BIOPSYCHOSOCIAL FACTORS ASSOCIATED WITH INTEREST IN AMYLOID IMAGING FOR ALZHEIMER'S DISEASE

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BIOPSYCHOSOCIAL FACTORS ASSOCIATED WITH INTEREST IN AMYLOID IMAGING FOR ALZHEIMER'S DISEASE

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Early detection of Alzheimer's disease (AD) allows patients and families extended time for care planning, often facilitated by social workers. Detection methods are continually improving as research efforts focus on creating more reliable and valid diagnostic tests across dementia types. Imaging amyloid in the brain, a hallmark of AD, may allow for the detection of AD pathology before memory symptoms are noticeable, or at the earliest stages of illness. Although social workers provide critical support to patients and families throughout the diagnostic process and the progression of illness, social work research has yet to substantially address dementia diagnostic technologies and their potential to impact care management approaches.

This dissertation explores what biopsychosocial factors, including demographic, cognition, health, and family-related factors, are associated with amyloid imaging (AI) research interest for AD, for those with varied levels of cognitive impairment, as well as for individuals with dementia (IWDs). Applying a biopsychosocial framework to the investigation of who seeks to use such technologies, and – possibly more importantly - who misses out, brings a social work perspective to this research area. Using a secondary data sample extracted from registry data of an Alzheimer Disease Center, multinomial logistic regression was used to model biopsychosocial factors associated with differing levels of AI research interest and participation.

For the full sample, younger age, better cognition, and experience of cognitive diagnostic change were related to both AI interest and participation. For IWDs, absence of medical comorbidity and having a spousal or partner care relationship were associated with AI interest and participation. Participation in diagnostic disclosure, and the receipt of extended social work support, points to the critical role social workers may play in facilitating amyloid imaging research participation. Older age groups and those with more impaired cognition may benefit from tailored counseling approaches that address concerns and needs. For IWDs, medical comorbidity may create a barrier to seeking AI, while the significance of spousal and partner care relationships intimates that these care partners have more time to devote to AI. These findings support social work roles in multidisciplinary dementia care teams using AI, and enrich the content of AI counseling protocols by identifying participant-specific factors that impact AI participation.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

PREFACE

Dedicated to my dad, Don Egner. I know this would have made your day!

Thank you to my committee, Danny Rosen, Jennifer Lingler, Ray Engel, and Fengyan Tang, for helping me see this work through. Your thoughtful insights across all aspects of this work were truly appreciated and valued. Thank you for hanging in there with me.

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To my family, Brady, Thomas, and Benjamin. Thank you for all your support and love. Now we get to embark on a true adventure together!

1.0 INTRODUCTION

James Watson, who won a Nobel Prize for discovering the structure of DNA, agreed to be the very first person to complete gene sequencing. He had just one condition: "I didn't want to know its prediction for Alzheimer's. There's nothing you can do to prevent it, so why would you want to know?"

-Morning Edition, National Public Radio, 2012

1.1 PURPOSE OF THE STUDY

We are experiencing a dynamic time in research on Alzheimer's disease (AD) - a progressive and devastating illness for which currently no cure exists. Diagnostic methods for dementia, in particular, are improving as research efforts focus on creating more reliable and valid diagnostic tests across dementia types. One such method uses positron emission tomography (PET) and an intravenous compound to image amyloid in the brain – a hallmark of AD. This type of imaging may be able to detect amyloid in the brain before memory symptoms are noticeable or at the earliest stages of illness. When and how to counsel individuals on the use of such testing has only just begun to be considered, and have focused on their use in research settings (Lingler & Klunk, 2013; Roberts, Dunn, & Rabinovici, 2013). Most work has examined AI testing through a medical model lens. Just one pilot study has examined patient and family views regarding the AI

testing counseling approaches, as well as the personal utility attributed to such testing (Lingler et al., 2015).

Additionally, although social workers provide a substantial amount of support to patients and families throughout the diagnostic process and the progression of illness - and are especially intrinsic to the care process given the current limitations of medical treatments - social work research has yet to substantially address dementia diagnostic technologies and their potential impact on care management approaches. Applying a biopsychosocial framework to the investigation of who seeks to use such technologies, and – possibly more importantly - who misses out, brings a social work perspective to this research area and informs social work practice with adults facing cognitive impairment and their families. In particular, acknowledging that variations in participant interest for amyloid imaging exist imports the social work tenet of self-determination in care decision-making into these changing and emerging care protocols for dementia.

As Dr. Watson's opening quote implies, interest in biomarker testing likely differs across individuals, and for varying reasons, which are not understood. This dissertation explores what factors are associated with interest in amyloid imaging research for Alzheimer's disease; for those with varied levels of cognitive impairment, as well as for individuals diagnosed with dementia. Individuals with comprehensive cognitive assessment data from standardized measures comprise the sample and include a subsample of individuals with dementia, those who were the initial focus of amyloid imaging research. Using a secondary data sample extracted from the University of Pittsburgh Alzheimer Disease Research Center (ADRC) database, multinomial logistic regression was used to model biopsychosocial factors associated with differing levels of interest in AI research participation. A second set of binomial regression

modeling examines biopsychosocial factors associated with participation in AI research. The following objectives are the focus of this dissertation:

- Among all ADRC participants, examine factors (demographic, cognition, health, dementia family history) that are associated with level of interest in brain imaging research;
- Among all ADRC participants, examine factors (demographic, cognition, health, dementia family history) that are associated with participation in amyloid imaging;
- Among the ADRC participants diagnosed with dementia, examine factors (demographic, cognition, health, dementia family history, and care partner relationship) that are associated with level of interest in brain imaging research; and
- Among the ADRC participants diagnosed with dementia, examine factors (demographic, cognition, health, dementia family history, and care partner relationship) that are associated with participation in amyloid imaging research.

Differing levels of interest in AI were captured using the following categories: 1) AI participants (Participators); 2) individuals who declined AI participation but indicated interest in imaging studies (Avoiders); and 3) individuals who indicated they did not want to be contacted for imaging studies (Refusers). Refusers and Avoiders were aggregated to one group, Non-Participators, and compared to Participators. For the full ADRC sample, the following factors were included in analysis and compared across AI interest groups and AI Participator/Non-Participator groups: 1) demographic characteristics (age, race, gender, and education); 2) neurocognitive status (ADRC diagnosis, Mini-Mental State Exam Score, change in ADRC diagnosis); 3) health (presence of psychiatric diagnosis, presence of physical health

comorbidity); 4) family history of dementia (participant report of immediate relatives with dementia). For ADRC patient with dementia, the following factors were examined: 1) demographic characteristics (age, race, gender, and education); 2) neurocognitive status (Mini-Mental State Exam Score, age at onset of cognitive symptoms); 3) health (presence of psychiatric diagnosis, presence of physical health comorbidity); 4) family history of dementia (participant report of immediate relatives with dementia); and 5) care partner relationship. This chapter presents a rationale for investigating participation in amyloid imaging, and its relevance to social work practice.

1.2 BACKGROUND AND SIGNIFICANCE

Access to amyloid testing has been mainly limited to research settings where, per protocol and due to concerns about lack of clinical significance of the results gained from findings, results have not been provided to participants. However, investigating AI interest within this population is an important starting point because this group represents the early adopters, those that will be the first to be approached about the potential for receiving results, as well as those most likely to express interest in results. A recent study comparing interest in cognition-focused research results disclosure between a sample of cognitively intact individuals who had been registry participants in an Alzheimer Disease Center (ADC) and a general population sample reported that the ADC sample expressed significantly more interest in disclosure than the general population, even when the risks and benefits of disclosure were enumerated and discussed (Gooblar, Roe, Selsor, Gabel, & Morris, 2015). The ADRC registry additionally provides a substantially-sized sample with a range of cognitive diagnoses and a dataset using uniform,

standardized measures that are not readily available from clinical settings. This work lays initial groundwork for understanding patient acceptance of amyloid imaging in clinical practice settings, which has not been examined to date.

While literature examining participation in genetic susceptibility testing for AD (e.g. Green et al., 2009; Roberts, 2000; Roberts et al., 2004) and memory screening and cognitive evaluation (e.g. Boustani et al., 2011; Werner & Heinik, 2004) provide a basis for understanding how demographics, cognition, and health relate to AI research interest, no studies have quantitatively explored whether there are biopsychosocial factors that may influence interest in neuroimaging. Additionally, most studies that explore factors impacting interest in genetic or cognitive testing for AD rely on the presentation of hypothetical scenarios to study participants, rather than examine true uptake of such diagnostic tools. As later described, interest reported in relation to hypothetical scenarios may not accurately reflect the percentages of actual utilization, or the factors associated with such participation. This dissertation will examine what demographic, cognition-related, health-related, and family-related factors, are associated with real participation in AI, rather than hypothetical use.

Also differing from previous studies, three levels of interest in brain imaging will be modeled using multinomial logistic regression. Previous studies have only reported findings using a dichotomous outcome variable, as in the genetic testing and memory screening literature. These three levels of interest will help to tease out whether differences do exist between those who express interest in neuroimaging (paralleling intent or willingness to test studies) and actual participation.

Overall, the increasing prevalence of this progressive and terminal illness warrants the need for an examination of diagnostic tools that may determine whether AD hallmark pathology

can be detected in the brain. Early detection means individuals have an opportunity to: 1) make decisions about care and service needs with support from family and care providers; 2) enroll in medication and other clinical trials; 3) create financial and health care advance directives; 4) consider safety issues in advance, such as driving; and 5) better allow for determining whether symptomatology is caused by a reversible process, such as depression or thyroid issues (Alzheimer's Association, 2011). Social workers offer integral coordination and support across these domains of care. Additionally, as more effective and preventative treatments develop, social workers may aid in the process of identifying those who will most benefit from detection technologies, including amyloid imaging.

Recommendations for who should complete AI have primarily focused on clinical presentation as the primary consideration and several research groups have presented thoughtful and varying considerations of who should be given results from amyloid testing, and what information should be presented (e.g. Grill, Johnson, & Burns, 2013; Lingler & Klunk, 2013; Roberts, Dunn, & Rabinovici, 2013). They additionally acknowledge that the information derived from amyloid testing, including its predictive value, or information regarding the risk of development of AD, remains sketchy (Roberts, Dunn, & Rabinovici, 2013). Clinicians involved in studies using amyloid imaging voice varied opinions about providing test results, though there is general agreement that patients need to have say in whether test results are revealed (Shulman, Harkings, Green & Karlawish, 2013). It is important to note that clinical recommendations are only just emerging regarding the diagnostic presentations that would warrant amyloid imaging (Johnson et al., 2013) and for disclosing AI results (Lingler, Roberts, Schulz & Klunk, 2012) which remain to be influenced by scientific additions to our understanding of the implications of a positive amyloid finding. Therefore the question of which participants actually consent to

uptake is important to tease out, as it provides an understanding of whether those individuals deemed to benefit from AI are in fact pursuing, and receiving, access.

As Dr. Watson's quote implies above, interest in biomarker testing likely differs across patients and may be influenced by many factors. Understanding who participates in diagnostic testing, such as AI, can help researchers better understand the decision-making process that individuals tackle in response to the opportunity for diagnostic testing. This process may be driven by personal characteristics, such as psychological status, perceptions surrounding family history, and cognition and health factors. Taking the impact of these factors into account will aid in tailoring social work-inclusive counseling protocols to address the concerns of individuals who express hesitancy regarding AI participation. As social workers play critical roles in diagnostic disclosure and care management post diagnosis, their role facilitating in AI counseling should be a point of key consideration.

1.3 RESEARCH QUESTIONS AND HYPOTHESES

This study examined the factors associated with two domains of interaction with amyloid imaging: interest and participation of individuals who have completed a cognitive assessment for memory impairment. Each domain was examined among a sample of ADRC participants, and again among ADRC participants diagnosed with dementia. The following research questions and hypotheses were the focus of this dissertation:

Q.1 What factors are associated with level of interest in brain imaging among ADRC participants?

H.1 Individuals who express greater interest in participation in brain imaging research: 1) are younger; 2) have less cognitive impairment (via ADRC diagnosis and/or Mini-Mental State Exam score); 3) have experienced a change in cognition diagnosis; 4) have more physical health comorbidity; 5) have a psychiatric diagnosis; and 6) have a family history of dementia; when controlling for sex, race and education level.

Q.2 What factors are associated with participation in amyloid imaging research among ADRC participants?

H.2 Individuals who participate in amyloid imaging research: 1) are younger; 2) have less cognitive impairment (via ADRC diagnosis and/or Mini-Mental State Exam score); 3) have experienced a change in cognition diagnosis; 4) have more physical health comorbidity; 5) have a psychiatric diagnosis; and 6) have a family history of dementia; when controlling for sex, race and education level.

Q.3 What factors are associated with level of interest in brain imaging research among ADRC participants diagnosed with dementia?

H.3 Individuals with dementia who express greater interest in brain imaging research: 1) are younger; 2) have less cognitive impairment (Mini-Mental State Exam score); 4) have more physical health comorbidity; 5) have a psychiatric diagnosis; 6) have a family history of dementia; and 7) have spousal/partner care support; when controlling for sex, race and education level.

Q.4 What factors are associated with participation in amyloid imaging research among ADRC participants diagnosed with dementia?

H.4 Individuals with dementia who participate in amyloid imaging research: 1) are younger; 2) have less cognitive impairment (Mini-Mental State Exam score); 4) have more physical health comorbidity; 5) have a psychiatric diagnosis; 6) have a family history of dementia; and 7) have a spousal/partner care support; when controlling for sex, race and education level.

1.4 SIGNIFICANCE TO SOCIAL WORK PRACTICE AND RESEARCH

Gaining an understanding of who agrees to diagnostic testing lays the groundwork for identifying the rationale behind interest in biomarker testing for AD and opens avenues for targeted, social work-inclusive interventions that may address the concerns of those pursuing AI, as well as those who opt out of its use. It informs the current multidisciplinary approach to assessment, diagnosis, and treatment planning in which social work is an integral part of the care team. The current investigation is the first known social work-based study to explore uptake of amyloid imaging. Examining the use of such diagnostic testing from a social work perspective grounds this research in a social work model of care and promotes social work as a key leader in the advancement of this research.

Many of the factors explored here that likely influence patient and family decision-making regarding diagnostic testing also comprise the components of a social work assessment, follow the biopsychosocial model of care, and fit well within the established frameworks for

diagnostic disclosure protocols and genetic counseling procedures. Social workers already play a significant role in AD care, across the domains of assessment, diagnosis, and care planning. Within Alzheimer Disease Research Centers, social workers partner with physicians in delivering the diagnosis, supporting the patient and family through the process of understanding the potential implications of the diagnosis, and linking individuals to appropriate services. Given the limitations of the current anti-dementia treatments on the market, psychosocial support and service planning provided by social workers may be the most critical points of care post diagnosis. Therefore, the social work profession naturally extends itself to involvement in the protocol development, assessment and utilization of pre and post counseling for dementia biomarker testing, as well as follow-up care.

Shifting care models, including partnerships between primary care practices and memory clinics (Callahan et al., 2011) and the adoption of the medical home model for dementia care within these partnerships (Boustani et al., 2005; Callahan et al., 2006; French et al., 2014) all apply a patient-centered, collaborative care approach to dementia in a primary care setting. The objective of this model for dementia care is to improve screening, diagnosis and treatment in the primary care setting, with support from a multidisciplinary memory care staff, inclusive of social workers. Although current recommendations advise that amyloid imaging is not indicated in the routine assessment process that a primary care provider would employ (Geldmacher & Kerwin, 2013), this emerging dementia medical model is a fitting home for AD biomarker testing, including amyloid imaging, with pre- and post-counseling protocols melded into existing processes for assessment, diagnosis, and follow-up.

The number of individuals served by these existing and emerging care models is likely on the rise. Diagnostic advances may mean that more individuals will be diagnosed in the earliest

stages of illness and have the capacity to participate in care planning and counseling. These advances are also expected to lead to a paradigm shift in social work and a movement from a focus on supporting the family through the illness process to engaging the person pursuing such testing, and their family, in care decisions. Social work roles will range from supporting the individual and their family through navigating care services, to counseling individuals coping with the diagnosis of a terminal illness, and framing these discussions within an understanding of emerging cognitive change. Most noteworthy is the additional counseling support that will be needed for clients and families to make decisions about participation in early diagnostic testing and understanding the ramifications of positive, negative, or inconclusive findings. This shift in focus coincides with a greater practice focus on understanding the experience of the person with cognitive impairment, in part by adopting a social model of care in which supporting the unique experience of the individual is a central theme. It also upholds the general movement towards a multidisciplinary approach to dementia care as the practice ideal, in which social workers collaborate with other health care professionals, including neurologists, psychiatrists, and nurse practitioners around assessment, diagnosis, treatment, counseling, and referral.

