Marcusson, & Wressle (2015) also found substantial variation in both participant's and care partner's experiences in their sample comprised of both MCI and mild dementia participants and care partners. The variation in experiences, especially at and after ADRC visit, may be related to this diverse sample, specifically for those with an MCI diagnosis, as this is still considered a new or novel diagnosis when compared to the more commonly recognized AD diagnosis (Grundman et al., 2004; Petersen et al., 2014).

Our findings demonstrate that dyads made conscious, pointed efforts to seek out information and care in response to cognitive changes prior to ADRC diagnosis. This is in contrast to previous work where rural health care providers identified a lack of awareness of cognitive changes and less use of resources early in the disease process for rural-dwelling patients (Morgan, Semchuk, Stewart, & D'Arcy, 2002). Based on our study findings, dyads did not seem to lack awareness, but rather they shared that they lacked clarity and consistency in the health care services and diagnoses provided locally. Dyads traveled about two hours to seek out specialty health care services in an urban ADRC. By the time of ADRC evaluation, over half the dyads had already sought out local specialty health care services. The long distance traveled and additional specialty

care services at an ADRC demonstrate both dyad's information and answer-seeking approach to cognitive symptom identification as well as possible lack of resources or specialist care in rural areas.

There was a range in participant's cognitive functioning and ADRC diagnoses as well as rurality of dyad residence, both of which may have impacted the shared experiences across all three time periods. For example, a participant with MCI may note fewer changes in cognitive functioning and no impact on activities of daily living, whereas a participant with AD and/or his care partner may notice activities of daily living are impacted (e.g., driving or balancing the checkbook). Participant with cognitive impairment inclusion criteria included a minimum MMSE score to try and reduce cognitive symptom variation in symptoms, however due to the multiple cognitive diagnoses of the sample, there was diversity in symptoms described by the sample. Similarly, as our study aimed to describe rural-dwelling adult's experiences, the range of rural classifications and state residence of participants may be considered both a strength and possible weakness. Finally, findings reflect the perceptions and experiences of an information-seeking and proactive sample, representing only part of a continuum of those receiving cognitive diagnoses. It is also important to explore experiences of individuals who did not actively seek answers to cognitive symptoms in order to better describe rural-dwelling adults across a continuum of care-seeking behaviors. Noting these considerations, the primary objective was to examine older, rural-dwelling adult's experiences surrounding a diagnostic evaluation, and this study is the first to begin to explore unique experiences in this underserved and underrepresented population.

A strength of the study was that there were standardized feedback sessions held for the preliminary cognitive impairment diagnosis for dyads with both a neurologist and social worker

111

present. This approach to disclosing diagnosis and reviewing evaluation results is ideal for both members of the dyad and for research purposes. For dyads, it provides the opportunity to learn about the testing performed and ask questions about the diagnosis or resources, with both a clinician and social worker; for research, it provides a standardized method to ensure dyads receive the same information and are given the opportunity to ask questions or discuss new cognitive diagnoses in person. In rural settings, initiating a team approach at diagnosis to promote cognitive health encourages sustained dialogue with providers and family from the beginning. This team approach to disclosure may be especially useful in rural settings, where there is limited access to health care services and resources and having multidisciplinary team may help consolidate resources.

Another strength of this study is that the perspective and experiences of both the rural care partner and rural participant were captured concurrently. Previous work in rural areas has shown that care partners/ caregivers tend to express needs (e.g., information about the disease, prognosis, and treatment) more than the participant care recipient with cognitive concerns (Edelman, Kuhn, Fulton, & Kyrouac, 2006), and thus provides rich data from two perspectives to better understand context and social support. Teel (2004)'s work examining dementia diagnosis in a rural setting found that family recognition and acknowledgement of cognitive changes was largely responsible for a shorter time from symptom onset to time of clinician diagnosis, which is crucial in cognitive disease management. It is important to note that the ADRC evaluation was the only time point in which interviews probed dyads consistency experiences across the nine interviews, as this was how it was directed by the interview guide. Although probed, different ADRC evaluation experiences were presented by participants, and additional, explicit probing into typical ADRC

112

events may have provided richer accounts of the visit itself. Future qualitative work should continue to use narratives from both members of the dyad to explore the time periods presented in this work in real-time so that participants are not reporting their feelings and experiences retrospectively, but rather reporting them as they are experiencing them. Thus, interviews can capture experiences and feelings during the period of interest and avoid participant recall bias. For example, time periods may include: 1) cognitive symptom recognition, but after an ADRC evaluation is scheduled, 2) immediately following ADRC visit, and 3) 1-, 3-, 6-, and/or 12- month follow-ups after ADRC visit.

In conclusion, there was variation in dyad descriptions of living with cognitive changes across interviews for all three time periods explored. However dyad experiences reinforced previous work that captured differences in dyad descriptions of cognitive changes, dyad reactions to cognitive changes and diagnosis, and dyad life changes following diagnosis. Our rural-dwelling sample illustrated a range of reactive and information-seeking individuals learning to live with their own or loved one's cognitive diagnosis. Future work should more narrowly focus on rural-dwelling adults' experiences in real-time at each of the three time periods rather than reflecting on the past or looking towards the future. As an underserved and underrepresented population, the narratives of rural-dwelling adults can help provide information and preferences to better direct resources and target early interventions to reduce health disparities and promote cognitive health.

6.0   SUMMARY OF STUDY

Quantitative and qualitative methods were used in this dissertation study to gain insight into older, rural-dwelling adults' cognitive health. The primary purpose was to determine if and how rural residence was a unique risk factor for delayed detection of early-stage cognitive impairment. A secondary data analysis of the National Alzheimer's Coordinating Center (NACC) Uniform Data Set (UDS) compared rural- and urban-dwelling adults' cognitive symptom severity, and found no significant difference in symptom severity at time of diagnosis between groups. However, findings showed that urban-dwelling adults had a greater number of years since onset of cognitive symptoms to diagnosis compared to their rural counterparts. This was an unexpected finding as rural-dwelling adults are typically diagnosed with chronic conditions later in the course of disease progression, compared to urban-dwelling adults. Qualitative methods used semi-structured, in-home interviews with participants with early cognitive changes and their care partners to explore rural-dwelling adults' perceived social determinants of health and reactions to cognitive symptoms and diagnosis. Themes emerged in interviews focusing on adoption of a healthy lifestyle, importance of relationships with others, and reasons to live in rural areas. Similarities were noted between most themes and those factors outlined in the Social Determinants of Health and Environmental Health Promotion Model (Schulz & Northridge, 2004). Dyads also described a variety of experiences surrounding cognitive diagnosis. Overall, dyads actively sought to learn more about cognitive symptoms and described the impact of cognitive changes on their everyday life. Based on the findings from our studies, there are several key points to highlight.

114

First, our quantitative work provides preliminary data on a typically underserved population that sought out specialty care at a research facility for cognitive changes. Although we did not find differences in symptom severity between older, rural- and urban-dwelling adults, this study provides a glimpse into a unique population: individuals who attend specialty research centers (such as an ADRC). The NACC UDS participants are not recruited through random selection by individual ADRCs, thus the secondary analysis using NACC UDS data does not provide an epidemiological comparison of rural-urban cognitive differences. Future studies should focus on recruitment of a randomly-recruited, rural-dwelling sample with diversity across multiple variables. Variables to consider include: degree of rurality (including different geographic classification scheme locations), state of residence, regional/state services available for cognitive health promotion and treatment diversity in individual's degree of resource- and information-seeking behaviors, and cognitive symptom severity at time of diagnosis. These recruitment considerations may provide a more accurate representation of rural-dwelling adults with cognitive impairment, which may be evidenced in future research through differences in sociodemographic characteristics and cognitive symptom severity when compared to urban-dwellers.

Few differences between older, rural and urban-dwelling adults with cognitive impairment were found in our quantitative studies, however urban-dwelling adults were found to have a greater number of years from onset of cognitive symptoms to diagnosis compared to their rural counterparts. There were no differences in sociodemographic characteristics or outcomes measures between rural and urban groups to explain this finding, which was unexpected. To better understand this observed difference, one potential explanation is that those living in rural areas may be more proactive in seeking out care and treatment at ADRCs to try and prevent dementia

symptoms or outcomes seen in other relatives with cognitive changes. Information-seeking actions in response to cognitive changes by rural-dwelling adults was supported by the significantly longer distance traveled by rural participants to ADRC site compared to urban participants in both our quantitative work as well as the reported 100 miles driven each way to ADRC traveled by qualitative study participants.

The rural-dwelling, ADRC-attending individuals and dyads in our studies may be a unique subset of rural-dwelling Americans based on similarities found in the quantitative analyses as well as their self-described proactive or reactive approaches to handling cognitive changes in one's self or loved ones. This further supports our claim that older, rural-dwelling adults who attended these ADRCs may not be typical of most older, rural-dwelling adults, and future work should focus on targeting individuals that are not as proactive or knowledge-seeking as ADRC participants. Qualitative findings reflect the perceptions and experiences of an information-seeking and proactive sample, representing only part of a continuum of those receiving cognitive diagnoses. Thus, it is important to explore experiences of individuals who did not actively seek out answers to cognitive symptoms in order to better describe rural-dwelling adults across a continuum of care-seeking behaviors. Inclusion of these individuals would provide further insight into diagnostic and management in this underserved population.

Qualitative findings highlighted critical aspects of rural adults' perceived determinants of health and reactions to cognitive symptoms and diagnosis, which may be used to help target earlier diagnosis and improve long-term disease management in rural-dwelling adults. Specifically, newly adopted or long-term changes to health behaviors that emerged in discussion of determinants of health demonstrated awareness that diet and physical activity play a

preventive role in cognitive health and may improve long-term cognitive health. Targeted health behavior interventions focused on diet or physical activity prior to diagnosis, at time of diagnosis, and beyond may help promote adoption of self- or dyad-management behaviors surrounding a pivotal diagnosis like cognitive impairment. Social connectedness to both family and community was also highlighted by participants and provides a foundation by which interventions are rooted and supported by loved or trusted friends or family.

Interviews with dyads provided evidence that dual participant and care partner participation at ADRC visits may provide an ideal platform by which to provide and launch health care services. Having two people involved in participant diagnosis and care outside of the clinical setting may be a key reason why dyads reported being proactive in their response to cognitive changes and sought out an ADRC. Furthermore, both diagnostic and long-term care sessions would ideally use the multidisciplinary approach used at the ADRC standardized feedback session for the preliminary cognitive impairment diagnosis, where the dyad meets with multiple clinical team members at each appointment or session. Initiation of a team approach at diagnosis, including both members of the dyad, may promote cognitive health and encourage sustained dialogue with providers and family from the beginning. This team approach to diagnosis and management may be especially useful in rural settings, where there is limited access to health care services and resources and a multidisciplinary team may help consolidate resources and participant burden through fewer, more-targeted visits. Future research should consider implementation of this multidisciplinary, dyad-attended approach in smaller clinics in rural areas, with the support of both clinical and social resources.

Finally, there are policy implications for this research. The Health Outcomes, Planning, and Education (HOPE) for Alzheimer's Act, currently being considered in US Congress, would extend existing Medicare coverage of diagnostic services, including comprehensive care planning. There is currently no reimbursement for care planning services to Medicare beneficiaries or their caregivers following diagnosis of AD, but this act would provide reimbursement for comprehensive care planning, coordination of management of other medical conditions, and ways to eliminate barriers to receiving these services. Findings from our qualitative work reinforce the need for this policy change that would provide and extend support of much-needed services to rural-dwelling Americans dealing with cognitive concerns through awareness, access, and management initiatives at a national level.

In summary, this dissertation study presents important findings that may be used to better serve and target rural-dwelling adults with cognitive impairment. Specifically, dyads' perceived social determinants of health and reactions to cognitive symptoms provide valuable information about how to help provide an ideal setting for diagnosis and management of cognitive impairment in a typically low resource and limited access population. A comprehensive approach to diagnosing and managing cognitive impairment, starting with knowledge of and access to services prior to cognitive symptom recognition, could ultimately improve both cognitive and general health in rural-dwelling adults through incorporation of family or friend support, a multidisciplinary team approach, and national resources.