Appropriate use criteria for AI (Johnson et al., 2013) identifies who may clinically benefit from AI, while exploring the psychosocial and health factors related to AI interest identifies those individuals that view a personal utility to be gained from AI, as well as those who may be opting out of access to AI testing. The inclusion of psychosocial factors in this dissertation additionally offers a more holistic view – from the social work perspective – of the person considering AI testing, identifying aspects of the individual that exist beyond their diagnostic status. Exploring the psychosocial, cognition and health-related factors that are associated with AI participation may inform social work-inclusive counseling protocols that

address the concerns of individuals who have varying levels of interest in such testing and who may need additional support in gaining access to such testing.

Applying the above multidisciplinary approach to AI in a clinical practice setting may be happening soon. A multi-site study evaluating whether the clinical use of amyloid imaging improves health outcomes will begin in 2016, and aims to recruit over 18,000 Medicare patients via referrals from dementia specialist physicians (Zakaid, 2015). This will also be the first study to examine whether care coordination and counseling outcomes differ in relation to AI use and is ripe for a social work role in providing care management and support following results disclosure. Measured study outcomes include counseling for safety, medical and financial decision-making, advance directives, and community service referral (IDEAS Study, 2015).

The implications of diagnostic testing are numerous for social work roles and social work research to provide evidence for best-practice approaches. It must be remembered that social work has had a long history of involvement in dementia care research and practice. Psychosocial interventions for dementia have been an ongoing focus within social work research. Work initially focused on the dementia caregiver (Pinquart & Sörensen, 2006) and extended our understanding of the importance of supporting the experience of the person with dementia (Cotrell & Schulz, 1993). Dementia-related biomarker research is creating a new frontier for practice and research. Ensuring the inclusion of a social work perspective is paramount, as it will advance our research and practice, but most importantly better serve individuals and families who are facing cognitive impairment.

There is much potential for access and growth of amyloid imaging, where results are provided, and social work support needs to surround that process, informed by social work research. In addition to use in clinical settings, Centers for Medicare and Medicaid Services

(CMS) currently covers scans completed in clinical trials where the impact on health outcomes or treatment options is of interest. This offers many opportunities for social work-inclusive research testing psychoeducational interventions that address outcomes such as emotional response to testing, health behavior change, adherence to service referrals, and safety measures, all informing best practices. As noted previously, a large CMS-funded study, with plans to recruit over 18,000 participants, will examine use of AI in clinical settings, and test its impact on outcomes, that include counseling for safety, medical and financial decision-making, advance directives, and community service referral, as well as related follow-through (IDEAS Study, 2015). All would benefit from social workers embedded in physician practices that ensure these critical outcomes are met. In fact, whether CMS decides to approve reimbursement for AI in the clinical setting hinges on this study.

Finally, there is much potential for the future expansion of AI to asymptomatic individuals. In fact, work is already underway to understand how people who are cognitively intact but approached for, or seeking, AI testing should be counseled (Harkins et al., 2015; Karlawish et al., 2013). Preventive clinical trials targeting asymptomatic individuals currently use screening protocols which include AI testing to determine eligibility for study participation. Individuals may receive AI results *de facto*, when deemed eligible (positive) or ineligible (negative). The counseling included in these trials is an important consideration. A more critical concern is gauging and supporting patient and family emotional response to testing and the receipt of results. While to date no research helps us understand the psychological effects of disclosure, there is a greater risk of suicide in early stages of AD, when insight is most preserved, rather than later stages (Lim, Rubin, Coats, & Morris, 2005). However, counseling protocols developed for AD-related genetic susceptibility testing point to the potential for providing

information on AD risk without creating psychological harm (Green et al., 2009). All points to need for social workers to be advocating for and pursuing roles in this area.

2.0 REVIEW OF THE LITERATURE

This chapter provides a brief summary of Alzheimer's disease (AD), including, prevalence, risk factors, and estimated costs to society, all noting the urgency for clinical and social work research aimed at improving the diagnostic and care management processes for Alzheimer's disease. Next, current standards for diagnosis, treatment, and care management for cognitive impairment are summarized. This sets the stage for exploring how current social-work inclusive care protocols may be impacted by dementia detection advances, including a better understanding of the factors that impact patient uptake of such detection tools, in this case amyloid imaging. A brief summary of AI developments and their addition to diagnostic protocols are reviewed, setting the stage for conceptualizing and modeling AI research participation from a social work perspective using a biopsychosocial framework. The biopsychosocial domains under investigation and their potential for a significant relationship with AI interest and participation are reviewed in the context of research on preferences for cognitive assessment and screening, as well as AD susceptibility testing. This review provides a framework for characterizing individuals who express a preference for amyloid imaging and those who may be missing out on the potential benefits derived from AD diagnostic testing. Advances in diagnostic technology for AD are moving forward. An overarching aim of this dissertation was to both maintain and create space for social work research and practice in this arena.

2.1 PREVALENCE AND COSTS OF ALZHEIMER'S DISEASE

Dementia is a progressive and fatal brain disease that affects almost 14% of individuals over age 70 in the United States. Plassman et al. (2007). Approximately 5.3 million individuals in the U.S. have Alzheimer's disease, the most common form of dementia (L. E. Hebert, Weuve, Scherr, & Evans, 2013), accounting for 60-80% of dementia cases (Thies & Bleiler, 2011). Dementia causes a general decline in cognitive abilities that interfere with daily life, including remembering new information, problem solving, thinking abstractly, and making sound judgments (Alzheimer's Association, 2015).

Age is a key risk factor for AD. While approximately 11% of individuals over age 65 has AD, prevalence dramatically increases to almost 1 in 3 (32%) for those 85 years and older (Alzheimer's Association, 2015; L. E. Hebert et al., 2013). As life expectancies increase and the baby boom generation ages, the number of individuals with AD is expected to surge. By 2025 approximately 7.1 million older adults (65 years and older) will be affected, a growth of 40 percent from the 2015 estimate (Alzheimer's Association, 2015; L. E. Hebert et al., 2013). Mirroring an increase in prevalence, payments for health care, long-term care, and hospice for individuals with dementia are projected to grow from $226 billion in 2015 to more than $1 trillion in 2050 (Alzheimer's Association, 2015). Medicare and Medicaid shoulder the brunt of these costs, at a combined 68% (Alzheimer's Association, 2015).

Improved diagnostic and treatment protocols might positively impact the lived experience of AD for both patients and caregivers. Unpaid caregivers, predominantly family members, experience significant burden, clocking in an estimated 17.9 billion hours of unpaid care valued at more than $217 billion in 2014 (Alzheimer's Association, 2015). They report high levels of stress and depression, as their care roles adversely impact health, employment, and financial

status (Alzheimer's Association, 2015). Though less studied, and in addition to the progressive loss of cognitive and functional abilities, individuals diagnosed with dementia clearly experience negative outcomes from the disease, such as anxiety, depression, and psychosis (Lyketsos et al., 2002; Steinberg et al., 2003). Individuals with dementia also report experiencing a loss of autonomy and security (Steeman, De Casterlé, Godderis, & Grypdonck, 2006). Creating a diagnostic process that is more responsive to patient conditions and needs may improve patient and family outcomes following diagnosis. The chronic care model (Bodenheimer, Wagner, & Grumbach, 2002), and efforts to apply the patient-centered medical home model to dementia care (Callahan et al., 2011), have been proposed as viable approaches to address both the medical, emotional and social needs of the patient-family dyad seeking diagnosis and care, as well as reduce care costs (Callahan et al., 2006).

2.2 DIAGNOSIS AND TREATMENT OF ALZHEIMER'S DISEASE

New guidelines of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) for diagnosing cognitive impairment, including Alzheimer's disease, have renamed the categories for cognitive impairment to major and mild neurocognitive disorder (NCD) (American Psychiatric Association, 2013). The DSM-5 rubric for a diagnosis of major neurocognitive disorder describes symptoms that include a significant decline in memory or another cognitive ability (e.g. language, learning, or executive function) that interfere with independently carrying out one or more activities of daily living. Mild neurocognitive disorder is defined by a decline in cognitive ability that does not obstruct completion of daily activities, though it may mean that a certain activity requires more mental attention. Alzheimer's disease, considered an etiologic

subtype of both major and mild NCD, then follows as a diagnosis. AD would be differentiated from other types of dementias based on disease course and cognitive presentation, behavioral and/or psychological symptoms, known risk factors, and findings from brain imaging (American Psychiatric Association, 2013).

A diagnostic work-up for dementia is most often completed by a primary care provider and ideally includes a family and medical history, psychiatric history and an assessment of cognitive and behavioral changes (Alzheimer's Association, 2015). Patients might also complete neuropsychological tests and a neurologic examination. Brain imaging may be ordered to rule out other brain abnormalities such as a tumor or stroke. A review of studies examining diagnostic accuracy for AD, comparing diagnosis to autopsy findings, reported good sensitivities ranging from 65-95% (Dubois et al., 2007).

Mild cognitive impairment (MCI) now falls under the domain of mild neurocognitive disorder within the DSM-V (American Psychiatric Association, 2013) and captures those individuals who are experiencing declines in memory that are noticeable but not presentations of AD. Specifically, an MCI diagnosis means that an individual's ability to carry out daily activities is not wholly impeded by memory changes, as in the case of AD.

Estimates of conversion from MCI to AD range from 11% to 64%, after 2 years (Ganguli, Dodge, Shen, & DeKosky, 2004; Geslani, Tierney, Herrmann, & Szalai, 2005). Variation in sampling method drives the large range of conversion rates; university-based memory clinic samples (Geslani et al., 2005) have much higher rates of conversion than population-based samples (Ganguli et al., 2004). Population-based studies may include a potentially less rigorous assessment process that is most adaptable for administration in a range of community-based settings, but is unfortunately susceptible to information bias. However,

these studies benefit from the inclusion of a more sociodemographically diverse of individuals, applying a less rigorous inclusion criteria, for improved sampling. Study samples derived from university-based memory clinics, including the sample for this dissertation, may be impacted by selection bias; participants have self-selected to participate in assessment and also meet specific criteria for participation, a benefit for inclusion-specific clinical trials. Yet their strength is data collection using a highly standardized, comprehensive assessment (Kukull & Ganguli, 2012). Currently there is no single test that definitively reports whether an individual has or will develop AD, although the continued development of biomarker testing, with amyloid imaging being a key leader, moves science closer to an ideal and more accurate diagnostic protocol.

Unfortunately, no treatment exists that can delay or prevent AD, although many medication studies are underway that specifically target beta-amyloid accumulation and amyloid imaging is often included in the study protocol. In fact, amyloid imaging has been a significant catalyst for AD drug development, and much work has been directed toward determining the amyloid status of individuals diagnosed with AD, as well as individuals with MCI, or in another prodromal, or preclinical stage of dementia. Allowing for identification of amyloid status allows for an examination of whether changes in amyloid deposition occur over the course of the drug trial (Johnson et al., 2013).

Current medications may temporarily improve symptoms, although none alter the underlying course of the illness. Currently the best approach to care involves ongoing, active management of AD that includes the use of anti-dementia medications and management of co-occurring illnesses, but importantly also includes effective care coordination across health and social service needs (Vickrey et al., 2006). It is noteworthy that social work professionals are often leads or key participants in the care team, providing ongoing support for individuals with

AD and their families, either via home or long-term care coordination, or via psychosocial interventions (Parker & Penhale, 1998).

2.2.1 Amyloid imaging for the diagnosis and treatment of Alzheimer's disease

The amyloid hypothesis is a widely accepted theory that explains how the degeneration of brain cells occurs in AD (Hardy & Selkoe, 2002) and has accordingly driven neuroimaging research to detect amyloid in the brain. Research is even progressing to studies examining the clinical effectiveness of amyloid imaging. An upcoming multi-site study funded by the Centers for Medicare and Medicaid (CMS) plans to examine patient outcomes related to completion of AI for dementia diagnosis and is intended to inform future CMS reimbursement protocols for AI (IDEAS Study, 2015). The following section describes the amyloid hypothesis and the history of research on AI.

To summarize, the amyloid hypothesis reasons that problems with the production, build up or disposal of beta-amyloid (a protein fragment in the brain) results in AD pathology. Deemed chemically "stickier" than other protein fragments, beta-amyloid accumulation eventually results in amyloid plaques. This accumulation is believed to interrupt communication between brain cells and triggers immune cells to cause both overall inflammation and the build-up of disabled cells, all ultimately resulting in cell death and brain atrophy. Based on the amyloid hypothesis, the investigation of technologies to image amyloid in the brain has flourished (Klunk et al., 2004).

Considered a biomarker test, AI uses positron emission tomography (PET) to detect amyloid plaques in the brain using a radioactive compound that binds to amyloid-beta, making it visible in PET imaging. Pittsburgh Compound B, or PiB, is one of several compounds under

investigation for imaging amyloid-beta (Klunk et al., 2004) and is widely used in clinical trials and longitudinal studies of AD. Completing AI can help clarify whether an individual's neurocognitive symptomatology is originating from an AD source and even detect amyloid in the brains of individuals who are cognitively intact (Aizenstein et al., 2008). A review of PiB retention studies reports that over 50% of individuals diagnosed with MCI are positive for amyloid deposition while 25% of individuals who are cognitively normal are amyloid positive (Lingler & Klunk, 2013).

PiB, while not yet approved for clinical marketing by the FDA, has been widely used in studies investigating diagnosis and treatment protocols for AD (Mueller et al., 2005; Rinne et al., 2010). Developed by University of Pittsburgh researchers, an initial study comparing individuals diagnosed with AD to healthy controls showed significant retention of PiB in individuals with AD versus older adults with no cognitive impairment (Klunk et al., 2004). PiB has also been used to identify amyloid deposition in the brains of individuals with no cognitive impairment, indicating that AI may be used to detect a preclinical stage of AD (Mintun et al., 2006). Another study found that greater binding of PiB to cortical areas of the brain predicted progression from normal cognition to symptomatic AD (Morris, Roe, Grant, & et al., 2009).

Three other radiotracers have been developed for use in detecting beta-amyloid in the brain (Barthel et al., 2011; Clark et al., 2011; Vandenberghe et al., 2010). The compounds differ in length of stability; radiotracers with a longer half-life span allows for greater flexibility of its use in research and clinical settings. One radiotracer for detecting amyloid-beta, florbetapir, was approved for marketing to clinical settings by the U.S. Food and Drug Administration (FDA) just last year, in April 2012 (U.S. Food and Drug Administration, 2012). Florbetapir is indicated for use in individuals with cognitive impairment who are undergoing an evaluation for AD or

another type of cognitive decline. Indications and limitations of use specifically stipulate that florbetapir is not intended to "establish a diagnosis of AD" and should be used as an "adjunct to other evaluations" (Lilly, 2013). Comparisons of scan readings for PiB and florbetapir show a strong association and provide comparable findings (Landau et al., 2013; Wolk et al., 2012).

The estimated cost of a florbetapir scan, including a radiologist's read of the scan and the use of a PET scanner, is approximately $3,000. Hearings regarding reimbursement by CMS were held in January 2013, with no plan for reimbursement resulting (Centers for Medicare and Medicaid Services, 2013). In hearings, debate persisted over whether lack of effective AD treatments make florbetapir impractical with respect to care outcomes or whether the potential for care management following early diagnosis can result in cost savings and better care outcomes (Centers for Medicare and Medicaid Services, 2013). The IDEAS study, which will be initiating recruitment in 2016, will determine whether AI leads to an improved diagnostic process, more appropriate treatment and care recommendations, and better patient health outcomes (i.e. reduced emergency department admissions and hospitalizations) (IDEAS Study, 2015).

This first substantial clinical study was supported by years of research exploring the efficacy and use of PiB. Previous research includes cross-sectional and longitudinal studies of PiB, all with the aim of building a research base to document how PiB binds to amyloid in varying parts of the brain and under what symptomatic conditions amyloid might be visible. Patient interest in amyloid PET research studies conducted at the University of Pittsburgh ADRC, a primary home of AI research, comprised the outcome variable of this dissertation and allowed for a panoramic snapshot of early adopters of AI and their related ADRC biopsychosocial assessment data.