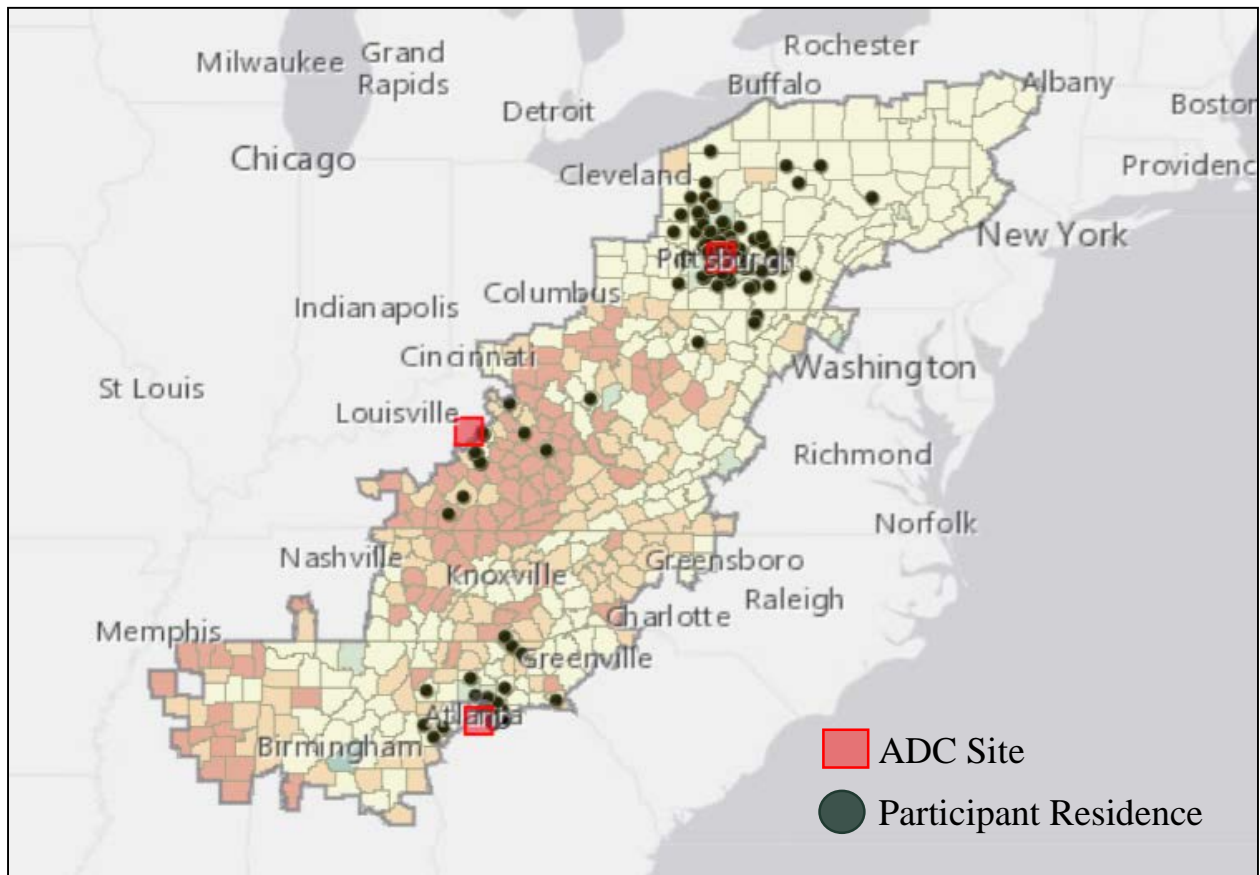# APPENDIX A

MAP OF THE APPALACHIAN REGION

White area = Appalachian region

Source: Appalachian Regional Commission

October 8, 2008

119
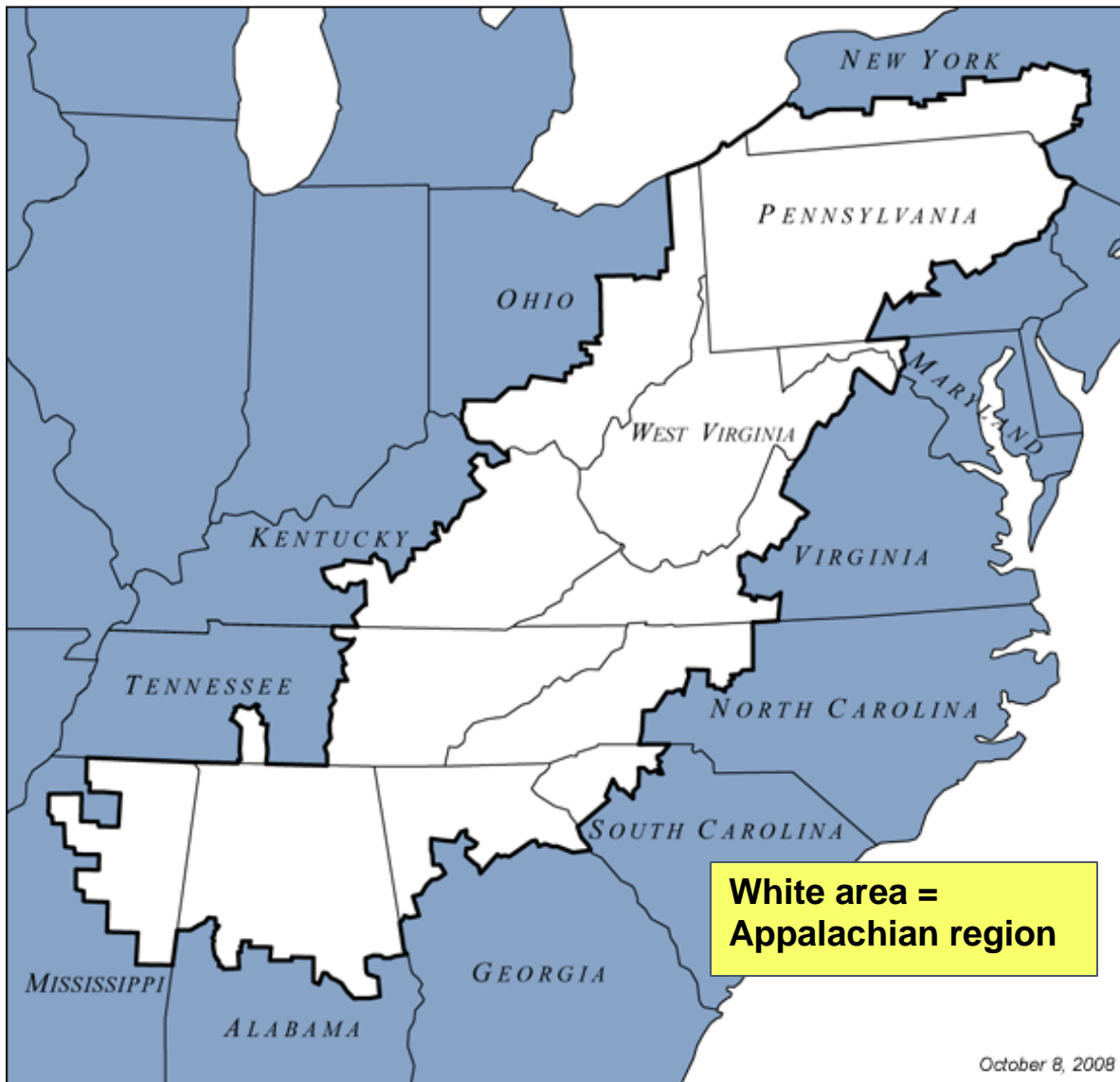
APPENDIX B

MAP OF ALZHEIMER'S DISEASE CENTER SITES AND PARTICIPANT RESIDENCE

WITHIN APPALACHIA

QUALITATIVE INTERVIEW GUIDE

Version 1. December 8, 2014

Opening questions:
- How are you feeling today?
- Besides the dyad, are there any family or friends in your home?
- Anything to be aware of before we begin?
- *NOTE TO INTERVIEWER: Proceed with casual discussion of rural residence.*
  <u>Probes</u>:
    - How long have you lived in this area?
    - Have you lived in this area for most of your life? If not, where else did you live?
    - Did you or do you want to live closer to or further away from the city?

1. Tell me about your last visit to the Alzheimer Disease Research Center in Pittsburgh.
   <u>Probes</u>:
    - When was your last visit to the ADRC?
    - What did the ADRC staff share with you?
    - What information was most helpful? Least helpful?
    - Do you think that you left with any additional resources, meaning ideas that you didn't have before you came in? If so, what?
    - How did you feel after the visit?

2. What does the term "mild cognitive impairment" mean to you?
   <u>Probes</u>:
    - Had you heard about MCI before your visit at the ADC?
    - Has your idea of MCI changed since that visit?
    - Do you think about MCI differently now than before you came to the ADC?

3. [Using the participant's preferred language (based on her or his response to question #2)], what do you believe might cause [these changes in memory or thinking – using participant's preferred phrasing to reference MCI symptoms]?
   <u>Probes</u>:
    - Are these things that you think could have been avoided?

121

  o Would you do anything differently knowing what you know now?

4. What does the term "healthy aging" mean to you?

5. [Using the participant's preferred language (based on her or his response to question #2)], what do you believe might cause [these changes in memory or thinking – using participant's preferred phrasing to reference MCI symptoms]?
Probes:
  o *NOTE TO INTERVIEWER: If they do not discuss brain/ cognitive function specifically, then ask about "healthy brain aging"*
  o Is healthy brain aging different from healthy body aging?

6. What are some things that you can do to maintain brain health?
Probe:
  a. Do you think that healthy brain aging is different from healthy body aging?

7. What, if anything, would you have liked to be told about [use of participant's preferred language for mild cognitive impairment symptoms] at your appointment or follow-up visits?
Probe:
  o What kind of information or referrals may have benefited you or your family at the time you were diagnosed?
  o What kinds of support would be helpful for you or your family now?

This next set of questions has to do with your daily experiences as a person who is living with [use of participant's preferred language for mild cognitive impairment].

8. What does a typical day look like for you?
Probes:
  o What time do you get up in the morning?
  o What do you typically eat at meals?
  o What do you do after breakfast?

9. How often do you leave the house to meet up with friends/family? Or do friends/family visit you? Who do you see most often and how often are you able to spend time together?

10. How do you keep in contact with friends/family?
Probes:
  o Via phone? How often and how long?
  o Via Internet? E-mail or chats? How often and how long?
  o If you have Internet, is it dial up or cable?

11. Do you wish that you spoke with or saw people more often? What helps you or makes it easier for you to stay connected with those you love? What, if anything, holds you back from connecting with friends and family as much as you might like to?
Probes:
o Use of Internet?
o Use of social media? Use of electronic support, cell phones?

12. Since learning of your diagnosis, have you sought out any professional organizations, support groups? If so, which ones? Where are they located?
Probes:
o If yes, did/does distance, cost, or convenience play a role in your involvement?
o Has distance, cost, or convenience kept you from participating in support groups or organization involvement?

APPENDIX D

IRB APPROVALS

D.1 UNIVERSITY OF PITTSBURGH, INSTITUTIONAL REVIEW BOARD, EXEMPT STATUS FOR AIM 1

University of Pittsburgh
Institutional Review Board

3500 Fifth Avenue
Pittsburgh, PA 15213
(412) 383-1480
(412) 383-1508 (fax)
http://www.irb.pitt.edu

Memorandum

To: Meghan Mattos MSN, RN
From: Sue Beers , Ph.D., Vice Chair
Date: 9/17/2014
IRB#: PRO14060033
Subject: Mild Cognitive Impairment in Older Rural Dwelling Adults

The above-referenced protocol has been reviewed by the University of Pittsburgh Institutional Review Board. Based on the information provided to the IRB, this project includes no involvement of human subjects, according to the federal regulations [§45 CFR 46.102(f)]. That is, the investigator conducting research will not obtain information about research subjects via an interaction with them, nor will the investigator obtain identifiable private information. Should that situation change, the investigator must notify the IRB immediately.

Given this determination, you may now begin your project.

Please note the following information:

- If any modifications are made to this project, use the **"Send Comments to IRB Staff"** process from the project workspace to request a review to ensure it continues to meet the determination.
- Upon completion of your project, be sure to finalize the project by submitting a **"Study Completed"** report from the project workspace.

Please be advised that your research study may be audited periodically by the University of Pittsburgh Research Conduct and Compliance Office.

D.2 UNIVERSITY OF PITTSBURGH, INSTITUTIONAL REVIEW BOARD, EXPEDITED STATUS FOR AIM 2

University of Pittsburgh
Institutional Review Board

3500 Fifth Avenue
Pittsburgh, PA 15213
(412) 383-1480
(412) 383-1508 (fax)
http://www.irb.pitt.edu

Memorandum

To: Meghan Mattos
From: Sue Beers , Vice Chair
Date: 9/21/2014
IRB#:   PRO14050205
Subject: Mild Cognitive Impairment in Older Rural Dwelling Adults

The University of Pittsburgh Institutional Review Board reviewed and approved the above referenced study by the expedited review procedure authorized under 45 CFR 46.110 and 21 CFR 56.110. Your research study was approved under:
45 CFR 46.110.(6)
45 CFR 46.110.(7)

This study is supported by the following federal grant application:
F31 NR015188 Mild Cognitive Impairment in Older, Rural Dwelling Adults

The risk level designation is Minimal Risk.

Approval Date: 9/21/2014
Expiration Date: 9/20/2015

This study meets the criteria for an extended approval period of three years. In the event that any type of federal funding is obtained during this interval, a modification must be submitted immediately so the IRB can reassess the approval period.

For studies being conducted in UPMC facilities, no clinical activities can be undertaken by investigators until they have received approval from the UPMC Fiscal Review Office.

Please note that it is the investigator's responsibility to report to the IRB any unanticipated problems involving risks to subjects or others [see 45 CFR 46.103(b)(5) and 21 CFR 56.108(b)]. Refer to the IRB Policy and Procedure Manual regarding the reporting requirements for unanticipated problems which include, but are not limited to, adverse events. If you have any questions about this process, please contact the Adverse Events Coordinator at 412-383-1480.

APPENDIX E

DETALIED DATA AND SAFETY MONITORING PLAN FOR PROPOSAL

AIM 1. Aim 1 is a secondary analysis that will use de-identified data from the National Alzheimer's Coordinating Center (NACC) Uniform Data Set (UDS), a repository for data collected at approximately 30 Alzheimer's Disease Centers (ADCs) throughout the US. Permission to use this de-identified data for research on cognitive impairment has been explicitly requested of participants during the informed consent process carried out during visits to the Alzheimer's Disease Centers that contribute data to the existing NACC UDS. The data used in the proposed research will be de-identified by an honest broker at the NACC UDS or University of Pittsburgh ADC before any members of the research team begin working with the data. Once transferred, this data will be stored in locked, confidential files (including password and firewall protected digital storage) at the University of Pittsburgh School of Nursing. As per University of Pittsburgh policy, data will be kept for a period of seven years after completion of the proposed research. Drs. Burke and Lingler will assume responsibility for long-term storage of the data.

AIM 2. Aim 2 will use interviews with older, rural-dwelling adults with mild cognitive impairment (MCI) and care partners to collect information about perceived support needs related to being an older adult living in a rural area with MCI. The source of materials for Aim 2 are abstracted data from an existing research data-base from the University of Pittsburgh ADRC,

interview-based self-reports, interview-based care partner reports, audio recordings of interviews, handwritten field notes, and electronically-entered transcribed interviews and field notes. Permission to extract data from existing databases has been explicitly requested of participants during the informed consent process from all Alzheimer's Disease Centers that contribute to the NACC UDS. Additional consent from both older adults with MCI and their care partner(s) will be obtained to conduct the interviews in participant or care partner homes.

Purposive sampling will be performed to include the most representative sample as possible. Time of diagnosis will be held constant for all participants, limiting it to participants who received an MCI diagnosis in the last 12 months. This approach will help minimize the possibility that participants may have advanced MCI symptoms or converted to AD or other dementias. Determinations of capacity to consent to the proposed research study will be based on a participant's ability to express an understanding the study's purpose, procedures, risks, and benefits during a one on one discussion with a member of the research team. Persons with MCI, by definition, have impaired memory and may have varying abilities to understand elements of the consent process. The PI will have received training to enhance subjects' ability to achieve decisional capacity during the consent process through formal training directed by Dr. Jennifer Lingler. For example, a one-page overview of key aspects of the study will be provided to supplement the lengthier informed consent document. Those who do not fulfill the criteria of being able to verbally express an understanding of the study's purpose, consent procedures, risks, and benefits, either during the preliminary phone contact or in-person, will be thanked for their interest in the study, but interviews or audio recordings will not be performed.

Every attempt will be made to protect human subjects in this study. For one, all participants

and care partners will be made aware of the research aims and informed that IRB approval is necessary to participate. Participants and care partners will also be explicitly told that they can decide not to participate and can stop the interview at any time. The audio portion of all interviews will be digitally recorded and stored on a password-protected computer with an additional copy produced after each meeting. Sensitive information such as participant and care partner(s) names, participant demographic information, IRB consents, tapes, and field notes will be kept in a secure location in the University of Pittsburgh School of Nursing in the Health and Community Systems department. Data will be recorded and identified by subject code numbers only. These materials will be kept in locked location, accessed only by the investigators listed on the grant and the data analysis team. Identities of participants will not be revealed in publications or presentations derived from this project.

This is a one-time interview that is expected to take approximately one hour. Participants, both the individual with MCI and the care partner, may experience boredom or fatigue during the interview. If at any point in the interview, the questions bother either the older adult with MCI or care partner, they do not have to continue. Additionally, presence of the participant's care partner may help mediate. If at any point in the interview, the investigator believes the participant(s) are experiencing excessive distress during the interview, the interview will cease, and they may be removed from the research study by the investigators without consent. If investigators learn that participants are in serious danger or risk for potential harm, they will inform, as required by Pennsylvania law, the appropriate agencies.

Another risk associated with participation is breach of confidentiality. The research team will attempt to preserve confidentiality by assigning a unique research code number to each

research record and by removing personal identifiers from stored information. Information linking the research code number to name and other personal identifiers will be stored in a separate secure location at the University of Pittsburgh School of Nursing in the Health and Community Systems Department. Access to any identifiable information contained within research records from the University of Pittsburgh ADRC will be limited to the investigators associated with the study. This research study will not result in identifiable information being placed into participant medical records at UPMC or the University of Pittsburgh ADRC.

As with Aim 1 and as per University of Pittsburgh policy, data will be kept for a period of seven years after completion of the proposed research. Co-chairs, Drs. Lora Burke and Jennifer Lingler, will assume responsibility for the long-term storage of the data.

APPENDIX F

LICENSE AGREEMENT FOR MANUSCRIPT 1

JOHN WILEY AND SONS LICENSE
TERMS AND CONDITIONS

Sep 29, 2016

This Agreement between Meghan K Mattos ("You") and John Wiley and Sons ("John Wiley and Sons") consists of your license details and the terms and conditions provided by John Wiley and Sons and Copyright Clearance Center.

License Number	3947680042437
License date	Sep 14, 2016
Licensed Content Publisher	John Wiley and Sons
Licensed Content Publication	Journal of Rural Health
Licensed Content Title	Older Rural- and Urban-Dwelling Appalachian Adults With Mild Cognitive Impairment
Licensed Content Author	Meghan K. Mattos,Beth E. Snitz,Jennifer H. Lingler,Lora E. Burke,Lorraine M. Novosel,Susan M. Sereika
Licensed Content Date	Aug 10, 2016
Licensed Content Pages	1
Type of Use	Dissertation/Thesis
Requestor type	Author of this Wiley article
Format	Electronic
Portion	Full article
Will you be translating?	No
Title of your thesis / dissertation	Mild Cognitive Impairment in Older, Rural-Dwelling Adults
Expected completion date	Dec 2016
Expected size (number of pages)	160
Requestor Location	Meghan K Mattos 1019 River Haven Circle Apt. N CHARLESTON, SC 29412 United States Attn: Meghan K Mattos
Publisher Tax ID	EU826007151
Billing Type	Invoice
Billing Address	Meghan K Mattos 1019 River Haven Circle Apt. N CHARLESTON, SC 29412 United States Attn: Meghan K Mattos
Total	**0.00 USD**

132

TERMS AND CONDITIONS

This copyrighted material is owned by or exclusively licensed to John Wiley & Sons, Inc. or one of its group companies (each a"Wiley Company") or handled on behalf of a society with which a Wiley Company has exclusive publishing rights in relation to a particular work (collectively "WILEY"). By clicking "accept" in connection with completing this licensing transaction, you agree that the following terms and conditions apply to this transaction (along with the billing and payment terms and conditions established by the Copyright Clearance Center Inc., ("CCC's Billing and Payment terms and conditions"), at the time that you opened your RightsLink account (these are available at any time at http://myaccount.copyright.com).

Terms and Conditions

- The materials you have requested permission to reproduce or reuse (the "Wiley Materials") are protected by copyright.

- You are hereby granted a personal, non-exclusive, non-sub licensable (on a stand-alone basis), non-transferable, worldwide, limited license to reproduce the Wiley Materials for the purpose specified in the licensing process. This license, **and any CONTENT (PDF or image file) purchased as part of your order,** is for a one-time use only and limited to any maximum distribution number specified in the license. The first instance of republication or reuse granted by this license must be completed within two years of the date of the grant of this license (although copies prepared before the end date may be distributed thereafter). The Wiley Materials shall not be used in any other manner or for any other purpose, beyond what is granted in the license. Permission is granted subject to an appropriate acknowledgement given to the author, title of the material/book/journal and the publisher. You shall also duplicate the copyright notice that appears in the Wiley publication in your use of the Wiley Material. Permission is also granted on the understanding that nowhere in the text is a previously published source acknowledged for all or part of this Wiley Material. Any third party content is expressly excluded from this permission.

- With respect to the Wiley Materials, all rights are reserved. Except as expressly granted by the terms of the license, no part of the Wiley Materials may be copied, modified, adapted (except for minor reformatting required by the new Publication), translated, reproduced, transferred or distributed, in any form or by any means, and no derivative works may be made based on the Wiley Materials without the prior permission of the respective copyright owner.**For STM Signatory Publishers clearing permission under the terms of the STM Permissions Guidelines only, the terms of the license are extended to include subsequent editions and for editions in other languages, provided such editions are for the work as a whole in situ and does not involve the separate exploitation of the permitted figures or extracts,** You may not alter, remove or suppress in any manner any copyright, trademark or other notices displayed by the Wiley Materials. You may not license, rent, sell, loan, lease, pledge, offer as security, transfer or assign the Wiley Materials on a stand-alone basis, or any of the rights granted to you hereunder to any other person.

- The Wiley Materials and all of the intellectual property rights therein shall at all times remain the exclusive property of John Wiley & Sons Inc, the Wiley Companies, or their respective licensors, and your interest therein is only that of having possession of and the right to reproduce the Wiley Materials pursuant to Section 2 herein during the continuance of this Agreement. You agree that you own no right, title or interest in or to the Wiley Materials or any of the intellectual property rights therein. You shall have no rights hereunder other than the license as provided for above in Section 2. No right, license or interest to any trademark, trade name, service mark or other branding ("Marks") of WILEY or its licensors is granted hereunder, and you agree that you shall not assert any such right, license or interest with respect thereto

- NEITHER WILEY NOR ITS LICENSORS MAKES ANY WARRANTY OR REPRESENTATION OF ANY KIND TO YOU OR ANY THIRD PARTY, EXPRESS, IMPLIED OR STATUTORY, WITH RESPECT TO THE MATERIALS OR THE ACCURACY OF ANY INFORMATION CONTAINED IN THE MATERIALS, INCLUDING, WITHOUT LIMITATION, ANY IMPLIED WARRANTY OF MERCHANTABILITY, ACCURACY, SATISFACTORY QUALITY, FITNESS FOR A PARTICULAR PURPOSE, USABILITY, INTEGRATION OR NON-INFRINGEMENT AND ALL SUCH WARRANTIES ARE HEREBY EXCLUDED BY WILEY AND ITS LICENSORS AND WAIVED BY YOU.

- WILEY shall have the right to terminate this Agreement immediately upon breach of this Agreement by you.

133

- You shall indemnify, defend and hold harmless WILEY, its Licensors and their respective directors, officers, agents and employees, from and against any actual or threatened claims, demands, causes of action or proceedings arising from any breach of this Agreement by you.

- IN NO EVENT SHALL WILEY OR ITS LICENSORS BE LIABLE TO YOU OR ANY OTHER PARTY OR ANY OTHER PERSON OR ENTITY FOR ANY SPECIAL, CONSEQUENTIAL, INCIDENTAL, INDIRECT, EXEMPLARY OR PUNITIVE DAMAGES, HOWEVER CAUSED, ARISING OUT OF OR IN CONNECTION WITH THE DOWNLOADING, PROVISIONING, VIEWING OR USE OF THE MATERIALS REGARDLESS OF THE FORM OF ACTION, WHETHER FOR BREACH OF CONTRACT, BREACH OF WARRANTY, TORT, NEGLIGENCE, INFRINGEMENT OR OTHERWISE (INCLUDING, WITHOUT LIMITATION, DAMAGES BASED ON LOSS OF PROFITS, DATA, FILES, USE, BUSINESS OPPORTUNITY OR CLAIMS OF THIRD PARTIES), AND WHETHER OR NOT THE PARTY HAS BEEN ADVISED OF THE POSSIBILITY OF SUCH DAMAGES. THIS LIMITATION SHALL APPLY NOTWITHSTANDING ANY FAILURE OF ESSENTIAL PURPOSE OF ANY LIMITED REMEDY PROVIDED HEREIN.

- Should any provision of this Agreement be held by a court of competent jurisdiction to be illegal, invalid, or unenforceable, that provision shall be deemed amended to achieve as nearly as possible the same economic effect as the original provision, and the legality, validity and enforceability of the remaining provisions of this Agreement shall not be affected or impaired thereby.

- The failure of either party to enforce any term or condition of this Agreement shall not constitute a waiver of either party's right to enforce each and every term and condition of this Agreement. No breach under this agreement shall be deemed waived or excused by either party unless such waiver or consent is in writing signed by the party granting such waiver or consent. The waiver by or consent of a party to a breach of any provision of this Agreement shall not operate or be construed as a waiver of or consent to any other or subsequent breach by such other party.

- This Agreement may not be assigned (including by operation of law or otherwise) by you without WILEY's prior written consent.

- Any fee required for this permission shall be non-refundable after thirty (30) days from receipt by the CCC.

- These terms and conditions together with CCC's Billing and Payment terms and conditions (which are incorporated herein) form the entire agreement between you and WILEY concerning this licensing transaction and (in the absence of fraud) supersedes all prior agreements and representations of the parties, oral or written. This Agreement may not be amended except in writing signed by both parties. This Agreement shall be binding upon and inure to the benefit of the parties' successors, legal representatives, and authorized assigns.

- In the event of any conflict between your obligations established by these terms and conditions and those established by CCC's Billing and Payment terms and conditions, these terms and conditions shall prevail.

- WILEY expressly reserves all rights not specifically granted in the combination of (i) the license details provided by you and accepted in the course of this licensing transaction, (ii) these terms and conditions and (iii) CCC's Billing and Payment terms and conditions.

- This Agreement will be void if the Type of Use, Format, Circulation, or Requestor Type was misrepresented during the licensing process.

- This Agreement shall be governed by and construed in accordance with the laws of the State of New York, USA, without regards to such state's conflict of law rules. Any legal action, suit or proceeding arising out of or relating to these Terms and Conditions or the breach thereof shall be instituted in a court of competent jurisdiction in New York County in the State of New York in the United States of America and each party hereby consents and submits to the personal jurisdiction of such court, waives any objection to venue in such court and consents to service of process by registered or certified mail, return receipt requested, at the last known address of such party.

134

WILEY OPEN ACCESS TERMS AND CONDITIONS

Wiley Publishes Open Access Articles in fully Open Access Journals and in Subscription journals offering Online Open. Although most of the fully Open Access journals publish open access articles under the terms of the Creative Commons Attribution (CC BY) License only, the subscription journals and a few of the Open Access Journals offer a choice of Creative Commons Licenses. The license type is clearly identified on the article.

The Creative Commons Attribution License

The Creative Commons Attribution License (CC-BY) allows users to copy, distribute and transmit an article, adapt the article and make commercial use of the article. The CC-BY license permits commercial and non-

Creative Commons Attribution Non-Commercial License

The Creative Commons Attribution Non-Commercial (CC-BY-NC)License permits use, distribution and reproduction in any medium, provided the original work is properly cited and is not used for commercial purposes.(see below)

Creative Commons Attribution-Non-Commercial-NoDerivs License

The Creative Commons Attribution Non-Commercial-NoDerivs License (CC-BY-NC-ND) permits use, distribution and reproduction in any medium, provided the original work is properly cited, is not used for commercial purposes and no modifications or adaptations are made. (see below)

Use by commercial "for-profit" organizations

Use of Wiley Open Access articles for commercial, promotional, or marketing purposes requires further explicit permission from Wiley and will be subject to a fee.

Further details can be found on Wiley Online Library http://olabout.wiley.com/WileyCDA/Section/id-410895.html

Other Terms and Conditions:

v1.10 Last updated September 2015

Questions? customercare@copyright.com or +1-855-239-3415 (toll free in the US) or +1-978-646-2777.