2.3 MODELING AMYLOID IMAGING PARTICIPATION

The following sections describe how this dissertation conceptualizes amyloid imaging interest, including how levels of interest are derived and what they potentially signify. Given this is the first known study that quantitatively explores interest in amyloid imaging, two bodies of research are summarized that explore the drivers of interest in AD genetic testing and cognitive screening and assessment. The biopsychosocial model is presented as a framework for understanding interactions across individual, social, and medical variables and with AI interest. All provide a useful backdrop for hypothesizing what characteristics are associated with AI interest.

2.3.1 Conceptualizing interest in amyloid imaging

Previous studies have explored interest in neuroimaging participation for AD from the patient perspective. Of research looking at patient preferences for neuroimaging, reported interest was lower in a sample of primary care patients (62.7%; Magin et al., 2015) than among participants in a university-based memory clinic (78%; Lingler, Rubin, & Saxton, 2010), although in each environment, the majority of respondents do express interest. Lingler and colleagues (2010) further found that one third of the sample indicated a different preference regarding brain imaging study participation one year later, and overall high interest continued. Of note, this work sets the stage for the conceptualization of AI interest in the current study, as the same data source for the dependent variable -- interest in neuroimaging research participation -- will be used.

When examining interest in dementia diagnostic status, irrespective of testing protocol, high percentages of individuals express a preference for knowing their dementia diagnostic status, according to a systematic review pooling samples of studies of individuals with no

cognitive impairment (90.7%) and individuals seeking assessment at a memory clinic (84.8%) (van den Dungen et al., 2014). These findings are somewhat supported by an international phone survey gauging public opinion about dementia testing. Among Americans sampled, 89% would go to a doctor if they were "exhibiting confusion and memory loss…to determine if the cause was Alzheimer's disease" (Blendon et al., 2012, p. 4). However, far fewer (29%) would be "very likely to get a diagnostic test if, in the future, one became available that would tell people before they had symptoms whether they will get Alzheimer's disease" (Blendon et al., 2012, p. 4). These differences are possibly due to differences in sample composition and the specific focus on preclinical state used in the public opinion poll.

Family caregivers also generally support diagnostic disclosure to the patient; although when family members do express concern about disclosure, worries regarding the emotional response of the patient are primary (Holroyd, Turnbull, & Wolf, 2002). Ethical guidelines for dementia diagnostic disclosure promote a consideration of patient wishes regarding disclosure and information sharing (Fisk, Beattie, Donnelly, Byszewski, & Molnar, 2007). While overall disclosure regarding diagnostic status is valued, preferences regarding testing in asymptomatic stages are likely to vary, for a range of reasons. The following section presents a framework for exploring factors related to AI interest.

As outlined earlier, the following categories capture interest levels in AI: 1) AI participants (Participators); 2) individuals who decline AI participation but indicate initial interest in imaging studies (Avoiders); and 3) individuals who indicate they do not want to be contacted regarding imaging studies, and in fact never agree in an AI study (Refusers). Refusers, Avoiders and Participators share the experience of being asked whether they would like to be contacted regarding participation in a neuroimaging study. Those who agree to contact (Avoiders

and Participators) and then delineated by whether they agree participation in an AI study. From these decision points, varying AI interest is derived and grouped into three categories.

Refusers are considered to have the strongest disinclination to participate in amyloid studies. This group may not perceive a value to be derived from participation in AI research, and social altruism may not be enough of a pull. They also have a shared experience of never receiving further information regarding the purpose and protocol involved in AI study participation, and may be more likely to have less knowledge of AI than Avoiders or Participators. Avoiders, who are open to discussion of AI participation with a study recruitment coordinator and then decline participation, experience a potentially more informed decision process. Their initial expression of interest likely means greater exposure to information about amyloid imaging and they decline following this knowledge gain. Avoiders and Participators share the experience of learning about the AI process and the rationale for such research, but diverge in their final decision about AI participation. The Participators group captures those with an active interest in AI – individuals who have agreed to both contact and have carried out participation in one or more AI studies.

While none of the Participators receive the results of AI imaging, other work has supported that there is an interest in receiving research results among university-based memory clinic participants (Gooblar et al., 2015), implying that hope may exist among participants that future disclosure is possible. This is supported by the University of Pittsburgh ADRC amyloid imaging study recruitment coordinator, who has noted that the majority of participants in AI studies would like to receive imaging results. Individuals diagnosed with MCI or normal with subjective complaints report interest in results, as do AD caregivers whose loved one has participated in AI imaging. Participants may also be motivated by the availability of additional

imaging that is apart from amyloid PET, is free of charge, and may provide new information regarding their condition. Maintaining a stronger connection to ADRC clinicians through study participation may also be valued by this group, with the hope that such a connection may lead to a deeper understanding of diagnosis or sense of closeness to the forefront of research, where access to the most advanced treatment options is more possible. Of note, while many studies do offer compensation of up to several hundred dollars and transportation as needed, anecdotally, few individuals describe this as a prime motivating factor.

2.3.2 Frameworks for exploring amyloid imaging interest and participation

In addition to modeling AI interest based on a biopsychosocial framework, participation in genetic testing for AD and cognitive screening or assessment serve as a framework for understanding the associations between demographics and family history, as well as cognitive status, health, and mental health status. In particular, these frameworks are used to generate hypotheses regarding the variable associations that are presented in the following sections.

Biopsychosocial model for amyloid imaging interest and participation

The medical model for dementia allowed for a movement from dementia viewed as a normal part of aging, to dementia conceptualized as an individualized disease process caused by progressive deterioration of the brain, that could be medically managed and treated (Lyman, 1989). It also, however, reduced social work and other allied health professionals to care assistants, under the direction of doctors and in supplemental or secondary roles (Kaplan & Andersen, 2013). It additionally considered the patient to be a passive actor in the care decision-making discussions (Kaplan & Andersen, 2013). Viewing dementia in a medicalized frame also

reduced the individual with dementia to their illness and symptom report, omitting the many dynamic psychosocial aspects of the individual that impact the illness experience and trajectory experience (Lyman, 1989; Spector & Orrell, 2010).

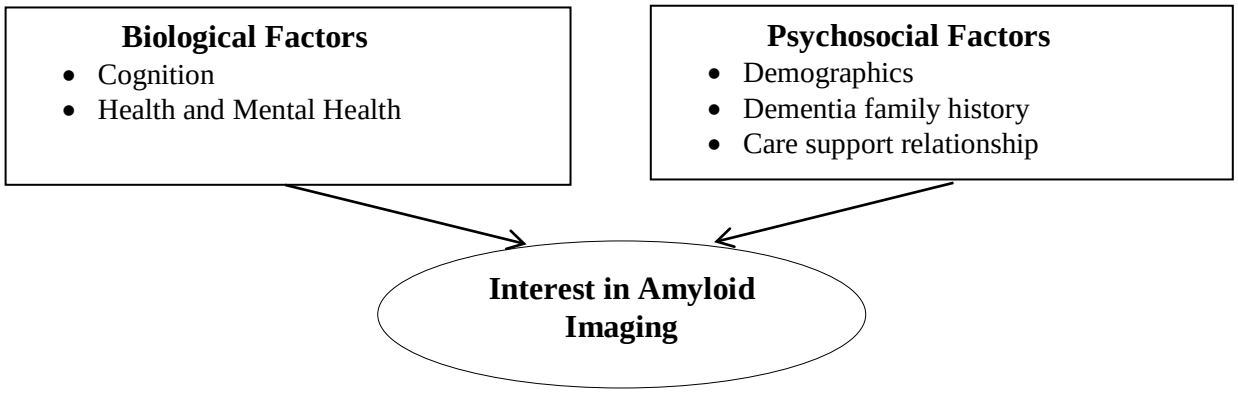
While written about to advocate a transformative model for medicine, the biopsychosocial model has long been embraced by social work as a tool for assessment and intervention with older adults (Greene, 2011; McInnis-Dittrich, 2005). The biopsychosocial model developed in response to a recognized need to move from independent and separate assessment of medical and psychosocial determinants surrounding assessment, diagnosis, and treatment to a merged model of care (Engel, 1977). It is derived from a general systems theory approach which considers varying factors surrounding an individual to be collectively and intrinsically linked. It also provides a connection between care delivery and the study of disease (Von Bertalanffy, 1950; Von Bertalanffy & Sutherland, 1974). Engel proposed the biopsychosocial model as a way to take into account varying patient-related and social-system factors as a part of care (Engel, 1977). Most importantly, patient report is given equal value to illness presentation (Engel, 1977).

It has been specifically applied to social work practice in dementia care (Kaplan & Andersen, 2013; Keady et al., 2013). For example, Spector and Orrell (2010) modeled a framework applying the biopsychosocial model to dementia care. They identified biological and psychosocial factors, both fixed and tractable, as well as related biological and psychosocial interventions, that impact dementia progression. Differentiating between fixed and tractable factors acknowledges those tractable biological and psychosocial factors that are amenable to change and may be impacted and improved. Factors may be considered risk factors or protective factors for dementia. Of note, dementia is modeled as a disease trajectory and progresses from

normal aging, through early organic change (without symptoms), through MCI and dementia diagnosis, to end-of-life care and death.

Applying the biopsychosocial model to this dissertation work allows for an exploratory examination of the associations between interest in AI and biological or medically determined variables (cognition, physical, and mental health status) and psychosocial variables (demographics, dementia family history, and informal care support; see Figure 1 for a pictorial representation). It additionally allows for exploration of interactions across independent variable groups, in relation to AI interest. To further delineate the potential relationships across these variables, a summary of the literature exploring interest in AD genetic testing, memory screening, and cognitive assessment literature is described in detail below.

Figure 1. Conceptual framework using the biopsychosocial model to depict interest in amyloid imaging



Genetic testing for Alzheimer's disease

Studies examining participation in genetic predictive and susceptibility testing for AD serve as one basis for exploring what factors may relate to participation in AI. Roberts et al. (2013) outline the key differences between susceptibility testing for AD and amyloid imaging, noting fixed results for genetic testing and potentially changing findings for AI, as amyloid status may change from negative to positive. A second important difference is that evidence for AI points to a more definitive determination of hallmark pathology, with a risk of clinical AD developing in the next 10-15 years for asymptomatic individuals. However, genetic testing shares many similarities with AI. Both allow individuals to know whether a condition exists that increases the likelihood of developing or having AD. Overall there are likely similarities in those who would express interest in completing each kind of diagnostic procedure, making the AD-related genetic testing literature an appropriate backdrop for the hypotheses generated in this study.

A range of studies have explored how genetic testing for AD risk is viewed, as well as what factors relate to participation in such testing. These studies employ a variety of research designs, ranging from hypothetical descriptions of genetic testing procedures (Roberts, 2000), to randomized controlled trials examining the feasibility and acceptance of genetic susceptibility testing (Green et al., 2009). Most samples include only individuals with first-degree relatives with AD, as their predisposition for AD may be all the more salient.

Across study designs, a high interest in testing is evident. Neumann et al. (2001) conducted phone interviews with a random sample of adults (N=314) and found that more than three-quarters would complete a predictive test for AD; however interest dropped to 49% for partially predictive testing. A study presenting differing hypothetical scenarios (e.g. varying

degrees of test accuracy, level of risk associated with a positive finding, and treatment availability) to adults with first degree family members with AD (N=203) reported that the majority of participants expressed interest in genetic testing, even when testing accuracy was limited (Roberts, 2000). Recruitment into a randomized controlled trial examining the delivery of AD genetic susceptibility testing results greatly exceeded expectations, warranting concerns that the current genetic counseling services available may not be sufficient to meet the anticipated demand for such testing (Roberts et al., 2004).

While limited treatment options inhibit the expansion of such testing and research points to fewer numbers of individuals expressing interest in genetic testing participation who actually follow through with participation, this high initial interest is worthy of consideration. The following sections will explore what psychosocial factors differentiate between those who express willingness to pursue testing and those who do not. Additionally, the drivers of initial interest in testing, compared to those factors associated with testing completion, will help establish a framework for exploring whether differences exist in the factors that define AI interest and participation groups.

Participation in cognitive screening and assessment

In addition to the literature on participation in AD-related genetic testing, a body of research has also explored factors associated with willingness to participate in initial memory screening or cognitive assessment. These studies provide a needed backdrop, as they offer a greater depth of exploration and theory testing, particularly in regards to the psychological factors related to testing interest. Another key aspect of this research is the addition of studies that explore factors associated with the decision to actually undergo a memory assessment, again

allowing for a review of factors that distinguish between who expresses intent to undergo memory testing and who actually completes such testing.

Eight sets of studies have explored this area, all including older adults with no known diagnosis of memory impairment. As in genetic studies, hypothetical scenarios were employed to explore whether there are differences in who expresses intent to undergo assessment and who declines (e.g. Boustani, Watson, Fultz, Perkins, & Druckenbrod, 2003; Boustani et al., 2011; Dale, Hemmerich, Hill, Hougham, & Sachs, 2008; Werner, 2003). Two studies incorporated scenarios in which respondents were asked to imagine different conditions under which they would express assessment intent, including concerns about memory changes (Dale et al., 2008; Werner & Heinik, 2004) or given a family history of AD (Werner, 2003). Two studies examined differences between those who completed memory screening and those who went on to complete diagnostic testing post screening (Boustani et al., 2006; Demirovic et al., 2003), while one study explored the reasons individuals who complete screening would pursue diagnostic testing (Williams, Tappen, Rosselli, Keane, & Newlin, 2010) and one explored factors impacting the decision to seek assessment among individuals with subjective memory complaints (Hurt, Burns, Brown, & Barrowclough, 2012).

Intention to participate in memory screening ranged across studies, from a low of 49% among older adults residing in independent living communities who were asked about interest in routine memory screening (N=500; Boustani et al., 2003), to high interest (97% reporting definitely or probably yes) in MCI screening when, hypothetically, a family member indicates concerns (N=199; Dale et al., 2008). For those interested in MCI screening, knowing as early as possible whether memory symptoms were an indication of AD was the most robust predictor of intent (Dale et al., 2008). Actual participation in cognitive assessment is substantially lower,

however. Among those who elected to complete a memory screening and, based on screening outcome, were referred for a diagnostic cognitive evaluation, less than half decided to pursue an evaluation (Boustani et al., 2006; Demirovic et al., 2003).

Compared to genetic testing studies, more variation in interest and completion of memory assessment is evident. Reasons for this variation seem to hinge on differences in sample composition and measurement, and will be explored in the following sections. Additionally, factors associated with intent to pursue such testing, in comparison to actual testing completion, seem to vary, and this difference is examined below.

Factors associated with interest and participation in AD genetic testing and cognitive assessment

Demographics. Age, race, gender, and education level may play a role in who chooses to participate in AI. The following section describes the varying relationships reported for genetic testing and cognitive screening intent and participation. Based on these findings, hypotheses are derived for AI interest and for each demographic.

Age. Overall, younger age groups seem to express more interest in genetic testing and assessment for AD. Older adult primary care patients with no dementia diagnosis (N=554) were more likely to express willingness to complete a memory screening if they fell in a younger age group (Fowler et al., 2012). In a sample of adults from a geriatric outpatient clinic (N=199), younger individuals (< 65 years) were more likely to express intentions to participate in MCI screening if memory symptoms were (hypothetically) evident (Dale et al., 2008).

The same finding held in relation to intent to participate versus actual participation in a cognitive evaluation. Werner (2003) reported that interest in cognitive assessment was more

evident among younger individuals with a first-degree family history of AD. The same was true for participation in a diagnostic cognitive assessment among a sample of older primary care patients (N=434; Boustani et al., 2006) and a community-based, multi-ethnic sample of older adults (N=310; Demirovic et al., 2003), when memory screening findings indicated need for follow-up. Among individuals with a family history of AD (N=196) who were approached for participation in a randomized clinical trial testing an AD genetic risk assessment counseling intervention, those less than 60 years old were more likely to participate in the trial (Roberts et al., 2004).

Just two studies reported age was non-significant in modeling; one exploring willingness of individuals with a family history of AD to participate in genetic testing (Roberts, 2000) and another exploring intent of first degree relatives to participate in a cognitive assessment (Werner & Heinik, 2004). A potential interaction between family history and age may alter findings and both variables will be included in this dissertation to further tease out a relationship.