APPENDIX G

DATA-BASED MANUSCRIPT 1 WITH TABLES

THE JOURNAL OF RURAL HEALTH

Older Rural- and Urban-Dwelling Appalachian Adults With Mild Cognitive Impairment

Meghan K. Mattos, MSN;[1] Beth E. Snitz, PhD;[2] Jennifer H. Lingler, PhD, CRNP;[3] Lora E. Burke, PhD, MPH, FAAN, FAHA;[4] Lorraine M. Novosel, PhD, CRNP, ANP-BC, GNP-BC;[5] & Susan M. Sereika, PhD[6]

1 Department of Health and Community Systems, University of Pittsburgh School of Nursing, Pittsburgh, Pennsylvania
2 Department of Neurology, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania
3 Department of Health and Community Systems, University of Pittsburgh School of Nursing, Medicine, and Clinical and Translational Science Institute, Pittsburgh, Pennsylvania
4 Departments of Health and Community Systems and Epidemiology, University of Pittsburgh School of Nursing, Graduate School of Public Health, and Clinical and Translational Science Institute, Pittsburgh, Pennsylvania
5 Department of Health Promotion and Development, University of Pittsburgh School of Nursing, Pittsburgh, Pennsylvania
6 Departments of Health and Community Systems, Epidemiology, and Biostatistics, University of Pittsburgh School of Nursing and Graduate School of Public Health and Clinical Translational Science Institute, Pittsburgh, Pennsylvania

Abstract

Purpose: Mild cognitive impairment (MCI) is a well-recognized risk state for Alzheimer's disease and other dementias. MCI is rapidly increasing among older adults in general and has not yet been examined in older adults within the Appalachian region. Our objective was to compare MCI symptom severity among older rural and urban Appalachian adults with MCI at an initial neuropsychological testing visit.

Methods: A cross-sectional, descriptive study of older Appalachian adults with MCI was conducted using data from the National Alzheimer's Coordinating Center Uniform Data Set. Symptom severity was conceptualized as neuropsychological composite scores across 4 cognitive domains and Clinical Dementia Rating-Sum of Boxes (CDR-SOB) score. For group comparisons, MANCOVA was used for cognitive domains and ANCOVA for CDR-SOB.

Results: The sample ($N = 289$) was about half male (54.3%), predominantly white (91.7%), and living with others (83.5%), with a mean ($\pm$SD) 74.6 $\pm$ 6.2 years of age and 15.4 $\pm$ 3.0 years of education. Rural and urban groups differed significantly in years since onset of cognitive symptoms (2.98 $\pm$ 1.91 in rural and 3.89 $\pm$ 2.70 in urban adults, $t[260] = -2.23$, $P = .03$), but they did not differ across sociodemographic features or comorbid conditions. Rural and urban participants were similar across the 4 cognitive domains and CDR-SOB ($P \geq .05$).

Discussion: No differences were found between rural and urban Appalachian residents on MCI symptom severity. However, urban residents reported a longer time lapse from symptom identification to diagnosis than their rural counterparts. Future studies using more representative population samples of Appalachian and non-Appalachian adults will provide an important next step to identifying disparate cognitive health outcomes in this traditionally underserved region.

Key words dementia, geriatrics, health disparities, mild cognitive impairment, older adults.

137

The Appalachian region of the United States, which spans from southern New York to northern Alabama, Mississippi, and Georgia, has a total population of almost 23 million inhabitants in over 400 counties and 13 states.[1] The Appalachian region suffers from inequalities in socioeconomic conditions,[2] behavioral risk factors for poor health outcomes, and higher mortality rates compared to the nation as a whole.[2] With over double the national percent of rural-dwelling adults within the Appalachian region[3,4] and a greater proportion of older adults,[3] older rural Appalachian adults are an important, understudied population. Appalachian rural adults have worse overall health and health outcomes when compared with the rest of the nation.[2,5-8] Additionally, behavioral risk factors such as smoking and a sedentary lifestyle[7,9] place rural Appalachian adults at greater risk for cardiovascular (CVD) and cerebrovascular disease. Poorer health outcomes in rural Appalachia continue to be addressed in the literature.[2,3,7,8] However, one condition that is rapidly increasing among older adults in general[10] and has not yet been examined in this population is the clinical syndrome, mild cognitive impairment (MCI), which is a well-recognized risk state for Alzheimer's disease (AD) and other dementias.

Rural-dwelling Appalachian adults are especially vulnerable to late-life cognitive impairment based on known health disparities and higher rates of risk factors among those living in rural Appalachia. Established risk factors for cognitive impairment include older age,[11-14] less education,[12,13] and female gender,[12,13] as well as hypertension,[11,15,16] heart disease,[11,15,16] diabetes,[17,18] depression,[11,19,20] and genetic factors.[11,12] Among these known risk factors for cognitive impairment, rural Appalachian residents have demonstrated lower levels of education[21,22] and higher rates of hypertension,[6] heart disease,[23] and diabetes.[23] Moreover, delayed detection of cognitive changes, possibly attributed to fewer rural-dwelling health care providers[7,24] and limited health services,[7] make rural Appalachian adults an especially vulnerable group. Since MCI is a recognized target for the secondary prevention of dementia, the time of MCI diagnosis may present a critical opportunity for interventions that help reduce health disparities.

The prevalence of MCI is estimated to be as high as 19% among older US adults.[25] An MCI diagnosis (1) involves decline in at least one cognitive domain (eg, memory), (2) requires maintenance of near normal functional activities, and (3) requires that the degree of cognitive impairment is not sufficient to warrant a diagnosis of AD or related dementia.[25,26] Subtle changes in cognition may not initially appear to directly affect daily living, but they often significantly worsen over time and can impact day-to-day activities. Based on known rural health disparities, especially later diagnosis of chronic diseases, it is reasonable to hypothesize that MCI may present later in its course in rural adults; however, studies describing older, rural-dwelling adults with MCI have not been documented. The purpose of this study was to compare MCI symptom severity among older rural and urban Appalachian adults with MCI at an initial neuropsychological testing visit. It was hypothesized that older, rural-dwelling Appalachian adults with MCI would present with worse symptom severity, as evidenced by neuropsychological test scores, compared to their urban counterparts.

Methods

Design

A quantitative, cross-sectional, descriptive study of symptom severity data collected from older Appalachian adults with MCI was performed. De-identified data were obtained from the National Alzheimer's Coordinating Center (NACC) Uniform Data Set (UDS), a publicly available national database drawing on over 30 federally funded Alzheimer Disease Centers (ADCs).

Sample

The ADCs, which contribute to the NACC UDS repository, conduct clinical and biomedical research on AD and related cognitive disorders. Individuals who participate in ADCs are enrolled through a variety of methods that include referrals from clinicians, family, or self-referral, and targeted recruiting through community organizations. In addition to enrolling individuals with AD and related cognitive disorders, most centers also enroll healthy control participants. There are 2 cohorts that are targeted by the ADCs: cognitively normal controls and individuals with symptoms associated with dementia.

Data are collected at an initial visit and each annual follow-up visit by clinicians, neuropsychologists, and other ADC research personnel, using up to 18 standardized data collection forms at each visit. The parent study (NACC UDS) sample, from which the present study sample was selected, includes adults who completed a memory evaluation at one of the ADC sites that may serve the Appalachia region from September 2005 through September 2014 data freeze. ADC sites located within or close to the Appalachian region that contribute data to the larger UDS include the University of Pittsburgh Alzheimer Disease Research Center, the University of Kentucky Alzheimer's Disease Center, and Emory University's Alzheimer's Disease Research Center, as well as ADC ancillary sites affiliated with these centers.

Inclusion criteria for the present study were ≥65 years of age; any MCI diagnosis; Appalachian residence, based on county of residence; and having a designated informant/care partner. There were no additional exclusion criteria. For the current study, individual ADCs were contacted and additional data were requested, including 5-digit ZIP codes for the purpose of rural classification. ZIP code data were provided by the individual ADCs for participants meeting the inclusion/exclusion criteria determined by and provided by NACC. ZIP codes reflect the most recent ZIP code data provided by the participant and/or care partner. The University of Pittsburgh Institutional Review Board approval was obtained prior to data acquisition.

After merging NACC UDS and ADC data, there were a total of 3,086 ADC visits for 936 participants with an MCI diagnosis across the 3 centers. Applying the study's inclusion and exclusion criteria, only initial visit data were used, 135 participants were younger than 65 years of age, 446 were not living within Appalachia, and 66 were excluded for other reasons such as no ZIP code available for classification. Ultimately, 289 participants were available for analysis (urban n = 231, rural n = 58). Participants reported residence across 9 states within Appalachia including Georgia (n = 32, 15.6% rural), Kentucky (n = 18, 100% rural), Maryland (n = 2, 100% rural), North Carolina (n = 2, 100% rural), Ohio (n = 3, 33.3% rural), Pennsylvania (n = 228, 12.7% rural), and West Virginia (n = 4, 25.0% rural). Overall, 50.0% of the rural, Appalachian sample resided in Pennsylvania, and the University of Pittsburgh ADRC provided 86.1% of the urban sample.

Measures

Appalachia Classification

Appalachian residence was determined using the Appalachian Regional Commission classification of US counties located within the Appalachian region.[3] Five-digit ZIP codes were converted to counties using the US Census Bureau's online resource, "Locate a county by place name" to classify residents as living within the Appalachia region.[27]

Rural Classification

Once participants were determined to be of Appalachian residence, they were further classified according to United States Department of Agriculture Rural-Urban Commuting Areas Codes (RUCAs) using codes from 1 to 10. This classification scheme was developed by the US Department of Agriculture's Economic Research Service and the US Department of Health and Human Services,

where urban ("metropolitan") includes primary RUCA codes 1-3 and rural ("micropolitan," "small town," and "rural areas") includes codes 4-10.[28]

MCI Classification

We used the MCI criteria implemented by NACC: (1) cognition is determined to be not normal and (2) clinical dementia is not present.[29] We included all MCI subtypes, including (a) predominant focal amnestic disorder, (b) amnestic disorder plus changes in other cognitive domains, (c) focal nonamnestic disorder, and (d) nonamnestic disorder plus changes in other nonmemory cognitive domains.[29]

Descriptive, Comorbid Conditions, and Medication Measures

Sociodemographic variables included age (measured in years) and education (measured in years) as continuous variables and sex (male/female), race (white/nonwhite), living situation (living with someone/not living with someone), and marital status (married/not married) as binary variables. Comorbid conditions and family of a first degree relative with dementia were coded as binary variables (recent/active and remote/inactive or absent/present), except for body mass index (BMI, kg/m^2) and Geriatric Depression Score (GDS)[30] that were measured as continuous variables and collected by clinician. Age of onset of cognitive decline was also measured as a continuous variable, as determined by the participant and family/informant self-report. Time since onset of symptoms was calculated by subtracting the age of onset of cognitive decline from the current participant age (in years). Total number of self-reported medications was reported as the sum of all prescription, nonprescription, and vitamins/supplements reported.

Distance to ADC

ArcMap (Esri, Redlands, California) was used for geocoding ZIP codes and ADCs into separate layers. The ArcGIS Network Analyst Origin-Destination (OD) function was used to compute driving distance between resident ZIP code and ADC address. The new OD cost matrix extension calculated distance between the 2 locations with a gravity model for access, assigning the same weight for each participant.

Outcome Variables: Neuropsychological Measures

To examine MCI symptom severity, we clustered neuropsychological measures conceptually across 4 cognitive

139

domains: Memory (Wechsler Memory Scale-R Logical Memory IA – Immediate and Delayed), Language (Boston Naming Test and Category Fluency – animals or vegetables), Attention/Psychomotor Speed (Trailmaking Test A, Wechsler Adult Intelligence Scale-Revised [WAIS-R] Digit Symbol Substitution Task [DSST], and Digit Span Forward), and Executive Functioning (Trailmaking Test B and Digit Span Backwards). Neuropsychological measures are described below.

Memory

Wechsler Memory Scale-R Logical Memory IA – Immediate is a measure of memory in which a brief story is read to the participant, who is asked to recall it immediately. Logical Memory IIA is a measure of delayed recall, where the participant recalls the same story after 30 min. The primary performance measure is number of story units recalled,[31] scored 0-25, with a higher score indicating better performance.[32]

Language

The Boston Naming Test[31] measures ability to name line drawings of objects, for a total possible score of 60. For the NACC UDS, only the score of the odd-numbered items are presented (scored 0-30). Category Fluency is a measure of semantic memory (verbal fluency, language) where the participant is asked to name different exemplars of a given semantic category. For the NACC UDS, the total number of animals or vegetables named in 60 seconds are scored from 0 to 77.[33]

Attention/Psychomotor Speed

Attention and psychomotor speed is measured by 3 assessments: Trailmaking A,[34] Wechsler Adult Intelligence Scale-Revised (WAIS-R) Digit Symbol Substitution Task (DSST),[35] and Digit Span Forward.[36] The Trailmaking Test A requires the participant to connect randomly placed encircled numbers that are strewn across a sheet of normal-sized paper. The participant is asked to connect all numbers with a pen/pencil, in order beginning with 1, as fast as possible, for a maximum of 150 seconds.[34] Scores include seconds to complete (0-150), number of errors (0-48), and number of correct lines drawn (0-24). WAIS-R DSST asks participants to take digit-symbol pairs and write the corresponding symbol for a list of digits in 90 seconds with a maximum of 93 items (0-93, total number of items correctly completed). Digit Span Forward is when the participant is read number sequences of increasing length and asked to repeat them. Measures of performance include: the number of digit sequences

recalled correctly, up to 2 consecutive errors (0-12), and the length of the highest digit sequences the participant is able to repeat correctly (0-8).

Executive Functioning

Trailmaking Test B requires the participant to connect both numbers and letters in order in an alternating pattern (eg, 1-A-2-B) in a maximum of 300 seconds.[37] Scores include seconds to complete (0-300), number of errors (0-48), and number of correct lines drawn (0-24). Digit Spans Backward is used to measure working memory. The participant is read number sequences of increasing length and then asked to repeat each sequence backward.[36] The primary measure of performance is the number of digit sequences correctly reversed with up to 2 consecutive errors at the same digit length (0-12). The digit span backward length is the length of the highest digit sequences the participant is able to reverse (0-7).