Race. The relationship between race and preferences for testing are mixed. African Americans are reported to be significantly more likely to express willingness to participate in MCI screening (Dale, Hougham, Hill, & Sachs, 2006) and to seek a cognitive assessment (Demirovic et al., 2003) than whites. Another study reported that younger African Americans were significantly more likely to complete a cognitive assessment than younger whites (less than 80 years of age) or older African Americans (aged 80 or older) (Boustani et al., 2006). African Americans are reported to be less likely to be interested in pursuing AD-related genetic testing than whites and report fewer reasons for participation in such testing (Hipps, Roberts, Farrer, & Green, 2003). No studies were found that examined AD genetic susceptibility testing in relation to other racial or ethnic groups. In fact, in some studies race was not explored as a factor

associated with interest in genetic testing due to the limited racial variability in the sample (Roberts, 2000; Roberts et al., 2004). An awareness of greater dementia prevalence among African Americans may be stimulating this interest in assessment and may be partially driving the overall findings in these studies (Gurland et al., 1999). A review of qualitative studies exploring the experience of diagnostic disclosure reported greater evidence of stigma related to dementia among minority ethnic groups than whites (Bunn et al., 2012), indicating the potential for lessened interest in AI. The present study will further explore this relationship, with a sample comprised of African American (7.5%) and white (92.5%) participants.

Sex. Less is known regarding the relationship between gender and AD testing interest. Just one study found an association between AD genetic testing interest and gender, in which men were significantly more likely to express interest in testing participation than women (Roberts, 2000). Additionally, Boustani et al. (2003) reported that older adult males living in a continuing care retirement community were more likely than females to express interest in memory screening. Other studies have reported no significant associations with gender (Dale et al., 2008; Demirovic et al., 2003; Green, Clarke, Thompson, Woodard, & Letz, 1997). A larger proportion of women do have AD; however this trend is largely explained by the longer life expectancy of women (Hebert, Scherr, McCann, Beckett, & Evans, 2001). Given this greater prevalence, it may be that women perceive greater harms from testing or screening (Boustani et al., 2003), although this seems to be a deficient rationale for any trend and it could be that a non-association is present.

Education level. Green et al. (1997) reported an association between lower education level and interest in a hypothetical, highly accurate, predictive genetic test for AD. Similarly, Dale et al. (2008) reported that individuals with a lower level of education were more likely to

express interest in MCI screening if a family member suggested memory problems were present, possibly indicating less comfort with their ability to self-identify memory changes. However, no differences in education level were reported in studies examining who goes on to participate in diagnostic assessment (Boustani et al., 2006; Demirovic et al., 2003). Furthermore, a study examining participation in genetic risk assessment counseling, as part of a randomized clinical trial, found those with at least a college education were more interested in participation. Overall, findings are mixed, possibly due to varied samples and the range of assessment involvement participants are questioned about.

While drawing firm conclusions regarding demographic factors associated with testing participation is not possible, they provide a starting point for the further investigation of these factors. The following hypotheses are derived based on these findings for the full sample and individuals with dementia: Younger age will be significantly related to interest in, as well as participation in, AI. No significant relationships regarding gender, race, or education level are anticipated.

Neurocognitive status. Self-perception of cognitive impairment has been the primary way that the relationship between cognition and interest in dementia testing has been explored, with varied findings reported. In an Israeli study sampling individuals with a first degree relative with dementia (N=93), having subjective memory complaints was predictive of interest in seeking a cognitive assessment (Werner & Heinik, 2004). However, among studies examining participation interest in memory screening, individuals who actually believed they had a memory problem were less likely to report interest in seeing a doctor for MCI screening if an instance of memory change was occurring (Dale et al., 2008). Another study found that self-report of a

memory problem was not indicative of interest in regular memory screening (Boustani et al., 2003).

Among studies employing measures of cognitive status, findings also differed. In one study older adults with worse performance on screening instruments had a higher probability of following through with the completion of a dementia assessment than those with better screening scores who were also referred for diagnostic assessment (Boustani et al., 2006). Another study using hypothetical scenarios to explore participant willingness to participate in AD research found that overall interest in AD-related study participation did not differ between individuals with and without cognitive impairment (Kim, Cox, & Caine, 2002). However, among individuals with mild to moderate AD (N=34), greater decisional impairment was associated with less interest in research participation.

Younger age at onset of cognitive symptoms may relate to whether an individual completes AI. Misdiagnosis of early onset AD is common and accuracy in diagnosis is critical to disease management as well as patient and family care planning (Werner, Stein-Shvachman, & Korczyn, 2009). For individuals with a young-onset dementia disorder, increasing diagnostic certainty regarding the cognitive disorder may be all the more critical for access to care and disability services. Although not in place when the individuals in the current study sample were approached about AI interest and participation, criteria for the clinical use of amyloid imaging include individuals presenting with early-onset AD among those who may benefit from its use (Johnson et al., 2013). Each of these aspects may make AI more attractive for younger individuals with dementia.

Receiving information about cognitive status, particularly the news that cognition is declining and mild cognitive impairment or dementia has been detected, may impact patient

interest and participation in neuroimaging. One study in which semi-structured interviews were completed with individuals diagnosed with MCI found that many participants felt that imaging was onerous to complete and did not seem appropriate in relation to their symptoms (Dean, Jenkinson, Wilcock, & Walker, 2014). Perceptions and preferences for neuroimaging are likely affected by the information exchange and communication dynamics that occur throughout the assessment and diagnostic process among patient, family members, and clinicians. A social work study completing qualitative interviews with individuals recently diagnosed with cognitive impairment and their families found an expressed interest in receiving more information about their diagnostic status, with one participant expressing, "knowing everything was better than not knowing" (Abley et al., 2013). This may be equated with an interest dementia study participation that is deemed to improve patient and family understanding of the patient's diagnostic status.

How individuals view the seriousness of their subjective memory complaints may explain the variation in findings. Among those comprising the current study sample and who are presenting to the Alzheimer Disease Research Center with memory complaints, as well as actively pursuing evaluation, there is certainly a greater worry regarding memory symptoms. Therefore, when considering the relationship between cognitive status and AI participation, we surmise that an inverse association may be present. Individuals with less impairment (e.g. MCI or no dementia but possibly subjective memory complaints) may express a greater interest in AI, as there may be more interest in gaining additional insight about their individual potential for a disease process. Less impairment also indicates greater ability to discern the meaning of participation in such a process, allowing better understanding and therefore acceptance of testing. It is important to note that for individuals with a diagnosis of dementia, family members may play a greater role in determining participation in AI.

To conclude, given the range of findings in relation to cognitive status and taking into account the unique nature of AI, we hypothesize that the following factors will be significantly associated with AI interest and participation: 1) having a diagnosis of no cognitive impairment, or mild cognitive impairment, rather than dementia; 2) better performance on cognitive testing, in this case the Mini Mental State Exam; 3) younger age at onset of cognitive symptoms; and 4) change in diagnostic status. Among individuals with dementia, we hypothesize that 1) better performance on cognitive testing; and 2) younger age at onset of cognitive symptoms will be significantly associated with AI interest and participation.

Family history. Given that a higher risk of AD is associated with family history of dementia (Green et al., 2002), several studies have limited sample composition to individuals who have an immediate family member diagnosed with AD (Roberts, 2000; Roberts et al., 2004). These individuals are considered to have a high interest in genetic testing for AD, which is supported by study findings (Roberts, 2000). Understanding how individuals perceive the importance of family history is especially salient as it may also play a role in determining who is referred for AI.

Three genetic testing studies have further explored the relationship between family history and genetic testing interest by including individuals with and without a family history and using varied samples, including: a community-based convenience sample (Green et al., 1997); a general population sample via random-digit dialing (Neumann et al., 2001); and a matched comparison group sample of individuals with no family history compared to individuals with a living parent diagnosed with AD (Cutler & Hodgson, 2003). Results from these studies were somewhat mixed; there was a trend toward more interest among individuals with family history

of AD, although the difference was significant in just one study (Green et al., 1997). Individuals asked about interest in completing a hypothetical, highly accurate predictive test for AD were significantly more likely to express interest if they had an AD family history (Green et al., 1997). Of studies with non-significant findings, Neumann et al. (2001) found that those with a family history reported greater interest in predictive testing than those without a family history (90% versus 77%), while interest in partially predictive testing was more similar (49% versus 44%). One limitation was that the definition of family history varied, in one case extending beyond immediate family members to grandparents (Neumann et al., 2001), potentially skewing risk perception. Cutler and Hodgson (2003) also found that adult children asked about participating in 100% accurate, predictive testing had a slightly greater interest (68%) than individuals with no family history (62%), but again the difference was non-significant.

Across studies examining interest in memory screening or uptake of cognitive assessment, findings are also somewhat mixed. One study's sample included only individuals with a first degree relative with AD, who reported moderate interest (42%) in cognitive assessment within the next one to 5 years (Werner & Heinik, 2004). Another found that older adults expressed more interest in cognitive evaluation when presented with a scenario in which they had a relative with AD (Werner, 2003). A third study supported these findings, based on semi-structured interviews completed with a multi-ethnic sample of older adults who were more receptive to both memory screening and cognitive evaluation when a family history of AD was evident (Williams et al., 2010).

Family caregivers of individuals with dementia had a lower acceptance of dementia screening than non-caregivers, and although information regarding family relationship was not available, caregivers in the sample were significantly more likely to believe they were at risk for

developing AD than non-caregivers (Boustani et al., 2011). Additionally, caregivers who were supporting family members with dementia-related behaviors reported lower intention to complete a cognitive evaluation (Werner & Heinik, 2004). It may be that personal experience caring for a loved one with dementia may alter views about the utility of testing and enhances perceptions of AD as a threat with significant repercussions.

Given the above findings and the potential for differing outcomes based on type of family history, the following hypothesis is derived for the full sample and the subsample of individuals with dementia: having family history of AD will be significantly associated with AI interest and participation.

Health status. Other health conditions may take precedence over AI participation, although few studies have examined how comorbid health issues impact interest in cognitive testing. Having two or more medical comorbidities was significantly related to greater interest in routine memory screening among older adults residing in a retirement community (Boustani et al., 2003). However, a history of stroke was not associated with participation in cognitive assessment following memory screening referral (Demirovic et al., 2003). Given the strong association between cardiovascular health and the higher risk of AD (Alzheimer's Association, 2012), it seems important to note whether the presence of health conditions, such as cardiovascular disease, diabetes, high cholesterol, and hypertension, all of which negatively impact cardiovascular health, lead individuals to pursue testing for AD. Based on the above findings and the association between cardiovascular health and AD, the following hypothesis will be tested: presence of health comorbidity will be significantly associated with AI interest and participation for both the full sample and subsample of individuals with dementia.

Mental Health Status. Studies examining the relationship between mental health and AD testing participation have primarily focused on documenting whether testing engagement leads to psychological distress, particularly following diagnostic disclosure. In fact, studies have documented that after a disclosure of a dementia diagnosis (Carpenter et al., 2008) or results of genetic testing indicating AD susceptibility (Green et al., 2009), psychological distress, including depressive symptoms, do not significantly increase. These findings seem to be in line with the link between other types of genetic testing and related emotional consequences (Broadstock, Michie, & Marteau, 2000). One might surmise that these findings may be due to self-selection; individuals who might experience testing-related distress opt out of participation.

Unfortunately, with regards to the prior depressive status of who might seek testing, less is known. Studies exploring the factors associated with willingness to complete memory screening for MCI or dementia report mixed results in relation to depressive symptoms. One study explored intent to participate in screening for MCI in varying hypothetical scenarios, including: 1) subjective memory complaints; 2) no memory complaints; 3) or family member-relayed memory concerns (Dale et al., 2008). Findings were mixed, in that depressive symptoms were associated with less interest in memory screening only in the instance of hypothetical memory changes. Across groups, anxiety was not associated with willingness to participate in MCI screening. Another study examining interest in memory screening among individuals with actual subjective memory complaints found no significant difference in depressive symptoms between individuals who had sought help for memory concerns and those who had not (Hurt et al., 2012). Yet, diagnostic testing could be considered useful in teasing out whether memory symptoms are caused by depression or dementia. In one study exploring intent to participate in

predictive testing for AD, self-reported history of depression was a significant predictor (Green et al., 1997).

Exploring the relationship between mental health and interest in AI may help tease out whether there is a need for pre-test counseling, inclusive of a significant focus on baseline distress. A systematic literature review examining the psychological implications of predictive genetic testing reported that in over half of studies reviewed, emotional status prior to testing was significantly related to level of distress following testing completion (Broadstock et al., 2000). It follows that a psychological assessment pre-testing may then help to better target post-test counseling support, as it has been documented that individuals with current depression may be more vulnerable to adverse effects of testing (Lerman et al., 2002).

Given the literature base, the following hypotheses are derived: 1) for the full sample, having a psychiatric diagnosis will be significantly associated with AI interest and participation; and 2) for the subsample of individuals with dementia, presence of a psychiatric disorder will not be significantly associated with AI interest and participation.

Informal care support relationship. Among individuals with dementia, care partner relationship may have implications for AI interest and participation, as the individual accompanying the patient to their cognitive assessment appointment(s) is likely also an important participator in the decision-making process for neuroimaging study involvement. One study, using an Alzheimer Disease Center registry cohort, examined caregiver willingness to have their loved one participate in an AD medication trial (Cary, Rubright, Grill, & Karlawish, 2015). The authors found that spousal care partners were significantly more likely to express research participation willingness and expressed a more positive attitude regarding research than adult

child care partners. The authors surmised that the finding might be due to greater time availability of spousal care partners and heightened interest in meaningful activities for the person with dementia. Based on the current research, we hypothesize that for the subsample of individuals with dementia, spousal care support will not be significantly associated with AI interest and participation.

2.4 CONCLUSIONS

Dr. Watson may be in the minority when it comes to interest in biomarker testing for Alzheimer's disease, as, overall, there seems to be high interest in such testing. Given this level of receptiveness, examining the rates of interest in AI may be especially critical for anticipating and responding to the demand for AI. With the number of individuals and families anticipated to face AD growing exponentially, the number of those interested in AI can be expected to rise. The continued development of tools for dementia detection, in the earliest stages of illness, will help target treatments and care planning support to those who need it most.

Modeling interest in AI offers some initial groundwork for understanding who is likely to be more accepting of such testing and, therefore, how to best develop protocols for pre- and post-test counseling for individuals undergoing AI. These protocols would be grounded in a biopsychosocial framework that views the individual from a holistic perspective, acknowledging the biological and psychosocial factors that personify them. The hypotheses derived above provide a premise for exploring the relationships between patient demographics, family history, and medical status variables with AI interest and participation. The following chapter will further

describe how these variables were operationalized and the sample from which they were derived, as well as present the analysis plan.

3.0 METHODOLOGY

3.1 STUDY DESIGN AND RATIONALE

The focus of this dissertation was to: Aim 1) determine what biopsychosocial factors are significantly associated with interest in and participation in amyloid imaging research among registry participants at an Alzheimer Disease Center; and Aim 2) determine what biopsychosocial factors are significantly associated with interest in and participation in amyloid imaging research among a subsample of individuals diagnosed with dementia (IWDs). A secondary dataset comprised of baseline and aggregated longitudinal data from the University of Pittsburgh Alzheimer Disease Research Center (ADRC) and capturing all ADRC participants approached for an amyloid imaging (AI) research study from 2003-2013 was analyzed (N=449). This dataset provides a substantial sample of individuals who, fairly uniquely, have completed annual comprehensive cognitive assessments, range in their cognitive status, and have been queried at each assessment point regarding their willingness to participate in amyloid imaging research. Of note, social workers often facilitate the initial discussion with patients and families that explores interest in neuroimaging research. The full sample includes individuals with no cognitive impairment, mild cognitive impairment (MCI), or dementia to determine whether cognitive status is significantly related to AI interest or participation. To further explore significant associations with AI uptake among patients who have been the first and most frequent

users of such technology, a second set of analyses examined interest in amyloid imaging among a subset of individuals diagnosed with dementia.

This dataset also allowed for greater delineation of interest in AI, via grouping into three levels of interest in AI participation: 1) amyloid imaging study participants (Participators); 2) individuals who declined amyloid imaging study participation but originally indicated interest in being contacted about imaging studies (Avoiders); and 3) individuals who did not want to be contacted for imaging studies or if they were first contacted regarding study participation, never agreed to an AI study (Refusers). These categories were derived from one or more contacts for each ADRC participant, in which they were either queried about their willingness to be contacted for a neuroimaging study or they were contacted about participation in an AI study. This approach allowed for the inclusion of all ADRC participants approached regarding AI studies from the time when recruitment for AI studies was first initiated. Three category groupings also allowed for a look at whether significant relationships with biopsychosocial factors varied by depth of interest in AI, rather than just participation. For comparison, a second set of analyses examined significant associations between biopsychosocial factors and participation in AI, in which Participators were compared to Non-Participators (Avoiders and Refusers).

The following sections provide detail on: 1) sample procedures, including the ADRC setting, sample description, and sampling strategy; 2) sources of data, including the data collection process and a description of each variable included in analysis; and 3) the data analysis plan.

3.2 PROCEDURES FOR SAMPLING

3.2.1 Setting

The ADRC is one of 29 federally-funded Alzheimer Disease Centers that conducts research with the goal of improving diagnosis and treatment for AD and other dementias. All centers offer comprehensive memory assessments for individuals who have concerns about their memory, as well as those who have no memory complaints but have an interest in memory research engagement. Individuals who participate in the ADRC registry complete annual memory evaluations that include neurological and psychiatric evaluations, brain imaging, a comprehensive neuropsychological assessment, and a psychosocial evaluation (Lopez, Becker, Klunk, Saxton, Hamilton, Kaufer, et al., 2000). Participation is voluntary and longitudinal. Participants and their family members may drop out from the ADRC at any time, although follow-up can continue until the death of the participant.

To be eligible for participation in the ADRC, participants must: 1) be English speaking at an early age; 2) have a family member or friend who can attend the assessment and answer questions about the participant's level of functioning (informant); 3) have a seventh grade or higher level of education; 4) have adequate visual and auditory abilities to complete neuropsychological testing; and 5) have no history of brain tumor or severe psychotic disorder. These requirements serve to enhance specificity and sensitivity of the final diagnosis. Almost all individuals are able to provide consent to ADRC participation. A minority assent to participation and an informant provides proxy consent. As a part of the consent process, all agree to their data being used by researchers who are ancillary to the ADRC. Following the memory evaluation, a multidisciplinary team of clinicians who assessed the participant meet to determine a diagnosis.

After an initial evaluation or when any change in diagnosis occurs following assessment, the participant and their family members are invited to return to the ADRC to meet with a neurologist and social worker to review the results of the assessment. At this time, in addition to discussion of treatment and social service support options, participants are also queried about their willingness to be contacted for neuroimaging studies at this time – a component of the outcome variable for this dissertation. Contact with an amyloid imaging study coordinator may also occur for individuals who are eligible for AI studies.

3.2.2 Sample description

Participants typically learn of the ADRC through doctor referral (primary care physician, neurologist, or psychiatrist) or self-refer after learning of the ADRC from internet searches, discussion with family/friends, or ADRC outreach programming. Individuals often initiate appointments due to memory concerns, although a cohort of individuals with no cognitive impairment enter the ADRC because of interest in dementia research or apprehension related to a family history of dementia.

All individuals included in this dissertation study sample have completed at least one ADRC assessment and have received the results of the assessment. The following were criteria for dataset inclusion: 1) meeting the ADRC inclusion criteria described above; and 2) completing an ADRC assessment between 2003 (when recruitment for AI studies was initiated) and 2013; and 3) queried about neuroimaging study contact and/or AI study participation. Exclusion criteria include: 1) exclusion from the ADRC following the completion of an ADRC initial assessment; 2) expressing interest in neuroimaging study contact, but never being contacted for AI study participation.

Individuals who are contacted for an AI study may share the following experiences. At the time of a diagnostic meeting or during the annual assessment, they are asked whether they wish to be contacted regarding participation in brain imaging studies, which are primarily comprised of amyloid imaging protocols. During this discussion the clinician or social worker describes the general purpose and procedure typically expected for such studies. While there is no formal script, staff are trained to note (in lay terms) that neuroimaging studies are mainly comprised of protocols using an amyloid imaging positron emission tomography (PET) tracer, in most instances Pittsburgh Compound B (PiB). Participants are told that the purpose of amyloid imaging is to assess the usefulness of this tracer for diagnosing dementia at varying stages of the disease process. Any questions about what is described are addressed and typically include the length of study participation and risks associated with exposure to a radioactive tracer during PET imaging, or imaging itself. Individuals who agree to contact may then be contacted by an AI study coordinator. Those who refuse contact were included in the Refusers group for this dissertation.

Within this study sample, individuals expressing interest in study contact were contacted by a study coordinator about participation in an AI study, and provided with further detail regarding study purpose and procedures. Studies may include one or more visits to complete amyloid imaging; in several instances participants complete up to three rounds of amyloid imaging over the course of three years. Additional procedures may also include other imaging and neuropsychological testing. As required with any consent protocol, the risks and benefits of study participation are described and the voluntary nature of study participation is emphasized. The risks described are those typically associated with participation in imaging (e.g. exposure to radioactivity, muscle aches from being immobile, anxiety from being in an enclosed space).

Risks also include the possibility of an unanticipated finding from imaging, such as the presence of a stroke or brain tumor. The study coordinator also emphasizes that there is no direct benefit gained from participation, although the aim of the study is to benefit society by improving our understanding of the relationship between beta-amyloid deposits and brain functioning. Those who agree to participation in an amyloid imaging study sign a consent form for the specific study and are deemed a Participator for the purpose of this dissertation. Those who refuse participation in an amyloid imaging study, after discussing the study with the coordinator, comprise the Avoiders group. A subset of individuals were contacted by the AI study coordinator between 2003-2005, prior to the adoption process for determining willingness to be contacted. Individuals who refused any study participation during this time period were deemed Refusers.

3.2.3 Sampling strategy

A convenience sample was derived from the ADRC participant registry, applying the above eligibility criteria, and included all individuals with data documenting one or more queries about participation in an AI study, or contact regarding neuroimaging study participation, from 2003 and through 2013. This approach allowed for the inclusion of a significant portion of individuals approached for AI research, over a range of study protocols that included individuals with different diagnoses. The study sample is derived from the ADRC registry sample, which is convenience in design and comprised of research-friendly individuals who have an interest in learning more about their cognitive functioning.

3.3 SOURCES OF DATA

3.3.1 Data collection

Three separate ADRC databases were accessed and merged to comprise the final dissertation dataset. Independent variables were extracted from two datasets, including the National Alzheimer's Coordinating Center Uniform Data Set (NACC UDS). Standardized clinical and neuropathological research data comprise the NACC UDS database and were collected by NACC-trained clinicians. For the purposes of this dissertation, only NACC UDS data collected by the University of Pittsburgh ADRC was accessed. In addition to UDS data, diagnostic data, including cognitive and psychiatric disorder diagnoses, were extracted from the University of Pittsburgh ADRC Registry. Diagnostic data extracted from the ADRC Registry were matched to UDS data by ADRC participant unique identifier and assessment date. Data collection using the UDS was initiated in 2005. Therefore, approximately half of the sample (n=251; 55.9%) have *initial* assessment data collected via UDS measures. For individuals who were ADRC participants prior 2005, their first *annual* assessment data collected via the UDS were instead extracted.

Data for the dependent variables, AI interest and participation in amyloid imaging, were extracted for each participant from the ADRC Ancillary Study dataset for the given time period (2003-2013). While amyloid imaging studies initiated recruitment in 2003, tracking of interest in being contacted for neuroimaging studies did not start until 2006. This impacted the criteria used to determine assignment to amyloid imaging interest categories, as it included a subset of individuals who were asked about participating in an AI study before being queried about

willingness to be contacted for neuroimaging research. Figure 1 provides a flowchart illustrating the criteria system used, which will also be described in more detail in the next section.

3.3.2 Study variables and operationalization

Table 1 summarizes the dependent variables and each independent variable under investigation, while the following sections provide further description for each variable, including how each is measured. Several categorical variables had additional response options (e.g. race, education, ADRC diagnosis, modified Charlson Comorbidity Index, and care support relationship). While this table presents the final categories examined in bivariate and multivariate analysis, the full set of categories for each is examined in descriptive analysis. Reasons for category aggregation are discussed in the Results section.

Table 1. Description of variables

Variable List	Variable Type	Variable Description	Data Source
Dependent Variables			
Interest in amyloid imaging research	Categorical	1=participated in amyloid imaging ("Participators"); 2=declined amyloid imaging participation but initially indicated interest in being contacted about brain imaging ("Avoiders"); and 3=did not want to be contacted for imaging studies ("Refusers")	ADRC Ancillary Database
Participation in amyloid imaging research	Dichotomous	1=participated in amyloid imaging ("Participators"); 0=did not participate in amyloid imaging ("Non-Participators")	ADRC Ancillary Database
Independent Variables			
Demographics			
Age	Continuous	Age at assessment visit, years	UDS
Sex	Categorical	0=Female; 1=Male	UDS
Race	Categorical	0=White; 1=African American	UDS
Education	Categorical	1=Less than HS/HS/GED 2=Some college/ Associate's/Bachelor's 3=Graduate work/Graduate degree	UDS
Cognition			
ADRC diagnosis	Categorical	1=no cognitive impairment 2=mild cognitive impairment 3=dementia	ADRC Registry
Mini Mental State Exam	Continuous	Global measure of cognitive impairment (potential range 0-30)	UDS
Age at onset of symptoms	Continuous	Reported age when symptoms began (for those diagnosed with cognitive impairment)	UDS
Change in ADRC diagnosis	Dichotomous	0=no change in diagnosis; 1=change in diagnosis	ADRC Registry
Health Status			
Modified Charlson Comorbidity Index	Dichotomous	0=Absence of physical health comorbidity; 1=presence of physical health comorbidity	UDS
Psychiatric diagnosis	Dichotomous	Presence or absence of a psychiatric disorder (0=No; 1=Yes)	Electronic ADRC Registry
Family History			
First degree family members diagnosed with dementia	Dichotomous	0=No; 1=Yes	UDS
Care Support*			
Care partner relationship	Categorical	1=Spouse/Partner; 2=Adult child; 3=Other	UDS

Note: *Care support relationship was analyzed only for individuals with dementia.
ADRC=Alzheimer Disease Research Center; HS=high school; GED=General Equivalency Diploma

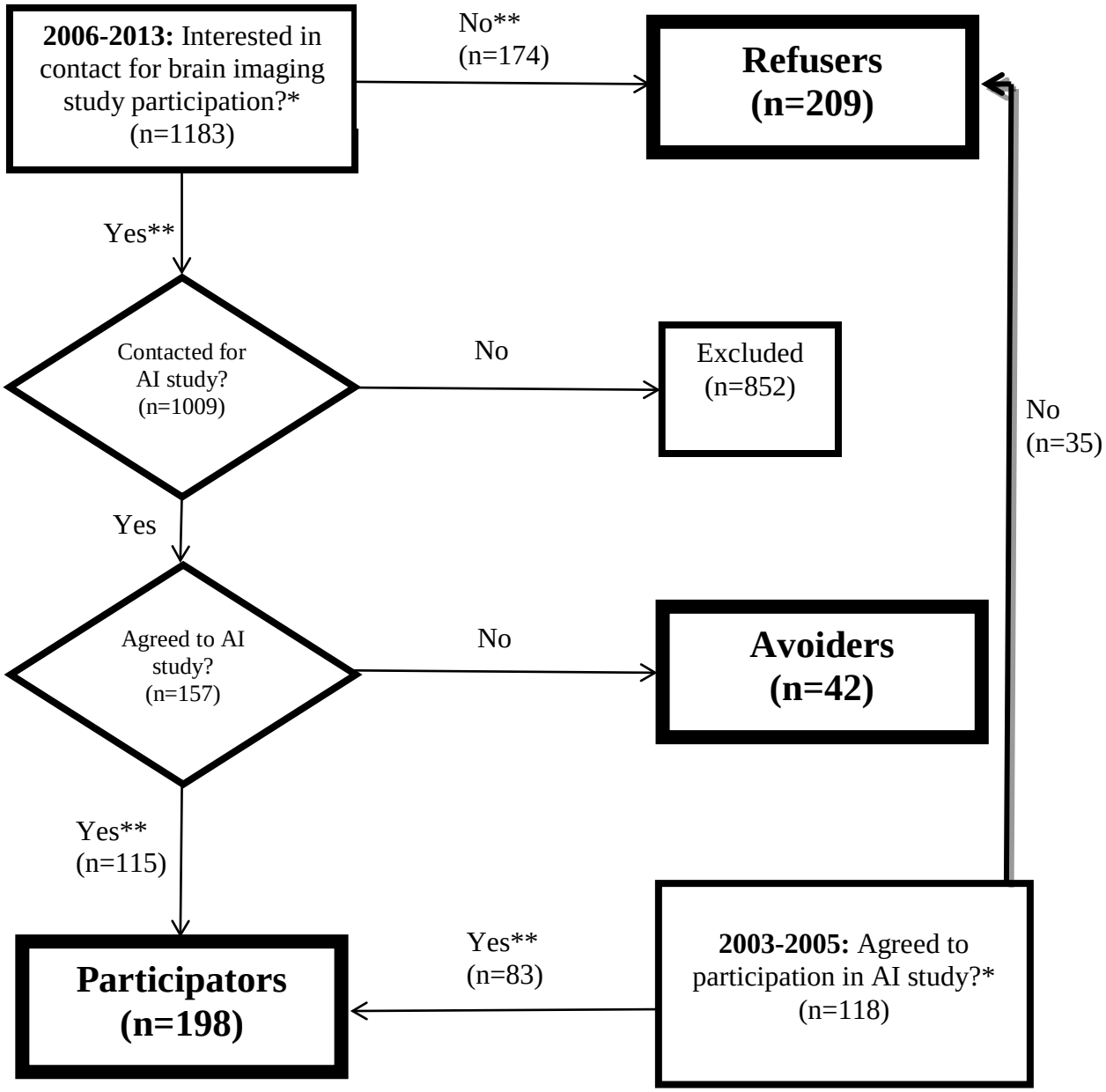
Dependent variable: Interest in amyloid imaging

The variable of focus measures level of interest in amyloid imaging and is a three-level, categorical variable where: 1=amyloid imaging participants ("Participators"); 2=individuals initially indicated interest in being contacted about neuroimaging studies, but later declined amyloid imaging participation ("Avoiders"); and 3=individuals who did not want to be contacted for imaging studies or, if first queried about study participation, always refused ("Refusers"). (See Figure 2 for a flowchart illustrating interest category determination.) All participants were queried about study contact and/or study participation at least once throughout the course of their ADRC participation between 2003 and 2013.

Dependent variable: Participation in amyloid imaging

Participation in amyloid imaging was aggregated from the variable measuring interest in amyloid imaging. While the category Participators remains the same, Avoiders and Refusers were collapsed into one category, Non-Participators. This allowed for examining whether biopsychosocial factors significantly related to interest in AI differed in comparison to factors significantly related to AI participation.

Figure 2. Process for determining amyloid imaging (AI) interest level groupings among a sample of ADRC participants completing one or more cognitive assessments from January 2003 through October 2013



Notes: *Alzheimer Disease Research Center data collection on interest in study contact began in 2006. Individuals asked about AI study participation between 2003 and 2005 were not first asked whether they wanted to be contacted for a study.
**Individuals may have had varied responses (Yes or No) at different time points, and were branched according to their most common response. Individuals who participated in at least one study were deemed Participators.

For the full sample, independent variables were categorized into five groups: Demographic variables (age, sex, race, education); Cognition variables (ADRC diagnostic group, Mini Mental State Exam score, change in ADRC diagnosis, age at onset of cognitive decline); Health (presence of psychiatric diagnosis, modified Charlson Comorbidity Index score); and Family history of dementia. Additional variables included in modeling of the subsample of IWDs were the Cognition variable, age at onset of cognitive symptoms, and Care support relationship. Modeling for IWDs omitted ADRC diagnosis.

Demographic variables

Demographics, including age, sex, race, and education level were extracted for all individuals included in the sample. Age (measured in years), sex (0=Female; 1=Male), race (0=White; 1=African American), and education (1=Less than high school, high school diploma, general equivalency diploma; 2=Some college, Associate's degree, Bachelor's degree; 3=Graduate work, graduate degree) were collected as a component of the social work assessment, and included in the UDS dataset. All other demographic data for each ADRC registry participant were collected from the initial assessment or the first annual assessment using the UDS.