Clinical Dementia Rating Sum of Boxes

The Clinical Dementia Rating-Sum of Boxes (CDR-SOB) score was also considered as an independent outcome. CDR-SOB is calculated by summing 6 domain box scores (memory, orientation, judgment and problem solving, community affairs, home and hobbies, and personal care) obtained from the Clinical Dementia Rating (range: 0-18).[38,39] This is included as a measure of symptom severity based on clinician judgment and participant account of his/her ability to perform activities of daily living, rated independently of neuropsychological test performance.

MCI symptom severity was measured using these 9 objective neuropsychological tests spanning 4 cognitive domains and individually for CDR-SOB. Composite scores were derived based on this mapping of individual neuropsychological tests to conceptual domains to provide averaged adjusted z-scores for each cognitive domain composite. For all neuropsychological measurements, age-, sex-, and education-adjusted z-scores were used, as adjusted using the normative calculator for the UDS neuropsychological test battery[40] and provided by the NACC UDS. The initial visit neuropsychological assessment measurements were used for analysis, and the time since onset of symptoms was considered as a covariate in the analysis of each outcome domain.

Analysis

Data were analyzed using IBM SPSS Statistics (v.23, IBM Corp., Armonk, New York). Initially data were screened for anomalies (eg, outliers, missing data, violations of statistical assumptions) using descriptive and

exploratory data analysis methods to characterize the sample overall and by rural/urban classification. Group comparisons were conducted for all sociodemographic variables by rural/urban classification using 2-sample t tests for continuous-type descriptors and chi-square or Fisher exact tests for categorical characteristics prior to proceeding with analysis of the neuropsychological outcome variables. All sociodemographic variables were examined as covariates for each outcome variable.

Mean adjusted z-scores for each cognitive domain composite were analyzed using multivariate analysis of covariance (MANCOVA) by examining the set of 4 cognitive domain composites simultaneously to compare MCI symptom severity between rural and urban groups using the multivariate F-test. Effect sizes were reported as partial eta-squared. Sociodemographic variables (eg, sex, education, age) were also examined for possible associations with cognitive outcome variables and, if significant associations were found, were controlled for in the analysis. Analysis of covariance (ANCOVA) was used to compare CDR-SOB scores between rural and urban samples while controlling for sociodemographics. For all analyses, the level of statistical significance was set at .05 for 2-sided hypothesis testing.

Results

Our final sample (N = 289; 231 urban, 58 rural) included participants who were, on average (± SD), 74.6 ± 6.2 years of age, predominantly white (91.7%), male (54.3%), and with a reported mean 15.4 ± 3.0 years of education. Most reported living with at least one person (83.5%) and being married (77.5%). Of those participants living with someone, 93.7% were married; of those participants who were not married, 75.8% lived alone. Rural and urban groups did not differ significantly across any sociodemographic features. See Table 1 for more detailed sociodemographic information.

Gender and education had statistically significant associations across outcome variables. Male gender was associated with lower adjusted z-scores for memory, language, and attention/psychomotor speed domains as well as higher CDR-SOB scores. Fewer years of education was associated with lower language and attention/psychomotor speed domain scores as well as higher CDR-SOB scores. Age had no statistically significant associations across outcome variables. Race was also considered; however, the small number of nonwhite participants in both rural and urban groups did not provide sufficient variability to warrant inclusion as a confounder. The identified significant associations for each outcome variable were adjusted for, and similar results were obtained for each outcome variable.

Overall there were no statistically significant differences in most comorbid conditions between rural and urban participants ($P \geq .05$). However, there was a difference in the time since onset of cognitive symptoms between groups (2.98 ± 1.91 years in rural adults and 3.89 ± 2.70 in urban adults, $t[260] = -2.23$, $P = .03$). Table 2 presents prevalence of comorbid conditions and distance traveled for the total sample as well as rural and urban samples. Rural- and urban-dwelling participants did, however, have significant differences in distance traveled to ADC. Rural participants traveled, on average, 65.03 ± 36.06 miles (range: 23.13-181.50) to ADC, compared to urban participants who traveled on average 17.20 ± 16.49 miles (range: 0.59-138.55) ($t[287] = 14.926$, $P < .001$).

There were no significant differences between rural and urban participants across the 4 objective cognitive domains or CDR-SOB: Memory ($F[1,287] = 1.35$, $P = .25$, partial $\eta^2 < 0.01$); Language ($F[1,287] = 0.12$, $P = .73$, partial $\eta^2 = <0.01$); Attention/Psychomotor Speed ($F[1,287] = 0.07$, $P = .79$, partial $\eta^2 < 0.01$); Executive Function ($F[1,287] = 0.90$, $P = .34$, partial $\eta^2 < 0.01$); and CDR-SOB ($t[287] = -0.15$, $P = .88$). When looking at individual neuropsychological tests, there were also no differences between rural- and urban-dwelling adults, except for 2 tests within the Attention/Psychomotor Speed domain, Trailmaking A and Digit Span Forward. Older, rural adults with MCI scored significantly worse in the Trailmaking A test compared to urban adults ($t[286] = -3.16$, $P < .01$), while older, urban adults with MCI scored significantly worse in Digit Span Forward compared to rural adults ($t[287] = 2.27$, $P = .02$). Table 3 presents results for individual neuropsychological tests.

Discussion

We hypothesized that older, rural-dwelling Appalachian adults would have worse cognitive symptom severity than their urban counterparts at an initial neuropsychological testing visit. This hypothesis was not supported by our analyses. Across 4 cognitive domains and CDR-SOB, we found significant differences within the attention/psychomotor speed domain for 2 of the individual tests, Trailmaking A and Digit Span Forward tests. However, the differences for the 2 tests were in different directions, and thus we believe that these are isolated findings likely due to chance and should not be overinterpreted regarding their clinical significance. There was no evidence of rural/urban differences at the domain level.

Of note, our analysis revealed a significant difference in the length of time from onset of symptoms to MCI

Table 1   Sociodemographic Features of Older, Appalachian-Dwelling Adults With MCI, Rural and Urban, N = 289

Variable	Total Sample (N = 289)	Rural (n = 58)	Urban (n = 231)	Test Statistic	P Value
Age, mean years ± standard deviation (SD)	74.64 ± 6.17	74.10 ± 6.15	74.78 ± 6.18	$t(287) = -1.41$	.16
Education, mean years ± SD	15.39 ± 3.03	14.90 ± 3.18	15.52 ± 2.98	$t(287) = -0.75$	.46
Sex, % male	54.3	46.6	56.3	$X^2(1) = 1.77$	.18
Race, % white	91.7	96.6	90.5	[a]	.18
Marital Status, % married	77.5	81.0	76.6	$X^2(1) = 0.52$	.47
Living Situation, % live with someone (n = 285)	83.5	87.9	82.4	$X^2(1) = 1.03$	.31

[a]Fisher exact test was used due to cells with expected count less than 5.

Table 2   Comorbid Conditions of Older, Appalachian-Dwelling Adults With MCI, Rural and Urban, N = 289

Comorbid Condition[a]	Total Sample (N = 289)	Rural (n = 58)	Urban (n = 231)	Test Statistic	P Value
Heart attack/arrest, % yes	11.4	17.2	10.0	$X^2(1) = 2.43$	.12
Atrial Fibrillation, % yes	11.1	13.8	10.4	$X^2(1) = 0.55$	.46
Angioplasty/ Endarterectomy, % yes	12.1	19.0	10.4	$X^2(1) = 3.20$	.07
Cardiac bypass procedure, % yes	10.7	15.5	9.5	$X^2(1) = 1.74$	.19
Pacemaker, % yes	6.6	3.4	7.4	[b]	.38
Congestive HF, % yes	2.1	5.2	1.3	[b]	.10
Stroke, % yes	8.3	3.4	9.6	[b]	.18
Hypertension, % yes	55.4	48.3	57.1	$X^2(1) = 1.48$	.23
Hypercholerolemia, % yes	61.6	65.5	60.6	$X^2(1) = 0.47$	.49
Diabetes, % yes	17.0	19.0	16.5	$X^2(1) = 0.21$	.65
Active depression, % yes	34.0	29.3	35.2	$X^2(1) = 0.72$	.40
Alcohol abuse, % yes	3.1	5.2	2.6	[b]	.39
Cigarette smoking, past 30 days, % yes	2.8	1.8	3.1	[b]	1.00
Cigarette smoking, > 100 in lifetime, % yes	48.6	50.9	48.0	$X^2(1) = 0.15$	.70
Other psychiatric disorders, % yes	6.6	5.2	6.9	[b]	.77
First degree relative with dementia, % yes	52.8	52.4	54.4	$X^2(1) = 0.07$	.79
Body Mass Index (kg/m^2), mean ± standard deviation (SD)	27.75 ± 5.05 (n = 273)	27.33 ± 5.51	27.85 ± 4.94	$t(271) = -0.67$	.50
Geriatric Depression Score, total score, mean ± SD	2.32 ± 2.57 (n = 288)	2.35 ± 2.40 (n = 57)	2.32 ± 2.61 (n = 231)	$t(280) = 0.09$	.93
Number of total medications, mean ± SD	6.56±3.57	6.47±4.01	6.58±3.46	$t(286) = -0.19$	.85
Time since onset of symptoms (y), mean ± SD	3.72 ± 2.59 (n = 262)	2.98 ± 1.91 (n = 49)	3.89 ± 2.70 (n = 213)	$t(260) = -2.23$	**.03**
Distance from Alzheimer's Disease Center (miles), mean ± SD	26.80 ± 29.03	65.03 ± 36.06	17.20 ± 16.49	$t(287) = 14.93$	**<.001**

[a]All comorbid conditions present a "history of" the condition (past and present).
[b]Fisher exact test was used due to cells with expected count less than 5.

diagnosis between older rural and urban adults, where rural adults were presenting for diagnosis earlier than their urban counterparts. This was unexpected as breast, prostate, and colorectal cancers, as well as CVD have been found to be diagnosed at later stages for rural adults than their urban counterparts.[2,7,8,41] A recent systematic review examining barriers to cognitive screening in rural America found that lack of knowledge about cognitive changes, lack of knowledgeable providers to offer cognitive screening, and geographic distance are barriers to cognitive screening.[42] One reason for the shorter length of time from onset of symptoms to diagnosis for

rural-dwelling adults compared to urban-dwelling adults may be that rural-dwelling adults are more likely to take the time to seek out and use specialty health care services if they have a first degree relative with dementia. Although over 50% of both rural and urban adults with MCI reported having at least one first degree relative with dementia, those living in rural areas may be more likely to be proactive in seeking out care and treatment at ADCs to try and prevent dementia symptoms or outcomes seen in their relatives. This may be explained by the significant difference in distance traveled by rural participants to ADC site compared to urban participants, with

Table 3 Neuropsychological Measures for Older, Appalachian-Dwelling Adults With MCI, Rural and Urban, N = 289

Neuropsychological Measures[a]	Total Sample (N = 289)	Rural (n = 58)	Urban (n = 231)	Test Statistic	P Value
Clinical Dementia Rating- Sum of Boxes (CDR-SOB, range 0-17)	1.59 ± 1.27	1.57 ± 1.27	1.60 ± 1.27	$t(287) = -0.15$	.88
Memory					
Logical Memory 1A- Immediate	−0.76 ± 1.07	−0.89 ± 1.15	−0.72 ± 1.05	$t(287) = -1.07$	.29
Logical Memory 1A- Delayed	−0.95 ± 1.00	−1.09 ± 1.09	−0.92 ± 0.98	$t(287) = -1.18$	.24
Language					
Boston Naming Test Score	−0.55 ± 1.00	−0.69 ± 1.12	−0.52 ± 0.97	$t(287) = -1.16$	.25
Category Fluency, Animals	−0.56 ± 0.88	−0.52 ± 0.87	−0.57 ± 0.88	$t(287) = 0.34$	.73
Category Fluency, Vegetables	0.10 ± 1.19 (n = 288)	0.29 ± 1.05 (n = 58)	0.06 ± 1.22 (n = 230)	$t(286) = 1.35$	.18
Attention/Psychomotor Speed					
Trailmaking A Score	−0.17 ± 1.13 (n = 288)	−0.58 ± 1.75 (n = 58)	−0.06 ± 0.89 (n = 230)	**$t(286) = -3.16$**	**<.01**
WAIS-R Digit Symbol Substitution	−0.22 ± 0.91 (n = 288)	−0.35 ± 0.93 (n = 58)	−0.19 ± 0.91 (n = 230)	$t(286) = -1.23$	.22
Digit Span Forward	−0.29 ± 0.97	−0.03 ± 0.86	−0.35 ± 0.98	**$t(287) = 2.27$**	**.02**
Digit Span Forward Length	−0.25 ± 0.95	−0.05 ± 0.87	−0.30 ± 0.97	$t(287) = 1.83$	.07
Executive Functioning					
Trailmaking B Score	−0.55 ± 1.27 (n = 287)	−0.75 ± 1.36 (n = 58)	−0.51 ± 1.24 (n = 229)	$t(285) = -1.31$	.19
Digit Span Backward	−0.22 ± 0.91	−0.27 ± 0.96	−0.21 ± 0.90	$t(287) = -0.46$	.64
Digit Span Backward Length	−0.25 ± 0.86	−0.27 ± 0.90	−0.25 ± 0.86	$t(287) = -0.19$	.85

[a]All reported values are age, sex, and education-adjusted *z*-scores except for CDR-SOB.

consideration for the fact that most specialty health care services are located within urban centers. Additionally, symptom identification by family members familiar with cognitive symptoms or knowledge of specialty health care centers may also play a role in bringing older, rural-dwelling adults to specialty centers earlier.

Historically, recruitment for research in rural America can be challenging,[43,44] and recruitment for cognitive changes may be compounded because cognitive symptoms may be dismissed as normal aging.[42] However, once involved in memory research, Hunsaker et al[45] found that both rural and urban research participants believed memory research benefited the participant, family, and society. For example, participation in memory research allowed them to understand age-related memory changes and provided family members with "an enhanced understanding of the disease process."[45]

Interpretation of results is limited as the older adults living in rural areas who attended the ADCs may not be typical of most older, rural-dwelling adults in Appalachia, as seen in the sociodemographic characteristics presented. For example, only 20.1% of the total sample lived in rural areas compared to 42% of the Appalachian population living in rural areas.[3] Within the Appalachian region, 55% are married, compared to 77.5% married in our total sample; 26% live alone in Appalachia compared to 16.5% of our total sample.[46] Our study participants also had a greater number of years of formal education (almost 3 years of college) compared to only 20.7% of adults over 25 years of age attaining a bachelor's degree or more residing in the Appalachian region.[47]

ADCs also employ various recruitment strategies and patient populations were not randomly selected. However, each center continuously monitors cohorts to try and match overall characteristics and recruit to include rural county inhabitants and minorities. Both participant characteristics and recruitment strategies support selection bias,[48,49] and generalizations to all older adults in Appalachia are not presumed. This is apparent in the similarities between the rural and urban samples. We also acknowledge that there are regions within Appalachia that are not well represented in this analysis, which could be attributed to location or recruitment strategies of ADCs within the region. However, we have included all participants living within Appalachia as it provides important new information about an underserved population receiving cognitive evaluations at a specialty research center. With consideration for the limitations of this study, NACC UDS provided the unique opportunity to use national multicenter data with detailed standardized neuropsychological testing to describe a region underrepresented in research settings.

143

Conclusion

This study can serve as an initial description of MCI in the underserved Appalachian region. Findings did not show differences in MCI symptom severity between older rural and urban residents within this region; this may be due to the lack of variability in the sample, as all participants lived within the Appalachian region, or because rural and urban Appalachian residents are more similar to each other than other rural/urban comparisons. Future studies of cognitive impairment using more representative population samples of Appalachian and non-Appalachian older adults will provide an important next step to identifying disparate cognitive health outcomes among residents in this traditionally underserved region.

References

1. US Department of Health and Human Services. *Health, United States, 2012: With Special Feature on Emergency Care.* Hyattsville, MD: US DHHS; 2013. Available at: http://www.cdc.gov/nchs/data/hus/hus12.pdf. Accessed April 8, 2013.
2. Halverson JA, Ma L, Harner EJ. *An Analysis of Disparities in Health Status and Access to Health Care in the Appalachian Region - Appalachian Regional Commission.* Washington, DC; 2004. Available at: http://www.arc.gov/research/research reportdetails.asp?REPORT_ID=82. Accessed June 23, 2013.
3. The Appalachian Region. *Appalach Reg Comm.* 2013. Available at: http://www.arc.gov/appalachian_region/The AppalachianRegion.asp. Accessed July 26, 2013.
4. USDA Economic Research Service - Rural Classifications. Available at: http://www.ers.usda.gov/topics/rural-economy-population/rural-classifications.aspx#.UVnPIqWLFjA. Accessed April 1, 2013.
5. Behringer B, Friedell G. Appalachia: where place matters in health. *Prev Chronic Dis.* 2006;5(4):1-4.
6. Eberhardt MS, Pamuk ER. The importance of place of residence: examining health in rural and nonrural areas. *Am J Public Health.* 2004;94(10):1682-1686.
7. Gamm L, Hutchison L, Bellamy G, Dabney BJ. Rural healthy people 2010: identifying rural health priorities. *J Rural Heal.* 2002;18(1):9-14.
8. Casey MM, Thiede Call K, Klingner JM. Are rural residents less likely to obtain recommended preventive healthcare services? *Am J Prev Med.* 2001;21(3):182-188.
9. Bennett KJ, Olatosi B, Probst J. *Health Disparities: A Rural—Urban Chartbook.* Columbia, SC: South Carolina Rural Health Research Center; 2008.
10. Alzheimer's Association. *Latest Facts & Figures Report.* Available at: http://www.alz.org/alzheimers_disease_facts_and_figures.asp#prevalence. Accessed May 15, 2013.
11. Sachdev PS, Lipnicki DM, Crawford J, et al. Risk profiles of subtypes of mild cognitive impairment: the Sydney Memory and Ageing Study. *J Am Geriatr Soc.* 2012;60(1):24-33.
12. Kryscio RJ, Schmitt FA, Salazar JC, Mendiondo MS, Markesbery WR. Risk factors for transitions from normal to mild cognitive impairment and dementia. *Neurology.* 2006;66(6):828-832.
13. Petersen RC. Prevalence of mild cognitive impairment is higher in men The Mayo Clinic Study of Aging. *Neurology.* 2010;75(10):889-897.
14. Ganguli B, Snitz BE, Hughes TF, Chang CH. Mild cognitive impairment incidence and vascular risk factors in a population-based cohort. *Neurology.* 2013;80(23):2112-2120.
15. Chen R-H, Jiang X-Z, Zhao X-H, et al. Risk factors of mild cognitive impairment in middle aged patients with type 2 diabetes: a cross-section study. *Ann Endocrinol (Paris).* 2012;73(3):208-212.
16. Ettorre E, Cerra E, Marigliano B, et al. Role of cardiovascular risk factors (CRF) in the patients with mild cognitive impairment (MCI). *Arch Gerontol Geriatr.* 54(2):330-332.
17. Cheng G, Huang C, Deng H, Wang H. Diabetes as a risk factor for dementia and mild cognitive impairment: a meta-analysis of longitudinal studies. *Intern Med J.* 2012;42(5):484-491.
18. Crane PK, Walker R, Hubbard RA, et al. Glucose levels and risk of dementia. *N Engl J Med.* 2013;369(6):540-548.
19. Spira AP, Rebok GW, Stone KL, Kramer JH, Yaffe K. Depressive symptoms in oldest-old women: risk of mild cognitive impairment and dementia. *Am J Geriatr Psychiatry.* 2012;20(12):1006-1015.
20. Johnson L, Mauer C, Jahn D, et al. Cognitive differences among depressed and non-depressed MCI participants: a project FRONTIER study. *Int J Geriatr Psychiatry.* 2013;28(4):377–82.
21. Billings DB, Blee DM. *The Road to Poverty: The Making of Wealth and Hardship in Appalachia.* New York, NY: Cambridge University Press; 2000.
22. Gillum RF, Mussolino ME. Education, poverty, and stroke incidence in whites and blacks: the NHANES epidemiologic follow-up study. *J Clin Epidemiol.* 2003;56:188-195.
23. Pearson T, Lewis C. Rural epidemiology: insights from a rural population laboratory. *Am J Epidemiol.* 1998;148(10):949-957.
24. Barley GE, Reeves CB, O'Brien-Gonzales A, Westfall JM. Characteristics of and issues faced by rural female family physicians. *J Rural Heal.* 2001;17(3):251-258.
25. Gauthier S, Reisberg B, Zaudig M, et al. Mild cognitive impairment. *Lancet.* 2006;367:1262-1270.
26. Petersen R, Doody R, Kurz A, et al. Current concepts in mild cognitive impairment. *Arch Neurol.* 2001;58:1985-1992.

144

27. QuickFacts: Locate a county by place name. Available at: http://quickfacts.census.gov/cgi-bin/qfd/lookup. Accessed April 24, 2015.

28. Rural Urban Commuting Area Codes Data. Available at: http://depts.washington.edu/uwruca/ruca-demographics.php. Accessed September 27, 2013.

29. Winblad B, Palmer K, Kivipelto M, Jelic V, Fratiglioni L. Mild cognitive impairment—beyond controversies, towards a consensus: report of the International Working Group on Mild Cognitive Impairment. *J Intern Med*. 2004;256:240-246.

30. Yesavage J, Brink T, Rose T, et al. Development and validation of a geriatric depression screening scale: a preliminary report. *J Psychiatr Res*. 1983;17(1):37-49.

31. Wechsler D. *Wechsler Memory Scale, Revised Manual*. San Antonia, TX: The Psychological Corportation; 1987.

32. Emilien G, Durlach C, Antoiniadis E, VanderLinden M, Maloteaux J. *Memory: Neuropsychological, Imaging and Psychopharmalogical Perspectives*. Hove, UK: Psychology Press; 2004.

33. Benton AL. Differential behaivoral effects in frontal love disease. *Neuropsychologia*. 1968;6:53-60.

34. Reitan RM. Validity of the Trail-Making Tests as an indication of organic brain damage. *Percept Mot Skills*. 1958;8:271-276.

35. Wechsler D. *Wechsler Adult Intelligence Scale*. 3rd ed. New York, NY: The Psychological Corportation; 1997.

36. Wechsler D. *Wechsler Adult Intelligence Scale, Revised Manual*. New York, NY: The Psychological Corportation; 1981.

37. Borkowski JG, Benton AL, Spreen O. Word fluency and brain damage. *Neuropsychologia*. 1967;6:135-140.

38. Morris MD, John C. The Clinical Dementia Rating (CDR): Current version and scoring rules. *Neurology*. 43(11):2412-2414.

39. O'Bryant SE, Waring SC, Cullum CM, et al. Staging dementia using Clinical Dementia Rating Scale Sum of Boxes scores: a Texas Alzheimer's research consortium study. *Arch Neurol*. 2008;65(8):1091-1095.

40. Shirk SD, Mitchell MB, Shaughnessy LW, et al. A web-based normative calculator for the uniform data set (UDS) neuropsychological test battery. *Alzheimers Res Ther*. 2011;3(6):32.

41. Campo S, Askelson NM, Routsong T, Graaf LJ, Losch M, Smith H. The green acres effect: the need for a new colorectal cancer screening campaign tailored to rural audiences. *Heal Educ Behav*. 2008;35(6):749-762.

42. Kirk Wiese L, Williams CL, Tappen RM. Analysis of barriers to cognitive screening in rural populations in the United States. *Adv Nurs Sci*. 37(4):327-339.

43. Cudney S, Craig C, Nichols E, Weinert C. Barriers to recruiting an adequate sample in rural nursing research. *Online J Rural Nurs Heal Care*. 2004;4(2):78-88.

44. Dibartolo MC, McCrone S. Recruitment of rural community-dwelling older adults: barriers, challenges, and strategies. *Aging Ment Health*. 2003;7(2):75-82.

45. Hunsaker A, Sarles CE, Rosen D, et al. Exploring the reasons urban and rural-dwelling older adults participate in memory research. *Am J Alzheimers Dis Other Demen*. 2011;26(3):227-234.

46. Haaga J. *Demographic and Socioeconomic Change in Appalchia: Households and Families in Appalachia*. Washington, DC: Population Reference Bureau and Appalachian Regional Commission; 2004.

47. Pollard K, Jacobsen L. *The Appalachian Region: A Data Overview from the 2009-2013 American Community Survey*. Washington, DC: Appalachian Regional Commission; 2015.

48. Kokmen E, Ozsarfati Y, Beard CM, O'Brien PC, Rocca WA. Impact of referral bias on clinical and epidemiological studies of Alzheimer's disease. *J Clin Epidemiol*. 1996;49(1):79-83.

49. Barnhart RL, van Belle G, Edland SD, et al. Geographically overlapping Alzheimer's disease registries: comparisons and implications. *J Geriatr Psychiatry Neurol*. 1995;8(4):203-208.

145

BIBLIOGRAPHY

Abner, E. L., Kryscio, R. J., Cooper, G. E., Fardo, D. W., Jicha, G., Mendiondo, M. S., Schmitt, F. (2012). Mild cognitive impairment: statistical models of transition using longitudinal clinical data. *International Journal of Alzheimer's Diseaseournal of Alzheimer's Disease*, *2012*, 291920. http://doi.org/10.1155/2012/291920

About Alzheimer's Disease: Treatment | National Institute on Aging. (n.d.). Retrieved August 7, 2013, from http://www.nia.nih.gov/alzheimers/topics/treatment

Aging, A. (2011). *A Profile of Older Americans : 2011 Administration on Aging*.

AHRQ. (2005). *Health Care Disparities in Rural Areas Selected Findings From the 2004 National Healthcare Disparities Report*. *Fact Sheet, AHRQ Pub No. 05-P022*.

Altheide, D. L., & Johnson, J. M. (1998). Criteria for Assessing Interpretive Validity in Qualitative Research. In N. K. Denzin & Y. S. Lincoln (Eds.), *Collecting and Interpreting Qualitative Materials* (pp. 283–312). Thousand Oaks: Sage Publications.

Alzheimer's Association. (2016). Support Groups. Retrieved July 19, 2016, from http://www.alz.org/apps/we_can_help/support_groups.asp

Ardila, A., Bertolucci, P. H., Braga, L. W., Castro-Caldas, A., Judd, T., Kosmidis, M. H., Rosselli, M. (2010). Illiteracy: the neuropsychology of cognition without reading. *Archives of Clinical Neuropsychology*, *25*(8), 689–712. http://doi.org/10.1093/arclin/acq079

Barley, G. E., Reeves, C. B., O'Brien-Gonzales, A., & Westfall, J. M. (2001). Characteristics of and Issues Faced by Rural Female Family Physicians. *Journal of Rural Health*, *17*(3), 251–258. http://doi.org/10.1111/j.1748-0361.2001.tb00962.x

Barnhart, R. L., van Belle, G., Edland, S. D., Kukull, W., Borson, S., Raskind, M., Larson, E. (1995). Geographically overlapping Alzheimer's disease registries: comparisons and implications. *Journal of Geriatric Psychiatry and Neurology*, *8*(4), 203–8. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/8561832

Beck, C. (1993). Qualitative Research: The evaluation of its credibility, fittingness and auditability. *WJNR*, *15*, 263.

Behringer, B., & Friedell, G. (2006). Appalachia: Where Place Matters in Health. *Preventing Chronic Disease*, *5*(4), 1–4.

Bello-Haas, V. P. M. D., Connell, M. E. O., & Morgan, D. G. (2014). Maintaining health and wellness in the face of dementia: an exploratory analysis of individuals attending a rural and remote memory clinic. *Rural and Remote Health*, *14*(3), 1–16.

Bennett, K. J., Olatosi, B., & Probst, J. (2008). *Health Disparities : Health Disparities : A Rural–Urban Chartbook*. Columbia.