Cognition variables

Cognitive status was captured through several variables, including: diagnostic group (1=dementia; 2=mild cognitive impairment ; 3=no cognitive impairment); and Mini Mental State Exam score (MMSE; Folstein, Folstein, & McHugh, 1975); age at onset of cognitive changes; and change in ADRC diagnosis (0=no change; 1=change in diagnosis). Diagnostic group was

extracted from the ADRC database and was determined by faculty/staff consensus for each participant assessment. Change in ADRC diagnosis was created using diagnostic data from: 1) the initial visit (data that is the primary focus of this dissertation); 2) the first assessment where data on interest in AI was also first collected (if it differed from the initial assessment visit); and 3) the last assessment completed by each study participant within the timeframe under investigation. Individuals converting from no cognitive impairment, mild cognitive impairment (MCI), or dementia to a different diagnosis, using the same three diagnostic categories, were deemed to have experienced a diagnostic change. ADRC diagnostic data were collected via the ADRC Registry. Age of onset was determined at the initial visit for all individuals reporting cognitive symptoms and collected as a part of the UDS system. This variable was included only in analysis for the subset of IWDs, as the full sample includes ADRC participants with no self-report of cognitive impairment.

The Mini Mental State Exam, administered by a trained neuropsychomotrist, is a global measure used to assess neurocognitive functioning and tests patients on memory, orientation, language, recall and attention (Folstein, Folstein, & McHugh, 1975). Scores range from 0 to 30 with higher scores indicative of less cognitive impairment. A review study reported satisfactory reliability and construct validity, as well as high levels of sensitivity for moderate to severe levels of cognitive impairment (Tombaugh & McIntyre, 1992). MMSE data were collected as a part of the UDS dataset.

Health status variables

UDS-based physical health history data were collected during the medical component of the ADRC assessment and were used to determine participant scoring on a modified version of

the Charlson Comorbidity Index (CCI; Charlson, Pompei, Ales, & MacKenzie, 1987; Gill, Koepsell, Hubbard, & Kukull, 2011). The CCI is a weighted index for classifying medical comorbidities according to number of comorbidities and severity of illness. Gill et al. (2011) applied a modified version of the CCI to UDS data, in which four comorbid conditions (cardiac arrest, congestive heart failure, cerebrovascular disease, and diabetes) were included with assigned weights of 1 for each condition. CCI scores range from 0 (no conditions) to 4 (all conditions). Although this modified version excludes comorbid conditions listed in the full version of the CCI because they are not collected by the UDS, most of the more severe conditions in the CCI would mean exclusion from the ADRC registry (e.g. tumor, leukemia, lymphoma, AIDS), and are therefore not applicable. The modified CCI was dichotomized for analysis purposes, where 0=no conditions and 1=1 or more conditions.

Mental health status was measured by the dichotomous variable, presence of psychiatric diagnosis, which was determined for each participant at the ADRC consensus meeting and based on ADRC psychiatric assessment data. Psychiatric diagnostic coding captures any presence of depression, anxiety, or other mental health diagnosis. This data was extracted from the ADRC Registry data.

Family history of dementia

A dichotomous variable indicating whether the participant has any immediate relative (parents, siblings, or children) with a diagnosis of dementia was extracted from UDS data. This variable was aggregated from an in-depth interview on family history completed as a part of the social work assessment. Family history of dementia is a key risk factor for developing the

disease and many ADRC participants point to their own family history as a prime motivator for completing an ADRC memory assessment.

Care support relationship

For the subsample of individuals with dementia, care partner relationship to ADRC participant will be extracted from the UDS dataset. Categories for care support relationship are 1=Spouse or partner; 2=Adult child; and 3=Other relationship.

3.4 DATA ANALYSIS PLAN

3.4.1 Descriptive analyses

Descriptive analyses were conducted to characterize the full sample and subsample of IWDs. For amyloid imaging interest and each categorical independent variable, frequencies were calculated. For continuous independent variables (age, MMSE, age at onset of cognitive symptoms), means and measures of dispersion (standard deviation, range, and skewness) were examined. Each continuous independent variable was examined for normality of distribution. Of note, according to Shapiro-Wilk testing, normality was violated for each continuous variable (See Table 2). One outlier in both age and age at onset of decline was present the Participators group and subsample of IWDS. This individual was kept in the sample throughout analysis because they represented an accurate addition to sample composition. Bivariate and multivariate analyses including and excluding this case resulted in no differences in significant findings. In preparation for bivariate

and multivariate analyses, frequencies of each categorical variable were analyzed and levels were collapsed for variable categories with small cell sizes, as appropriate.

Table 2. Test of normality for age, Mini Mental State Exam score, and age at onset of cognitive decline in the full sample

Continuous variables	Shapiro-Wilk *W*	*df*	*p*
Age	.98	49	<.001
MMSE score	.92	49	<.001
Age at onset of cognitive decline	.97	58	<.001

3.4.2 Bivariate analyses

Amyloid imaging interest groups – Participants, Avoiders, and Refusers – and each independent variable were compared across each biopsychosocial factor (independent variable) for the full sample and subset of IWDs. According to the Shapiro-Wilk *W* test, for the full sample the normality assumption for was not met for the Refusers group (See Table 3). Mean MMSE scores also violated the normality assumption for each AI interest group. When examining normality across groups for the IWD subsample, normality was not met for the Refusers group for age, MMSE score, or age at onset of cognitive decline (See Table 4). Although normality violations occurred, this dissertation continued with one-way fixed effects analysis of variance (ANOVA), as cell sizes were large and previous work points to a robustness of ANOVA, even when this

assumption violation occurs (Schmider, Ziegler, Danay, Beyer, & Bühner, 2015). For significant ANOVA findings, the pattern of differences in the continuous variable across amyloid imaging interest groups was examined with post hoc pairwise comparisons using the Scheffé adjustment. To support ANOVA findings, Kruskal-Wallis H tests were also used. Continuous variable distributions were dissimilar across AI interest groups, for the full sample and dementia subsample, as assessed by visual examination of boxplots. Therefore frequency distributions rather than medians were compared. In instances where significant differences resulted in frequency distributions, pairwise comparisons were performed using Dunn's procedure with a Bonferroni correction for multiple comparisons. Chi-square testing was used for each categorical variable in all instances when at least 80% of cells had frequencies of 5 or more. When cell sizes did not meet this criteria, Fisher's exact test was applied rather than chi-square testing.

Table 3. Test of normality for age and MMSE score for each amyloid imaging interest group, for the full sample

	Age			**MMSE**		
AI Interest Group	Shapiro-Wilk *W*	*df*	*p*	Shapiro-Wilk *W*	*df*	*p*
Refusers	.96	209	<.001	.95	209	<.001
Avoiders	.96	42	.15	.88	42	<.001
Participators	.99	198	.12	.88	198	<.001

Table 4. Test of normality for age, MMSE score, and age at onset of cognitive decline for each amyloid imaging interest group, for the subsample of individuals with dementia

	Age			**MMSE**			**Age at onset**		
AI Interest Group	Shapiro-Wilk *W*	*df*	*p*	Shapiro-Wilk *W*	*df*	*p*	Shapiro-Wilk *W*	*df*	*p*
Refusers	.94	146	<.001	.97	146	.001	.93	146	<.001
Avoiders	.97	24	.60	.93	24	.08	.95	24	.25
Participators	.98	90	.27	.97	90	.03	.98	90	.20

Additionally, two AI participation groups, Participators and Non-Participators, were compared for each biopsychosocial factor. Shapiro-Wilk *W* tests for the full sample revealed normality assumption violations in mean age for Non-Participators and mean MMSE score for both Participators and Non-Participators (See Table 5). For the IWD subsample, normality was violated for mean age, mean MMSE score, and mean age at onset of cognitive decline only for Non-Participators (See Table 6). Independent samples *t*-tests were completed to compare each continuous variable by AI participation group. While normality violations occurred, the robustness of the *t*-test may hold in the case of larger sample sizes (greater than 40) (Lumley, Diehr, Emerson, & Chen, 2002). To support *t*-test findings, Mann-Whitney U tests were also applied for two-group comparisons to continuous variables. As with the three-group comparisons, distributions of age and MMSE score for the full sample, and age, MMSE score, and age at onset of cognitive symptoms for IWDs, were dissimilar for each continuous variable and across AI participation groups, as assessed by visual inspection of boxplots. Therefore frequency distributions rather than medians were compared. As in the case of three-group

comparisons, chi-square testing was used for each categorical variable when at least 80% of cells had frequencies of five or more. Fisher's exact test was applied when cell sizes violated this rule.

Table 5. Test of normality for age and MMSE score for each amyloid imaging participation group, for the full sample

	Age			**MMSE**		
AI Interest Group	Shapiro-Wilk *W*	*df*	*p*	Shapiro-Wilk *W*	*df*	*p*
Non-Participators	.962	251	.000	.945	251	.000
Participators	.989	198	.116	.884	198	.000

Table 6. Test of normality for age, MMSE score, and age at onset of cognitive decline for each amyloid imaging participation group, for the subsample of individuals with dementia

	Age			**MMSE**			**Age at onset**		
AI Interest Group	Shapiro-Wilk *W*	*df*	*p*	Shapiro-Wilk *W*	*df*	*p*	Shapiro-Wilk *W*	*df*	*p*
Non-Participators	.946	170	.000	.967	170	.000	.935	170	.000
Participators	.983	90	.274	.969	90	.029	.980	90	.195

To address low cell sizes and to prepare for multivariate analysis, several variables were aggregated for bivariate analysis, as presented in Table 1. Education level was aggregated to 1.) Less than high school/high school diploma/GED, 2.) Some college/Associate's degree/ Bachelor's degree, and 3.) Graduate work/Graduate degree. Additionally, due to low cell frequencies, bivariate analysis included a comparison of only African American and white individuals. For the dementia subsample, care support relationship was collapsed to 1) Spouse/partner, 2) Adult children, and 3) Other (sibling, other relative, friend/neighbor, paid caregiver/provider, other – not specified).

3.4.3 Multivariate analyses

Due to the categorical nature of the dependent variable, multinomial logistic regression and binomial logistic regression were completed to model biopsychosocial factor associations with amyloid imaging interest and participation, respectively. One benefit of logistic regression is that is does not assume normality, linearity, or homoscedasticity. For the full sample, two models were run for each regression type to address the potential for multicollinearity between ADRC diagnostic group and MMSE score. For the subsample of IWDs one model was run using each regression approach.

Multivariate logistic regression included interest in amyloid imaging as the dependent variable comparing the groups, Refusers, Avoiders, and Participators. Refusers served as the reference group. The first multivariate run for the full sample (Model 1a) included the independent variables: Demographics (age, sex, race, and education level); Cognition (ADRC diagnosis and change in ADRC diagnosis); Health (presence of psychiatric diagnosis and presence of physical health comorbidity); and Dementia family history. The second multivariate

model (Model 1b) included MMSE score in place of ADRC diagnosis. Modeling for the dementia subsample (Model 3) included the following independent variables: Demographics (age, sex, race, and education level); Cognition (MMSE and age at onset of cognitive symptoms); Health (psychiatric diagnosis and presence of physical comorbidity); Dementia family history; and Care Support Relationship.

Binomial logistic regression examined biopsychosocial factors significantly associated with participation in amyloid imaging, comparing Participators to Non-Participators, and with Non-Participators serving as the reference group. For the full sample, two models were again run (Models 2a and 2b), mirroring the multinomial logistic regression modeling described above (Model 1a and 1b, respectively). Binomial logistic regression modeling (Model 4) for the subsample of IWDs was the same as that used in the multivariate modeling described above (Model 3).

All assumptions were met for completing logistic regression analysis, including a linear relationship between the continuous independent variables included in the model and the logit of the dependent variable, interest in amyloid imaging for multinomial logistic regression, and participation in amyloid imaging for binomial logistic regression. No outliers were identified after examining the influential statistics, leverage, Cook's distance, and Dfbeta values, for each regression model. Additionally, the potential for multicollinearity was assessed with no independent variables included in modeling noted to be redundant.

4.0 RESULTS

4.1 OVERVIEW OF RESULTS

Three sections comprise the results chapter. The first includes descriptive results for the dependent variable under investigation, interest in amyloid imaging, as well as descriptive findings for the full sample and the subsample of individuals with dementia (IWDs). Second, bivariate and multivariate analyses address the first research objectives: Examine what psychosocial factors were significantly associated with level of interest in and participation in amyloid imaging. The third section presents bivariate and multivariate results addressing the second research objectives: Among individuals with dementia, examine what psychosocial factors were significantly associated with level of interest in and participation in amyloid imaging.

4.2 DESCRIPTIVE FINDINGS

4.2.1 Interest in amyloid imaging study participation

A total of 449 Alzheimer Disease Research Center (ADRC) participants were queried regarding their interest in participation in an amyloid imaging (AI) study between 2003 and 2013. Table 1

presents the number and percentages of individuals comprising each AI interest group, for all ADRC participants and the subset of participants diagnosed with dementia. Participators, individuals who completed an AI study, and Refusers, those who refused any AI study contact or participation, comprised similarly sized groups (n=198, 44.1% and n=209, 46.5%, respectively; See Table 7). Avoiders, individuals who expressed initial interest in contact regarding AI studies, yet later refused participation, accounted for just 9.4% (n=42) of the sample. Among IWDs, a larger number comprised the Refusers group (n=146, 56.4%), compared to Participators (n=90, 34.4%) and Avoiders (n=24, 9.3%).

Table 7. Grouping of interest in amyloid imaging research participation

	All Participants (N=449)		**Participants with Dementia (n=260)**	
AI Interest Group	**Frequency**	**%**	**Frequency**	**%**
Refuser	209	46.5	146	56.2
Avoider	42	9.4	24	9.2
Participator	198	44.1	90	34.6

A minority of the sample altered their opinion regarding AI study contact or AI study participation (See Table 8). Approximately one fifth of the sample changed interest in being contacted regarding an AI study (n=86, 19.2%), while fewer IWDs changed their interest in contact (n=39, 15%). Smaller numbers of individuals fluctuated in their actual AI participation; when change occurred, more individuals participated in a study, then later refused participation, rather than refusing first and then participating (n=16, 3.6% vs. n=2, 0.4%). The same was true, albeit in smaller frequencies, for IWDs (n=7, 2.7% vs. n=2, 0.8%).

Table 8. Amount of fluctuation in amyloid study interest and participation

	All Participants (N=449)		**Participants with Dementia (n=260)**	
	Frequency	**%**	**Frequency**	**%**
Changed interest in contact	86	19.2	39	15.0
Changed interest in study participation	18	4.0	9	3.5
Participated, then refused participation	16	3.6	7	2.7
Refused participation, then participated	2	0.4	2	0.8

4.2.2 Descriptive results for the full sample

The following independent variables characterized the study sample (N=449) and comprised the psychosocial factors under investigation in relation to AI interest and participation. Table 9 presents frequencies and percentages for categorical variables, as well as means and standard deviations for continuous variables. Independent variables were categorized into five groups: Demographic variables (age, sex, race, and education level); Cognition variables (ADRC diagnostic group, Mini Mental State Exam score, change in ADRC diagnosis, and age at onset of cognitive decline); Health (presence of psychiatric diagnosis and modified Charlson Comorbidity Index score); Family history of dementia; and Care support relationship to the patient.

Demographic variables

Older adults comprise the majority of the sample (Mean age=72.93 years, Standard Deviation=9.71), with over three-quarters over age 65. Half of participants are women (53.7%), and a large majority of the sample is white (91.1%). Other racial groups in the sample, unfortunately in small numbers, include individuals who identify as African American (7.3%), Asian (0.7%), and Multiracial (0.9%). Due to these small numbers, multivariate analysis which includes race as an independent demographic variable, is limited to African American and white individuals.

Finally, educational attainment was high; almost half of the sample completed a Bachelor's degree (16.0%) or graduate work/graduate degree (30.1%). Just 5.6% did not complete high school, while over one quarter completed high school or their General Equivalency Degree (GED; 26.7%), and one fifth completed some college or an Associate's degree (20.3%). To create more equal groupings for analysis, education was aggregated for

bivariate and multivariate analysis to the following groups: less than high school/high school diploma or GED (32.3%); some college or Associate's degree/Bachelor's degree (36.3%); and graduate work or graduate degree (31.4%).