Benton, A. L. (1968). Differential behaivoral effects in frontal love disease. *Neuropsychologia*, *6*, 53–60.

Billings, D. B., & Blee, D. M. (2000). *The Road to Poverty: The Making of Wealth and Hardship in Appalachia*. New York: Cambridge University Press.

Blusi, M., Kristiansen, L., & Jong, M. (2015). Exploring the influence of Internet-based caregiver support on experiences of isolation for older spouse caregivers in rural areas: a qualitative interview study. *International Journal of Older People Nursing*, *10*(3), 211–20. http://doi.org/10.1111/opn.12074

Borak, J., Salipante-Zaidel, C., Slade, M. D., & Fields, C. a. (2012). Mortality disparities in Appalachia: reassessment of major risk factors. *Journal of Occupational and Environmental Medicine*, *54*(2), 146–56. http://doi.org/10.1097/JOM.0b013e318246f395

Borkowski, J. G., Benton, A. L., & Spreen, O. (1967). Word fluency and brain damage. *Neuropsychologia*, *6*, 135–140.

Borson, S., Scanlan, J. M., Watanabe, J., Tu, S.-P., & Lessig, M. (2006). Improving identification of cognitive impairment in primary care. *International Journal of Geriatric Psychiatry*, *21*(4), 349–55. http://doi.org/10.1002/gps.1470

Bradford, A., Kunik, M. E., Schulz, P., Williams, S. P., Singh, H., & Mph, J. (2009). Missed and Delayed Diagnosis of Dementia in Primary Care Prevalence and Contributing Factors. *Alzheimer Disease & Associated Disorders*, *23*(4), 311–314.

Buchner, A., Erdfelder, E., Faul, F., & Lang, A. (2009). G*Power (Version 3.1). Retrieved from http://www.uni-duesseldorf.de/home/fileadmin/fehlerseite.html

Busse, A., Hensel, A., Gühne, U., Angermeyer, M. C., & Riedel-Heller, S. G. (2006). Mild cognitive impairment: long-term course of four clinical subtypes. *Neurology*, *67*(12), 2176–85. http://doi.org/10.1212/01.wnl.0000249117.23318.e1

Campo, S., Askelson, N. M., Routsong, T., Graaf, L. J., Losch, M., & Smith, H. (2008). The green acres effect: the need for a new colorectal cancer screening campaign tailored to rural audiences. *Health Education & Behavior*, *35*(6), 749–62. http://doi.org/10.1177/1090198108320358

Casey, M. M., Thiede Call, K., & Klingner, J. M. (2001). Are rural residents less likely to obtain recommended preventive healthcare services? *American Journal of Preventive Medicine*, *21*(3), 182–8. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/11567838

Chen, R.-H., Jiang, X.-Z., Zhao, X.-H., Qin, Y.-L., Gu, Z., Gu, P.-L., … Zou, Y.-F. (2012). Risk factors of mild cognitive impairment in middle aged patients with type 2 diabetes: a cross-section study. *Annales D'endocrinologie*, *73*(3), 208–12. http://doi.org/10.1016/j.ando.2012.04.009

Cheng, G., Huang, C., Deng, H., & Wang, H. (2012). Diabetes as a risk factor for dementia and mild cognitive impairment: a meta-analysis of longitudinal studies. *Internal Medicine Journal*, *42*(5), 484–91. http://doi.org/10.1111/j.1445-5994.2012.02758.x

Cornwell, E. Y., & Waite, L. J. (2009). Measuring social isolation among older adults using multiple indicators from the NSHAP study. *The Journals of Gerontology*, *64 Suppl 1*, i38-46. http://doi.org/10.1093/geronb/gbp037

Crane, P. K., Walker, R., Hubbard, R. a, Li, G., Nathan, D. M., Zheng, H., … Larson, E. B. (2013). Glucose levels and risk of dementia. *The New England Journal of Medicine*, *369*(6), 540–8. http://doi.org/10.1056/NEJMoa1215740

Creswell, J. W. (2007). *Qualitative Inquiry and Research Design* (3rd ed.). Thousand Oaks: Sage Publications, Inc.

Cudney, S., Craig, C., Nichols, E., & Weinert, C. (2004). Barriers to recruiting an adequate sample in rural nursing research. *Online Journal of Rural Nursing and Health Care*, *4*(2), 78–88.

Dibartolo, M. C., & McCrone, S. (2003). Recruitment of rural community-dwelling older adults: barriers, challenges, and strategies. *Aging & Mental Health*, *7*(2), 75–82. http://doi.org/10.1080/1360786031000072295

DiNapoli, E. a., Wu, B., & Scogin, F. (2013). Social Isolation and Cognitive Function in Appalachian Older Adults. *Research on Aging*. http://doi.org/10.1177/0164027512470704

Eberhardt, M. S., & Pamuk, E. R. (2004). The importance of place of residence: examining health in rural and nonrural areas. *American Journal of Public Health*, *94*(10), 1682–6. Retrieved from http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=1448515&tool=pmcentrez&rendertype=abstract

Edelman, P., Kuhn, D., Fulton, B. R., & Kyrouac, G. a. (2006). Current Topics in Care of Persons With Alzheimer ' s Disease. *American Journal of Alzheimer's Disease & Other Dementias*, *21*(4), 226–233. http://doi.org/10.1177/1533317506290664

Eisenhardt, K. M. (1989). Making Fast Strategic Decisions in High-Velocity Environments.

Academy of Management Review, *14*(4), 532–550.

Emilien, G., Durlach, C., Antoiniadis, E., VanderLinden, M., & Maloteaux, J. (2003). *Memory: Neuropsychological, Imaging and Psychopharmalogical Perspectives*. Psychology Press.

Erlandson, D. (1993). Quality Criteria fo a Naturalistic Study. In D. Erlandson (Ed.), *Doing Naturalistic Inquiry: A Guide to Methods*. Sage Publications.

Ettorre, E., Cerra, E., Marigliano, B., Vigliotta, M., Vulcano, A., Fossati, C., … Marigliano, V. (2012). Role of cardiovascular risk factors (CRF) in the patients with mild cognitive impairment (MCI). *Archives of Gerontology and Geriatrics*, *54*(2), 330–2. http://doi.org/10.1016/j.archger.2011.04.025

Ford, J. A., Wong, G., Jones, A. P., & Steel, N. (2016). Access to primary care for socioeconomically disadvantaged older people in rural areas: a realist review. *BMJ Open*, *6*. http://doi.org/10.1136/bmjopen-2015-010652

Gamm, L., & Hutchison, L. (2003). Rural health priorities in America: where you stand depends on where you sit. *Journal of Rural Health*, *19*(3), 209–13. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/12839126

Gamm, L., Hutchison, L., Bellamy, G., & Dabney, B. J. (2002). Rural Healthy People 2010: Identifying Rural Health Priorities and Models for Practice. *Journal of Rural Health*, *18*(1), 9–14. http://doi.org/10.1111/j.1748-0361.2002.tb00869.x

Gamm, L., Hutchison, L., Bellamy, G., & Dabney, B. J. (2010). Rural Healthy People 2010: Identifying Rural Health Priorities. *The Journal of Rural Health*, 9–14.

Gamm, L., Hutchison, L., Dabney, B., & Dorsey, A. (2003). *Rural Healthy People A Companion Document to Healthy People 2010. College Station, Texas, Texas A&M University System Health Science Center, School of Rural Public Health, Southwest Rural Health Research Center* (Vol. I). College Station, Texas.

Ganguli, M., Dodge, H. H., Shen, C., & DeKosky, S. T. (2004). Mild cognitive impairment, amnestic type: an epidemiologic study. *Neurology*, *63*(1), 115–21. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/15249620

Ganguli, M., Fu, B., Snitz, B. E., Hughes, T., & Chang, C. (2013). Mild cognitive impairment Incidence and vascular risk factors in a population-based cohort. *Neurology*, *4*(80), 2112–20.

Gates, N. J., Sachdev, P. S., Fiatarone Singh, M. a, & Valenzuela, M. (2011). Cognitive and memory training in adults at risk of dementia: a systematic review. *BMC Geriatrics*, *11*(1), 55. http://doi.org/10.1186/1471-2318-11-55

Gauthier, S., Reisberg, B., Zaudig, M., Petersen, R. C., Ritchie, K., Broich, K., … Winblad, B.

(2006). Mild cognitive impairment. *Lancet*, *367*, 1262–1270.

Gillum, R. F., & Mussolino, M. E. (2003). Education, poverty, and stroke incidence in whites and blacks: The NHANES epidemiologic follow-up study. *Journal of Clinical Epidemiology*, *56*, 188–195.

Glaser, B. G., & Strauss, A. L. (1967). *The Discovery of Grounded Theory: Strategies for Qualitative Research*. Chicago: Aldine.

Gomersall, T., Astell, A., Nygård, L., Sixsmith, A., Mihailidis, A., & Hwang, A. (2015). Living with ambiguity: A metasynthesis of qualitative research on mild cognitive impairment. *The Gerontologist*, *55*(5), 892–912. http://doi.org/10.1093/geront/gnv067

Google Maps. (2016). Street Maps.

Grundman, M., Petersen, R. C., Ferris, S. H., Thomas, R. G., Aisen, P. S., Bennett, D. A., … Thal, L. J. (2004). Mild cognitive impairment can be distinguished from Alzheimer disease and normal aging for clinical trials. *Archives of Neurology*, *61*(1), 59–66. http://doi.org/10.1001/archneur.61.1.59

Haaga, J. (2004). *Demographic and Socioeconomic Change in Appalchia: Households and Families in Appalachia*.

Hall, S., Kaufman, J. S., & Ricketts, T. C. (2006). Defining urban and rural areas in U.S. epidemiologic studies. *Journal of Urban Health*, *83*(2), 162–75. http://doi.org/10.1007/s11524-005-9016-3

Halverson, J. A., Ma, L., & Harner, E. J. (2004). *An Analysis of Disparities in Health Status and Access to Health Care in the Appalachian Region - Appalachian Regional Commission. Appalachian Regional Commission*. Washington, D.C. Retrieved from http://www.arc.gov/research/researchreportdetails.asp?REPORT_ID=82

Han, A., Radel, J., McDowd, J. M., & Sabata, D. (2015). Perspectives of People with Dementia About Meaningful Activities: A Synthesis. *American Journal of Alzheimer's Disease and Other Dementias*, *98*(4). http://doi.org/10.1177/1533317515598857

Health, United States, 2012: With Special Feature on Emergency Care. (2013). Hyattsville, MD. Retrieved from http://www.cdc.gov/nchs/data/hus/hus12.pdf

Holstein, J. A., & Gubrium, J. F. (1995). *The Active Interview*. Thousand Oaks: Sage Publications.

Huberman, A. M., & Miles, M. B. (1998). Data Management and Analysis Methods. In *Collecting and Interpreting Qualitative Materials* (pp. 179–210). Thousand Oaks: Sage Publications.

Hughes, C. P., Berg, L., Daziger, W. L., Coben, L. A., & Martin, R. L. (1982). A new clinical state

for hte staging of dementia. *Journal of Psychiatry*, *140*, 566–572.

Hunsaker, A., Sarles, C. E., Rosen, D., Lingler, J. H., Johnson, M. B., Morrow, L., & Saxton, J. (2011). Exploring the reasons urban and rural-dwelling older adults participate in memory research. *American Journal of Alzheimer's Disease and Other Dementias*, *26*(3), 227–234. http://doi.org/10.1177/1533317511399569

Hunter, D., & Wilson, J. (2012). Promoting health equity. *BMJ*, *345*(aug08 1), e4881–e4881. http://doi.org/10.1136/bmj.e4881

Incalzi, R., Marra, C., Gemma, A., Capparella, O., & Carbonin, P. U. (1992). Unrecognized dementia: sociodemographic correlates. *Aging (Milano)*, *4*(4), 327–32. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/1294247

Jaffe, S. (2015). Aging in rural America. *Health Affairs*. http://doi.org/10.1377/hlthaff.2014.1372

Jeste, D. V, Palmer, B. W., Appelbaum, P. S., Golshan, S., Glorioso, D., Dunn, L. B., … Kraemer, H. C. (2007). A new brief instrument for assessing decisional capacity for clinical research. *Archives of General Psychiatry*, *64*(8), 966–974. http://doi.org/10.1001/archpsyc.64.8.966

Johansson, M. M., Marcusson, J., & Wressle, E. (2015). Cognitive impairment and its consequences in everyday life: experiences of people with mild cognitive impairment or mild dementia and their relatives. *International Psychogeriatrics / IPA*, *27*(6), 949–958. http://doi.org/10.1017/S1041610215000058

Johnson, L., Mauer, C., Jahn, D., Song, M., Wyshywaniuk, L., Hall, J. R., O'Bryant, S. E. (2013). Cognitive differences among depressed and non-depressed MCI participants: a project FRONTIER study. *International Journal of Geriatric Psychiatry*, *28*(4), 377–82. http://doi.org/10.1002/gps.3835

Jorgensen, D. (1989). *Participant Observation: A Methodology for Human Studies*. Newbury Park: Sage Publications.

Keppel, K. G., Pearcy, J. N., & Klein, R. J. (2004). *Measuring progress in Healthy People 2010. Healthy People 2010 statistical notes: from the Centers for Disease Control and Prevention/National Center for Health Statistics*. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/15446274

Kirk Wiese, L., Williams, C. L., & Tappen, R. M. (2014). Analysis of barriers to cognitive screening in rural populations in the United States. *Advances in Nursing Science*, *37*(4), 327–339. http://doi.org/10.1097/ANS.0000000000000049

Knopman, D., Donohue, J. A., & Gutterman, E. M. (2000). Patterns of care in the early stages of Alzheimer's disease: impediments to timely diagnosis. *Journal of the American Geriatrics Society*, *48*(3), 300–4. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/10733057

Kokmen, E., Ozsarfati, Y., Beard, C. M., O'Brien, P. C., & Rocca, W. A. (1996). Impact of referral bias on clinical and epidemiological studies of Alzheimer's disease. *Journal of Clinical Epidemiology*, *49*(1), 79–83. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/8598515

Kryscio, R. J., Schmitt, F. A., Salazar, J. C., Mendiondo, M. S., & Markesbery, W. R. (2006). Risk factors for transitions from normal to mild cognitive impairment and dementia. *Neurology*, *66*(6), 828–32.

Latest Facts & Figures Report. (2013). Retrieved May 15, 2013, from http://www.alz.org/alzheimers_disease_facts_and_figures.asp#prevalence

Lingler, J. (2014). No Title. Pittsburgh.

Lingler, J., Nightingale, M. C., Erlen, J. a, Kane, A. L., Reynolds, C. F., Schulz, R., & DeKosky, S. T. (2006). Making sense of mild cognitive impairment: a qualitative exploration of the patient's experience. *The Gerontologist*, *46*(6), 791–800. http://doi.org/10.1093/geront/46.6.791

Lofland, J. (1971). *Analzying Social Settings: A Guide to Qualitative Observation and Analysis*. Belmont: Wadsworth Publishing Co.

Long, K., & Weinert, C. (1999). Rural nursing: developing the theory base. 1989. *Scholarly Inquiry for Nursing Practice*, *13*(3), 257-69–4. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/10744513

Lopez, O. L., Becker, J. T., Klunk, W., Saxton, J., Hamilton, R. L., Kaufer, D. I., … DeKosky, S. T. (2000). Research evaluation and diagnosis of probable Alzheimer's disease over the last two decades: I. *Neurology*, *55*(12), 1854–1862. http://doi.org/10.1212/WNL.55.12.1854

Lopez, O. L., Jagust, W. J., DeKosky, S. T., Becker, J. T., Fitzpatrick, A., Dulberg, C., … Kuller, L. H. (2003). Prevalence and classification of mild cognitive impairment in the Cardiovascular Health Study Cognition Study: part 1. *Archives of Neurology*, *60*(10), 1385–9. http://doi.org/10.1001/archneur.60.10.1385

Malinowski, B. (1978). Argonauts of the Western Pacific. In P. J. Pelto & G. H. Pelto (Eds.), *Anthropological Research: The Structure of Inquiry* (p. 68). Cambridge: Cambridge University Press.

Manly, J. J., Jacobs, D. M., Touradji, P., Small, S. a., & Stern, Y. (2002). Reading level attenuates differences in neuropsychological test performance between African American and White elders. *Journal of the International Neuropsychological Society*, *8*(3), 341–348. http://doi.org/10.1017/S1355617702813157

Manly, J. J., Schupf, N., Tang, M.-X., & Stern, Y. (2005). Cognitive decline and literacy among ethnically diverse elders. *Journal of Geriatric Psychiatry and Neurology*, *18*(4), 213–7.

http://doi.org/10.1177/0891988705281868

Manusov, E. (2009). *The Rural Health Care Dilemma*. (S. B. Publishing, Ed.). New York.

Mattos, M., Snitz, B., Lingler, J., Burke, L., Novosel, L., & Sereika, S. (2016, Epub ahead of print). Mild Cognitive Impairment in Older, Appalachian Adults. *Journal of Rural Health*. doi:10.1111/jrh.12189

McKhann, G., Drachman, D., Folstein, M., Katzman, R., Price, D., & Stadlan, E. M. (1984). Clinical diagnosis of Alzheimer's disease: report of the NINCDS-ADRDA Work Group under the auspices of Department of Health and Human Services Task Force on Alzheimer's Disease. *Neurology*, *34*(7), 939–944. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/6610841

Medically Underserved Areas/Populations. (1995). Retrieved April 3, 2013, from http://www.hrsa.gov/shortage/mua/index.html

Miles, M. B., & Huberman, A. M. (1994). *Qualitative Data Analysis: An Expanded Sourcebook* (second ed.). Thousand Oaks: Sage Publications.

Mitchell, A. J., & Shiri-Feshki, M. (2008). Temporal trends in the long term risk of progression of mild cognitive impairment: a pooled analysis. *Journal of Neurology, Neurosurgery, and Psychiatry*, *79*(12), 1386–91. http://doi.org/10.1136/jnnp.2007.142679

Mitchell, A. J., & Shiri-Feshki, M. (2009). Rate of progression of mild cognitive impairment to dementia - Meta-analysis of 41 robust inception cohort studies. *Acta Psychiatrica Scandinavica*, *119*(4), 252–265. http://doi.org/10.1111/j.1600-0447.2008.01326.x

Morgan, D., Semchuk, K., Stewart, N., & D'Arcy, C. (2002). Rural families caring for a relative with dementia: Barriers to use of formal services. *Social Science and Medicine*, *55*(7), 1129–1142. http://doi.org/10.1016/S0277-9536(01)00255-6

Morgan, G. H., Garand, L. I., & Lingler, J. H. (2012). Self-initiated health behaviors following a diagnosis of mild cognitive impairment. *Research in Gerontological Nursing*, *5*(2), 94–100. http://doi.org/10.3928/19404921-20110831-02

Morris, J. (1993). The Clinical Dementia Rating (CDR): Current version and scoring rules. *Neurology*, *43*(11), 2412–2414.

Morse, J. (1989). *Qualitative Nursing Research: A Contemporary Dialogue*. Rockville: Aspen Publications.

O'Bryant, S. E., Waring, S. C., Cullum, C. M., Hall, J., Lacritz, L., Massman, P. J., Doody, R. (2008). Staging dementia using Clinical Dementia Rating Scale Sum of Boxes scores: a Texas Alzheimer's research consortium study. *Archives of Neurology*, *65*(8), 1091–5.

http://doi.org/10.1001/archneur.65.8.1091

Pearson, T., & Lewis, C. (1998). Rural epidemiology: insights from a rural population laboratory. *American Journal of Epidemiology*, *148*(10), 949–57. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/9829866

Pelto, P. J., & Pelto, G. H. (1978). *Anthropological Research: The Structure of Inquiry*. Cambridge: Cambridge University Press.

Petersen, R. (2010). Prevalence of mild cognitive impairment is higher in men The Mayo Clinic Study of Aging. *Neurology*, *75*(10), 889–897.

Petersen, R. C. (2004). Mild cognitive impairment as a diagnostic entity. *Journal of Internal Medicine*, *256*(3), 183–94. http://doi.org/10.1111/j.1365-2796.2004.01388.x

Petersen, R., Caracciolo, B., Brayne, C., Gauthier, S., Jelic, V., & Fratiglioni, L. (2014). Mild cognitive impairment: a concept in evolution. *Journal of Internal Medicine*, *275*(3), 214–28. http://doi.org/10.1111/joim.12190

Petersen, R., Doody, R., Kurz, A., Mohs, R., Morris, J., Rabins, P., … Wingblad, B. (2001). Current Concepts in Mild Cognitive Impairment. *Arch Neurol*, *58*, 1985–1992.

Petersen, R., Smith, G., Waring, S., Ivnik, R., Tangalos, E., & Kokmen, E. (1999). Mild Cognitive Impairment: Clinical Characterization and Outcome. *Arch Neurol*, *56*(3), 303–309.

Pollard, K., & Jacobsen, L. (2015). *The Appalachian Region: A Data Overview from the 2009-2013 American Community Survey*.

Reitan, R. M. (1958). Validity of the Trail-Making Tests as an indication of organic brain damage. *Perceptual and Motor Skills*, *8*, 271–276.

Ritchie, K., Artero, S., & Touchon, J. (2001). Classification criteria for mild cognitive impairment: a population-based validation study. *Neurology*, *56*(1), 37–42. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/11148233

Rodríguez-Sánchez, E., Mora-Simón, S., Patino-Alonso, M. C., García-García, R., Escribano-Hernández, A., García-Ortiz, L., … Gómez-Marcos, M. a. (2011). Prevalence of cognitive impairment in individuals aged over 65 in an urban area: DERIVA study. *BMC Neurology*, *11*(1), 147. http://doi.org/10.1186/1471-2377-11-147

Ross, G. W., Abbott, R. D., Petrovitch, H., Masaki, K. H., Murdaugh, C., Trockman, C., … White, L. R. (1997). Frequency and characteristics of silent dementia among elderly Japanese-American men. The Honolulu-Asia Aging Study. *JAMA*, *277*(10), 800–5. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/9052709

Rural Urban Commuting Area Codes Data. (n.d.). Retrieved July 24, 2013, from http://depts.washington.edu/uwruca/ruca-codes.php

Sachdev, P. S., Lipnicki, D. M., Crawford, J., Reppermund, S., Kochan, N. a, Trollor, J. N., … Brodaty, H. (2012). Risk profiles of subtypes of mild cognitive impairment: the sydney memory and ageing study. *Journal of the American Geriatrics Society*, *60*(1), 24–33. http://doi.org/10.1111/j.1532-5415.2011.03774.x

Sandelowski, M. (1986). The problem of rigor in qualitative research. *Adv Nurs Sci*, *8*(3), 27–37.

Sandelowski, M. (2000). Focus on Research Methods: Whatever Happened to Qualitative Description? *Research in Nursing & Health*, *23*, 334–340.

Sandelowski, M. (2010). What's in a name? Qualitative description revisited. *Research in Nursing & Health*, *33*(1), 77–84. http://doi.org/10.1002/nur.20362

Schulz, A., & Northridge, M. E. (2004a). Social determinants of health: implications for environmental health promotion. *Health Education & Behavior*, *31*(4), 455–71. http://doi.org/10.1177/1090198104265598

Schulz, A., & Northridge, M. E. (2004b). Social determinants of health: implications for environmental health promotion. *Health Education & Behavior*, *31*(4), 455–71. http://doi.org/10.1177/1090198104265598

Schulz, A., & Northridge, M. E. (2004c). Social determinants of health: implications for environmental health promotion. *Health Education & Behavior*, *31*(4), 455–71. http://doi.org/10.1177/1090198104265598

Shirk, S. D., Mitchell, M. B., Shaughnessy, L. W., Sherman, J. C., Locascio, J. J., Weintraub, S., & Atri, A. (2011). A web-based normative calculator for the uniform data set (UDS) neuropsychological test battery. *Alzheimer's Research & Therapy*, *3*(6), 32. http://doi.org/10.1186/alzrt94

Sperling, R. A., Aisen, P. S., Beckett, L. A., Bennett, D. A., Craft, S., Fagan, A. M., … Phelps, C. H. (2011). Toward defining the preclinical stages of Alzheimer's disease: Recommendations from the National Institute on Aging and the Alzheimer's Association workgroup. *Alzheimer's & Dementia*, *7*(3), 1–13. http://doi.org/10.1016/j.jalz.2011.03.005

Spira, A. P., Rebok, G. W., Stone, K. L., Kramer, J. H., & Yaffe, K. (2012). Depressive symptoms in oldest-old women: risk of mild cognitive impairment and dementia. *The American Journal of Geriatric Psychiatry*, *20*(12), 1006–15. http://doi.org/10.1097/JGP.0b013e318235b611

Sternberg, S. A., Wolfson, C., & Baumgarten, M. (2000). Undetected dementia in community-dwelling older people: the Canadian Study of Health and Aging. *Journal of the American Geriatrics Society*, *48*(11), 1430–4. Retrieved from

http://www.ncbi.nlm.nih.gov/pubmed/11083319

Teel, C. (2004). Rural practitioners' experiences in dementia diagnosis and treatment. *Aging & Mental Health*, *8*(5), 422–9. http://doi.org/10.1080/13607860410001725018

Teel, C., & Carson, P. (2003). Family Experiences in the Journey Through Dementia Diagnosis and Care. *Journal Of Family Nursing*, *9*(1), 38–58. http://doi.org/10.1177/1074840702239490

The Appalachian Region. (2013). Retrieved July 26, 2013, from http://www.arc.gov/appalachian_region/TheAppalachianRegion.asp

The Vision, Mission, and Goals of Healthy People 2020. (2011). Retrieved from http://www.healthypeople.gov/2020/

US Census Bureau Geography. (n.d.). *2010 Census Urban and Rural Classification and Urban Area Criteria*. Retrieved from https://www.census.gov/geo/reference/ua/urban-rural-2010.html

US Department of Agriculture Economic Research Service. (2013a). Rural Urban Commuting Area Codes Data. Retrieved September 27, 2013, from http://depts.washington.edu/uwruca/ruca-demographics.php

US Department of Agriculture Economic Research Service. (2013b). USDA Economic Research Service - Rural Classifications. Retrieved from http://www.ers.usda.gov/topics/rural-economy-population/rural-classifications.aspx#.UVnPIqWLFjA

US Department of Commerce. (2013). QuickFacts: Locate a county by place name. Retrieved April 24, 2015, from http://quickfacts.census.gov/cgi-bin/qfd/lookup

US Department of Health & Human Services, F. O. of R. H. P. (2015). Defining Rural Population. Retrieved October 1, 2016, from http://www.hrsa.gov/ruralhealth/aboutus/definition.html

Wechsler, D. (1981). *Wechsler Adult Intelligence Scale-Revised Manual*. New York: The Psychological Corportation.

Wechsler, D. (1987). *Wechsler Memory Scale- Revised Manual*. San Antonia, TX: The Psychological Corportation.

Wechsler, D. (1997). *Wechsler Adult Intelligence Scale- Third Edition*. New York: The Psychological Corportation.

Winblad, B., Palmer, K., Kivipelto, M., Jelic, V., & Fratiglioni, L. (2004). Mild cognitive impairment – beyond controversies , towards a consensus : report of the International Working Group on Mild Cognitive Impairment. *Journal of Internal Medicine*, *256*, 240–246.

Winters, C., & Lee, H. (Eds.). (2010). *Rural Nursing: Concepts, Theories and Practice* (3rd ed.). New York: Springer Publishing Company.

Yesavage, J., Brink, T., Rose, T., Lum, O., Huang, V., Adey, M., & Leirer, V. O. (1983). Development and validation of a geriatric depression screening scale: a preliminary report. *Journal of Psychiatric Research*, *17*(1), 37–49. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/7183759