Table 9. Biopsychosocial factors for the full sample and subsample of individuals with dementia

	Full Sample (N=449)	**Subsample of IWDs (n=260)**
Demographics		
Age, Mean (SD), Range	72.93 (9.71), 36-97	74.75 (9.90), 36-97
Sex, n (%)		
Female	241 (53.7)	139 (53.5)
Male	208 (46.3)	121 (46.5)
Race, n (%)		
African American	33 (7.3)	15 (5.8)
Asian	3 (0.7)	1 (0.4)
Multiracial	4 (0.9)	3 (1.2)
White	409 (91.1)	241 (92.7)
Education, n (%)		
Less than HS	25 (5.6)	21 (8.1)
HS or GED	120 (26.7)	87 (33.5)
Some college/Associate's degree	91 (20.3)	55 (21.2)
Bachelor's degree	72 (16.0)	38 (14.6)
Graduate work/Graduate degree	141 (31.4)	59 (22.7)
Cognition		
ADRC diagnosis, n (%)		
Normal	84 (18.7)	
MCI	105 (23.4)	
Dementia	260 (57.9)	260 (100.0)
MMSE Score, Mean (SD), Range	24.14 (4.90), 4-30	21.39 (4.49), 4-30
Change in ADRC diagnosis, n (%)		
No change	377 (84.4)	256 (98.5)
Normal to MCI	6 (1.3)	
Normal to Dementia	9 (2.0)	
MCI to Dementia	38 (8.5)	
MCI to Normal	12 (2.7)	
MCI to Dementia to MCI	1 (0.2)	
Dementia to MCI	4 (0.9)	4 (1.5)
Age at Onset of Cognitive Symptoms*, Mean (SD), Range	68.85 (9.72), 34-92	70.11 (9.43), 34-92

Table 9. (continued)

	Full Sample (N=449)	Subsample of IWDs (n=260)
Health		
Psychiatric diagnosis, n(%)	142 (31.6)	90 (34.6)
Modified CCI Score, n(%)		
0	330 (73.5)	185 (71.4)
1	89 (19.8)	57 (21.9)
2	24 (5.3)	13 (5.0)
3	5 (1.1)	5 (1.9)
4	0 (0.0)	0 (0.0)
Family History		
Family history of dementia, n(%)	237 (52.8)	132 (50.8)
Unknown	1 (0.2)	1 (0.4)
Care Support		
Relationship to patient**, n(%)		
Spouse/partner	267 (59.5)	154 (59.2)
Child	110 (24.5)	89 (34.2)
Sibling	8 (1.8)	5 (1.9)
Other relative	10 (2.2)	7 (2.7)
Friend/neighbor	13 (2.9)	3 (1.2)
Paid caregiver/provider	1 (0.2)	0 (0.0)
Other	5 (1.1)	2 (0.8)
Missing	35 (7.8)	0 (0.0)

Notes: *91 participants did not report memory symptoms; 78 had a diagnosis of Normal; 13 had a diagnosis of MCI

**35 participants did not have an informant; 34 had a diagnosis of Normal; 1 had a diagnosis of Mild Cognitive Impairment

ADRC: Alzheimer Disease Research Center; CCI: Charlson Comorbidity Index; IWD: Individuals with dementia; MCI: Mild cognitive impairment; SD: Standard deviation

Cognition variables

Over half of the sample had a diagnosis of dementia (57.5%), while 23.4% had a diagnosis of mild cognitive impairment (MCI) and 18.7% had no cognitive impairment. Dementia diagnoses included probable Alzheimer's disease (AD; n=212, 81.4%) and possible AD (n=9, 3.6%). While probable AD infers that other potential causes of dementia have been ruled out, a diagnosis of possible Alzheimer's disease is given when the diagnostic team believes that dementia may be due to another cause. Among those diagnosed with possible AD, cerebrovascular disease (n=4), preceding and concurrent depression (n=1), head injury (n=1), frontotemporal dementia (n=1), and other (non-specified) conditions (n=2) were dual diagnoses. Other dementia diagnoses included multiple infarct dementia (n=1, 0.4%), frontotemporal dementia (n=14, 5.4%), other (non-specified and unknown) dementias (n=16, 6.1%), and Lewy Body dementia (n=8, 3.1%). Among those with a non-specified dementia, six had a concurrent psychiatric diagnosis and three were diagnosed with cerebrovascular disease, both of which may contribute to a presentation of dementia symptoms.

Greater specificity of diagnosis also occurred for patients diagnosed with mild cognitive impairment. Amnestic MCI was the primary diagnosis (n=90, 85.7%), while a minority were diagnosed with non-amnestic MCI (n=15, 14.3%). Among patients diagnosed with no cognitive impairment, the majority (n=67, 79.8%) were controls; they neither reported nor exhibited any cognitive impairment symptoms. Within this subgroup of controls, it is worth noting that one participant had cerebrovascular disease and one had a head injury. A minority within the no cognitive impairment group also exhibited or reported symptoms, though not to the point of warranting a cognitive impairment diagnosis. Four (5.6%) had abnormal test scores yet no

subjective complaint, while 13 (15.5%) had complaints of cognitive problems yet normal scoring.

Mean Mini Mental State Exam (MMSE) score was in the mild impairment range for the sample (Mean = 24.14; Standard Deviation=4.90). Scores ranged from 4 to 30, with 11.8% (n=53) obtaining a perfect score (30), indicating a ceiling effect. Overall, 15.6% (n=70) of the sample experienced a change in ADRC diagnosis over the timespan in which amyloid study participation was examined. Change in diagnosis in most cases followed a typical negative trajectory of disease progression, including transitions from MCI to dementia (n=38, 8.5%), normal to dementia (n=9, 2.0%), or normal to MCI (n=6, 1.3%). Interestingly, there was also a handful of participants who "improved" in diagnosis. Twelve participants (2.7%) transitioned to having no cognitive impairment following an initial MCI diagnosis, and four (0.9%) transitioned from dementia to MCI. Just one participant (0.2%) experienced two diagnostic changes, from MCI to dementia, and back to MCI.

Finally, self- and/or informant-reported mean age at onset of cognitive symptoms was in the older adult range (Mean=68.85, Standard Deviation=9.72), and age at onset ranged from 34 to 92 years. Values for this variable were available only for those who reported cognitive symptoms (n=358). One outlier (34 years at onset) was identified.

Health variables

Of the full sample, 31.6% (n=142) had a psychiatric diagnosis identified by the ADRC. This diagnosis could be current and active or a past condition in remission and most commonly represented a depression or anxiety disorder. A modified Charlson Comorbidity Index (CCI) score was calculated for each participant, indicating the presence and severity of physical health

comorbidities. The sample was predominantly free of comorbidity (n=330, 73.5%). As scoring on the CCI increased, the percentage of individuals with each score declined; 19.8% (n=89) had a comorbidity score of one, 5.3% (n=24) had a score of two, 1.1% (n=5) had a score of three, and no participants scored four.

Dementia family history variable

Just over half of the sample reported a family history of dementia (n=237, 52.8%), indicating they had one or more first degree relatives (e.g. parents, siblings, or children) with dementia.

Care support relationship variable

Informant, or care support, relationships were predominantly spousal or partner (n=267, 59.5%), while almost one-quarter were adult children relationships (n=110, n=24.5%). Other included siblings (n=8, 1.8%), other relatives (n=10, 2.2%), friends or neighbors (n=13, 2.9%), paid caregivers (n=1, 0.2%), or other relations (n=5, 1.1%). A proportion of sample did not participate in the ADRC with an identified informant (n=35, 7.8%); most (n=34) had a diagnosis of no cognitive impairment. Although the current criteria for ADRC participation requires that participants are accompanied by an informant, long-time control participants (healthy volunteers with no cognitive impairment) were "grandfathered" in to the ADRC registry and encouraged, but not required, to have an accompanying informant. The protocol follows that if an ADRC control participant transitions to a cognitive impairment diagnosis, an informant must also participate in the diagnostic process. Due to missing data, predominantly comprising the

diagnostic group with no cognitive impairment, this variable was not included in bivariate and multivariate analysis for the full sample. Informant relationship is included in further analysis for the dementia subsample, and referred to as care support relationship, since in this subsample informants also have care partnering, or caregiving, relationships with the patient.

4.2.3 Descriptive results for the subsample of individuals with dementia

Demographic variables

As expected, mean age for IWDs was higher than for the full sample (Mean=74.75, Standard Deviation=9.90), and ages ranged from 36-97 years. An outlier (age 36 years) was also present in the dementia subsample. Similar to the full sample, women comprised the majority of the dementia subsample (n=139, 53.5%), and whites (n=241, 92.7%). African Americans were the second largest racial group (n=15, 5.8%), while the remaining racial groups represented were Asian (n=1, 0.4%) and Multiracial (n=3, 1.2%).

Compared to the full sample, educational attainment was lower among IWDs. Smaller percentages had completed a Bachelor's degree (14.6%, n=38) or graduate work/graduate degree (22.7%, n=59), while a similar percentage had completed some college or an Associate's degree (n=21.2%, n=55). A larger percentage of IWDs compared to the full sample had completed high school or obtained a GED (33.5%, n=87), or had less than a high school degree (8.1%, n=21).

Cognition variables

A description of the types of dementia included in this subsample was provided in the previous section (See Section 4.2.2). As noted, a large majority were diagnosed with probable Alzheimer's disease (81.4%). Mean MMSE score for IWDs was in the mild to moderate

impairment range (Mean=21.39, Standard Deviation=4.49) and scores ranged from four to 30. Mean age at onset of cognitive symptoms was 70.11 years (Standard Deviation=9.43) and ages ranged from 34 to 92 years. As with the full sample, an outlier with age of onset beginning at 34 years is included in this subsample.

Health variables

As with the full sample, approximately one-third of the dementia sample was diagnosed with a psychiatric disorder by ADRC clinicians (n=90, 34.6%). Modified CCI scores shared a similar distribution with the full sample. The majority of the sample scored 0, or had an absence of comorbidity (n=185, 71.4%). Over one quarter (28.8%, n=75) of the sample scored one or more on the index and as before percentages of individuals with each score decreased as CCI score increased (1=21.9%; 2=5.0%; 3=1.9%; 4=0.0%).

Dementia family history variable

As with the full sample, approximately half of the subsample of individuals with dementia had a first degree relative with dementia (50.8%, n=132).

Care support relationship variable

Relationships with care support were predominantly comprised of spouses or partners (n=154, 59.2%), followed by adult children (n=89, 34.2%). The remaining relationships included siblings (n=5, 1.9%), other relatives (n=7, 2.7%), friends or neighbors (n=3, 1.2%), and other relations (n=2, 0.8%).

4.3 BIOPSYCHOSOCIAL FACTORS ASSOCIATED WITH AMYLOID IMAGING INTEREST AND PARTICIPATION FOR THE FULL SAMPLE

This section addresses the research objective of examining biopsychosocial factors associated with interest in amyloid imaging for dementia diagnosis. Results of bivariate analyses are first described, comparing differences in AI interest groups (Refusers, Avoiders and Participators) for each biopsychosocial variable. Next, bivariate findings comparing Participators to Non-Participators (Refusers and Avoiders) are presented.

The results of four logistic regression models are presented. The first two models (Model 1a and Model 1b) apply multinomial logistic regression to examine factors associated with three amyloid interest groups. Refusers serve as the referent group, to which Participators and Avoiders are compared. Model 1a includes the cognition variable ADRC diagnosis (normal, MCI or dementia), while Model 1b uses the variable MMSE score in place of diagnosis. Two binomial logistic regression models follow (Model 2a and Model 2b), which again compare Participators to Non-Participators (referent group). As with multinomial logistic regression, Model 2a includes ADRC diagnosis and Model 2b uses MMSE score.

The full sample was limited to African Americans and whites, due to low cell frequencies for Asian (n=3) and Multiracial (n=4) individuals. Additionally one case (a Refuser) was missing data for dementia family history and a second case was missing comorbidity data, limiting multivariate analysis to N=440.

4.3.1 Bivariate findings for the full sample

Bivariate comparisons of Refusers, Avoiders and Participators

Table 10 presents bivariate findings comparing three AI interest groups. Although interpreted with caution due to normality violations, there was a significant difference in age across groups, $F(2, 446)=18.75$, $p < .001$, $\eta 2=.08$. In post hoc pairwise comparisons, Participators (M= 69.88, SE=.66) were significantly younger than both Refusers (M=75.34, SE=.65), $p<.001$ and Avoiders (M=75.29, SE=1.44), p=.01. There was no significant difference between Refusers and Avoiders. Applying non-parametric testing to the distributions of age scores also resulted in a significant difference between groups, $\chi 2(2)=38.43$, $p<.001$. Post hoc analysis pointed to significant differences in age between Participators (mean rank = 182.32) and Refusers (mean rank = 259.61) ($p<.001$), and Participators and Avoiders (mean rank = 253.99) ($p=.003$), but not between Refusers and Avoiders.

There was no difference in gender across groups. A comparison of African American and white individuals resulted in no significant differences across groups ($p=.42$). Educational attainment did differ across AI interest groups, $\chi 2$ (4, N=449) = 11.42, $p=.02$. An examination of aggregated education groups revealed that more individuals who had completed graduate work/graduate degrees participated in amyloid imaging (38.4%), than refused (25.4%) or avoided (28.6%) amyloid imaging. Refusers, Avoiders, and Participators were comprised of similar percentages of individuals with some college or Associate's or Bachelor's degrees (35.9%, 38.1%, and 36.4%, respectively). Individuals who completed less than high school, a high school diploma, or GED were comprised of more Avoiders (38.8%) and Refusers (33.3%) than Participators (25.3%).

ADRC diagnostic group (normal, mild cognitive impairment, dementia) also differed significantly across amyloid interest groups, $\chi 2$ (4, N=449) = 30.448, p<.001. More Refusers (69.9%) were individuals with dementia, although they also comprised a majority of Avoiders (57.1%) and were less dominant among Participators (45.5%). A greater percentage of individuals with MCI were Participators (33.3%) than Refusers (15.8%) or Avoiders (14.3%). Individuals with no cognitive impairment comprised more Avoiders (28.6%) than Participators (21.2%) or Refusers (14.4%). A significant difference was also noted among those experiencing a change in diagnosis, $\chi 2$ (2, N=449) = 20.023, p<.001. Participators had a greater percentage of individuals who experienced a diagnostic change (23.7%) than Refusers (7.7%) or Avoiders (16.7%).

MMSE scores significantly differed across groups, F(2, 446)=12.317, p <.001, $\eta 2$=.052. Participators (M=25.33, SE=.34) had significantly higher scores than Refusers (M=22.98, SE=.33), p<.001. There were no other significant differences in MMSE scores among amyloid imaging interest groups when comparing Participators to Avoiders (M=24.26, SE=.74), p=.420, or Refusers to Avoiders, p=.286. Non-parametric testing, completed due to normality violations, supported ANOVA findings. The distributions of MMSE scores were significantly different between groups, $\chi 2(2)$=24.61, p<.001. Post hoc analysis also revealed significant differences in MMSE scores between Participators (mean rank = 255.24) and Refusers (mean rank=193.08) (p<.001), but not Participators and Avoiders, or Refusers and Avoiders.

There was additionally a significant difference in the age memory decline began across AI interest groups, F(2, 355)=12.855, p <.001, $\eta 2$=.068. Participators (M=65.91, SE=.77) were significantly younger than Refusers (M=71.15, SE=.71) when memory decline was first noticed, p<.001). There were no other significant differences in age at onset among interest groups when

comparing Participators to Avoiders (M=70.07, SE=1.72), p=.089, or Refusers to Avoiders, p=.845. In non-parametric testing, the distributions of age at onset were significantly different between groups, $\chi 2(2)=26.37$, $p<.001$. Pairwise comparisons were again performed, revealing significant differences between Participators (mean rank = 146.91) and Refusers (mean rank = 205.23) ($p<.001$), but, as before, no significant differences between Participators and Avoiders, or Refusers and Avoiders.

Percentage of individuals with a psychiatric diagnosis was similar across amyloid interest groups and comprised approximately one-third of each group. Presence of comorbidity did significantly differ across AI groups, $\chi 2$ (2, N=448) = 6.890, p=.032. Participators had a greater percentage of individuals with no comorbidity (79.8%) than Refusers (68.8%) or Avoiders (69.0%). Finally, having a first degree relative with dementia did not differ across AI interest groups, $\chi 2$ (2, N=448) = 2.488, p=.288. Approximately half of each AI group was comprised of individuals with a dementia family history.

Table 10. Bivariate comparisons of Refusers, Avoiders, and Participators for the full sample

Independent Variables	Refusers (n=209)	Avoiders (n=42)	Participators (n=198)
Demographics			
Age, Mean (Standard Error)	75.34 (.65)	75.29 (1.44)	69.88 (.66)
F(2, 446)=18.794, p <.001, η2=.078			
Sex, n (%)			
Female	121 (57.9)	23 (54.8)	97 (49.0)
Male	88 (42.1)	19 (45.2)	101 (51.1)
χ2 (2, N=449)=3.27, p=.20			
Race, n (%)			
African American	15 (7.2)	5 (12.5)	13 (6.7)
White	194 (92.8)	35 (87.5)	180 (93.3)
Fisher's Exact Test, p=.42, n=442			
Education, n (%)			
Less than HS/HS or GED	81 (38.8)	14 (33.3)	50 (25.3)
Some college/Associate's degree/Bachelor's degree	75 (35.9)	16 (38.1)	72 (36.4)
Graduate work/Graduate degree	53 (25.4)	12 (28.6)	76 (38.4)
χ2 (4, N=449)=11.42, p=.02			
Cognition			
ADRC diagnosis, n (%)			
Normal	30 (14.4)	12 (28.6)	42 (21.2)
MCI	22 (15.8)	6 (14.3)	66 (33.3)
Dementia	146 (69.9)	24 (57.1)	90 (45.5)
χ2 (4, N=449)=30.45, p<.001			
Change in ADRC diagnosis, n (%)	16 (7.7)	7 (16.7)	47 (23.7)
χ2 (2, N=449)=20.02, p<.001			
MMSE score, Mean (SE)	22.98 (.33)	24.26 (.74)	25.33 (.34)
F(2, 446)=12.317, p <.001, η2=.052			
Age at onset of memory symptoms, Mean (SE)	71.15 (.71)	70.07 (1.72)	65.91 (.77)
F(2, 355)=12.855, p <.001, η2=.068			
Health			
Psychiatric diagnosis, n (%)	68 (32.5)	15 (35.7)	59 (29.8)
χ2 (2, N=449)=.71, p=.70			
Modified CCI score, n (%)			
0	143 (68.8)	29 (69.0)	158 (79.8)
1+	65 (31.3)	13 (31.0)	40 (20.2)
χ2 (2, N=448)=6.89, p=.03			
Family History			
Dementia family history, n (%)	104 (49.8)	20 (48.8)	113 (57.1)
χ2 (2, N=448)=2.49, p=.29			

Notes: ADRC: Alzheimer Disease Research Center; CCI: Charlson Comorbidity Index;
MCI: Mild cognitive impairment; MMSE: Mini Mental State Exam; SE: Standard error

Bivariate comparisons of Participators and Non-Participators

Overall, findings for bivariate comparisons of Participators and Non-Participators were similar to the above three-group differences. Table 11 presents these findings. Age significantly differed between groups, $t(401.53)=6.065$, $p < .001$. Participators were significantly younger than Non-Participators (M=69.88, SD=0.70; M=75.33, SD=.56, respectively). When comparing distributions using non-parametric tests to account for normality violations, Participators (mean rank = 182.32) were again significantly younger than Non-Participators (mean rank = 258.67), $U = 16{,}398$, $z = -6.19$, $p < .001$.

Participators and Non-Participators were roughly equal in percentages of males and females with no significant difference noted, $\chi 2$ (1, N=449) = 3.126, p=.086. There was also no significant difference in AI participation groups between African Americans and whites, $\chi 2$ (1, N=449) = 0.264, p=.716.

Educational attainment significantly differed between AI participation groups, $\chi 2$ (2, N=449) = 10.935, p=.004. Individuals with some college, Associate's, or a Bachelor's degree were roughly equal in percentages between Participators (36.3%) and Non-Participators (36.4%), yet Non-Participators had a greater percentage of individuals who completed less than high school, high school, or a GED than Participators (37.8% vs 25.9%). Inversely, Participators had a greater percentage individuals completing graduate work or a graduate degree than Non-Participators (38.4% vs. 25.9%).

ADRC diagnosis significantly differed between Participators and Non-Participators, $\chi 2$ (1, N=449) = 17.865, p<.001. Participators were comprised of larger percentages of individuals with no cognitive impairment or MCI than Non-Participators (21.2% vs 16.7% and 33.3% vs.

15.5%, respectively) and a smaller percentage of IWDs (45.5% vs 67.7%). Change in diagnosis also significantly differed between groups, $\chi 2$ (2, N=449) = 25.660, p<.001, with Participators comprised of a greater percentage of individuals with a diagnostic change than Non-Participators (23.7% vs. 9.2%).

A significant difference in MMSE score between groups provided an additional signal that Participators were less impaired that Non-Participators, t(444.777) = -4.789, p <.001. Non-parametric testing also pointed to a significant difference in score distributions. MMSE scores for Participators (mean rank = 256.24) were significantly higher than for Non-Participators (mean rank = 200.36), U = 31,034, z = 4.55, p <.001. Mean MMSE score was 25.33 (SE=0.32) for Participators and two points lower for Non-Participators (M=23.20; SE=0.32), falling in the mild dementia range.

Subjective report of age at onset of cognitive symptoms also differed between groups, t(304.302)=-4.966, p <.001. Participators were on the cusp of older adulthood when symptoms were first noted (M=65.91, SE=0.81), while Non-Participators were on average five years older (M=70.99, SE=0.63). Findings from non-parametric testing supported *t*-test findings; age at onset of cognitive decline occurred at a significantly younger age for Participators (mean rank = 146.91) than for Non-Participators (mean rank = 203.28), U = 10,707, z = -5.09, p <.001.

As with comparing the three amyloid interest groups, there was no difference between Participators and Non-Participators in psychiatric diagnosis, $\chi 2$ (1, N=449) = .547, p=.476. Approximately one-third of both Participators and Non-Participators received a psychiatric diagnosis (29.8% vs 33.1%, respectively). The modified CCI score again elicited a significant difference between groups, $\chi 2$ (1, N=448) = 6.888, p=.009. A greater percentage of Participators had an absence of physical health comorbidity (79.7%) than Non-Participators (68.8%).

Although Participators had a greater percentage of first-degree family members with dementia (57.1%) than Non-Participators (49.6%), the difference was not significant, $\chi 2$ (1, N=448) = 2.475, p=.116.

Table 11. Bivariate comparisons of Participators and Non-Participators for the full sample

Independent Variables	Non-Participators (n=251)	Participators (n=198)
Demographics		
Age, Mean (SE)	75.33 (.56)	69.88 (0.70)
t(401.53)=6.065, p <.001		
Sex, n (%)		
Female	144 (57.4)	97 (49.0)
Male	107 (42.6)	101 (51.0)
$\chi 2$ (1, N=449)=3.126, p=.086		
Race, n (%)		
African American	20 (8.0)	13 (6.7)
White	229 (92.0)	180 (93.3)
$\chi 2$ (1, N=442)=0.264, p=.716		
Education, n (%)		
Less than HS/HS or GED	95 (37.8)	50 (25.9)
Some college/Associate's degree/Bachelor's degree	91 (36.3)	72 (36.4)
Graduate work/Graduate degree	65 (25.9)	76 (38.4)
$\chi 2$ (2, N=449)=10.935, p=.004		
Cognition		
ADRC diagnosis, n (%)		
Dementia	170 (67.7)	90 (45.5)
Mild Cognitive Impairment	39 (15.5)	66 (33.3)
Normal	42 (16.7)	42 (21.2)
$\chi 2$ (1, N=449)=17.865, p<.001		
Change in ADRC diagnosis, n (%)	23 (9.2)	47 (23.7)
$\chi 2$ (2, N=449)=25.660, p<.001		
MMSE score, Mean (SE)	23.20 (0.32)	25.33 (0.31)
t(444.777)=-4.789, p <.001		
Age at onset of cognitive symptoms, Mean (SE)	70.99 (0.63)	65.91 (0.81)
t(304.302)=-4.966, p <.001		
Health		
Psychiatric diagnosis, n (%)	83 (33.1)	59 (29.8)
$\chi 2$ (1, N=449)=.547, p=.476		
CCI score, n (%)		
0	172 (68.8)	158 (79.7)
1+	78 (31.2)	40 (20.2)
$\chi 2$ (1, N=448)=6.888, p=.009		
Family History		
Dementia family history, n (%)	124 (49.6)	113 (57.1)
$\chi 2$ (1,N=448)=2.475, p=.116		

Note: ADRC: Alzheimer Disease Research Center; CCI: Charlson Comorbidity Index; MMSE: Mini Mental State Exam; MCI: Mild cognitive impairment; SE: Standard error

4.3.2 Multivariate findings for the full sample

Multinomial logistic regression for the full sample

Overall, Model 1a, using Refusers as the referent group, was statistically significant, $\chi 2$ (22) = 76.39, p<.001 and explained 19% (Nagelkerke R^2) of the variance in amyloid imaging interest. Table 12 presents findings from Model 1a. Two of the nine variables included in the model had statistically significant associations. Age was significantly related to being a Participator or a Refuser, b=-0.05, $\chi 2$ (1) = 18.05, p<0.001. With each year of decreased age, the odds of being a Participator, compared to being a Refuser, increased by 5% (OR=0.95, 95% CI, 0.93-0.97). Whether a change in diagnosis occurred was also significantly related to being a Participator or a Refuser, b=-0.84, $\chi 2$ (1)=5.18, p=0.02. Individuals who had experienced no diagnostic transition were almost half as likely to be a Participator as a Refuser (OR=0.43, 95%, 0.21-0.89). No biopsychosocial factors were significantly associated with being an Avoider versus being a Refuser.

Table 12. Model 1a: Multinomial logistic regression of factors associated with interest in amyloid imaging, with ADRC diagnosis included in modeling (N=440)

AI Interest Group		Estimate	Std. Error	Wald	df	*p*	Odds Ratio	95% Confidence Interval	
								Lower Bound	Upper Bound
Avoider	Intercept	0.38	1.93	0.04	1	0.845			
	Age	0.00	0.02	0.00	1	0.955	1.00	0.96	1.04
	Sex, female	-0.22	0.39	0.32	1	0.574	0.80	0.37	1.73
	Race, white	-0.65	0.59	1.24	1	0.266	0.52	0.16	1.65
	Education, <HS/HS/GED (referent)								
	Some college/Associate's/Bachelor's	-0.10	0.49	0.05	1	0.833	0.90	0.34	2.37
	Graduate work/Graduate degree	0.15	0.43	0.12	1	0.726	1.16	0.50	2.67
	ADRC Diagnosis, Normal (referent)								
	MCI	-0.89	0.46	3.70	1	0.054	0.41	0.17	1.02
	Dementia	-1.18	0.63	3.53	1	0.060	0.31	0.09	1.05
	Change in ADRC diagnosis, no	-0.77	0.60	1.66	1	0.197	0.46	0.14	1.49
	Psychiatric diagnosis, no	-0.38	0.39	0.98	1	0.324	0.68	0.32	1.45
	Modified CCI, 0	0.20	0.42	0.22	1	0.640	1.22	0.54	2.75
	Dementia family history, no	0.15	0.36	0.17	1	0.680	1.16	0.58	2.33
Participator	Intercept	4.36	1.18	13.64	1	0.000			
	Age	**-0.05**	**0.01**	**18.05**	**1**	**0.000**	**0.95**	**0.93**	**0.97**
	Sex, female	-0.30	0.23	1.60	1	0.206	0.75	0.47	1.18
	Race, white	-0.26	0.43	0.35	1	0.552	0.77	0.33	1.80
	Education, <HS/HS/GED (referent)								
	Some college/Associate's/Bachelor's	0.40	0.29	1.94	1	0.164	1.50	0.85	2.65
	Graduate work/Graduate degree	0.28	0.27	1.05	1	0.305	1.32	0.78	2.23
	Diagnosis, Normal (referent)								
	MCI	-0.43	0.31	1.94	1	0.163	0.65	0.36	1.19
	Dementia	0.12	0.36	0.11	1	0.746	1.12	0.55	2.28
	Change in ADRC diagnosis, no	**-0.84**	**0.37**	**5.18**	**1**	**0.023**	**0.43**	**0.21**	**0.89**
	Psychiatric diagnosis, no	0.25	0.24	1.01	1	0.316	1.28	0.79	2.06
	Modified CCI, 0	0.49	0.26	3.47	1	0.062	1.63	0.98	2.72
	Dementia family history, no	-0.26	0.22	1.41	1	0.235	0.77	0.50	1.18

Note: R^2=.16 (Cox & Snell), .19 (Negelkerke). Model $\chi 2(22)=76.39$, $p<.001$.
HS=high school; GED=General Equivalency Diploma; ADRC=Alzheimer Disease Research Center; CCI=Charlson Comorbidity Index

Model 1b, with Refusers as the referent group and the cognition variable, ADRC diagnosis, replaced with MMSE score, is presented in Table 13. The logistic regression model was statistically significant, $\chi 2(20)=75.20$, $p<.001$, and again explained 19% (Nagelkerke R^2) of the variance in amyloid imaging interest. Four of the nine variables included in the model had statistically significant associations. Age remained significantly associated with being a Participator or a Refuser, b=-0.05, $\chi 2(1)=18.96$, $p<.001$. With each year of decreased age, the odds of being a Participator, compared to a Refuser, increased by 5% (OR=0.95, 95% CI, 0.93-0.97). MMSE score was also significantly related to whether an individual participated in or refused amyloid imaging, b=0.07, $\chi 2(1)=7.28$, p=0.01. With each additional point increase in MMSE score, the odds of being a Participator, rather than a Refuser, increased by 7% (OR=1.07, 95% CI, 1.02-1.12). Change in diagnosis continued to have a significant relationship with being a Participator versus a Refuser, b=-0.96, $\chi 2(1)=8.47$, $p<.001$. Those who had no change in diagnosis were one-third as likely to be a Participator compared to a Refuser (OR=.38, 95% CI, 0.20-0.73). Lastly, presence of health comorbidities (measured by the modified Charlson Comorbidity Index) emerged as having a significant relationship to being a Participator compared to a Refuser, b=0.51, $\chi 2(1)=3.86$, p=.049. Participators were 1.7 times as likely as Refusers to have no comorbidities (OR = 1.67, 95% CI, 1.00-2.77). No psychosocial factors were significantly associated with being an Avoider versus being a Refuser.

Table 13. Model 1b. Multinomial logistic regression of factors associated with interest in amyloid imaging, with MMSE score included in modeling (N=440)

AI Interest Group		Estimate	Std. Error	Wald	df	*p*	Odds Ratio	95% Confidence Interval	
								Lower Bound	Upper Bound
Avoider	Intercept	-2.01	2.18	0.85	1	0.356			
	Age	0.00	0.02	0.03	1	0.861	1.00	0.96	1.04
	MMSE score	0.05	0.04	1.32	1	0.251	1.05	0.97	1.13
	Sex, female	-0.13	0.39	0.11	1	0.742	0.88	0.41	1.88
	Race, white	-0.67	0.58	1.34	1	0.247	0.51	0.16	1.59
	Education, <HS/HS/GED								
	Some college/Associate's/Bachelor's	-0.06	0.50	0.01	1	0.904	0.94	0.36	2.49
	Graduate work/Graduate degree	0.21	0.42	0.25	1	0.616	1.24	0.54	2.84
	Change in ADRC diagnosis, no	-0.58	0.54	1.17	1	0.279	0.56	0.19	1.60
	Psychiatric Diagnosis, no	-0.28	0.38	0.55	1	0.460	0.76	0.36	1.58
	Modified CCI, 0	0.30	0.41	0.52	1	0.469	1.35	0.60	3.03
	Dementia family history, no	0.16	0.36	0.21	1	0.649	1.18	0.59	2.36
Participator	Intercept	2.77	1.32	4.39	1	0.036			
	Age	**-0.05**	**0.01**	**18.96**	**1**	**0.000**	**0.95**	**0.93**	**0.97**
	MMSE score	**0.07**	**0.03**	**7.28**	**1**	**0.007**	**1.07**	**1.02**	**1.12**
	Sex, female	-0.34	0.23	2.10	1	0.147	0.71	0.45	1.13
	Race, white	-0.26	0.43	0.36	1	0.547	0.77	0.33	1.80
	Education, <HS/HS/GED								
	Some college/Associate's/Bachelor's	0.28	0.30	0.87	1	0.350	1.32	0.74	2.35
	Graduate work/Graduate degree	0.20	0.27	0.55	1	0.459	1.22	0.72	2.08
	Change in ADRC diagnosis, no	**-0.96**	**0.33**	**8.47**	**1**	**0.004**	**0.38**	**0.20**	**0.73**
	Psychiatric Diagnosis, no	0.23	0.24	0.93	1	0.336	1.26	0.79	2.03
	Modified CCI, 0	**0.51**	**0.26**	**3.86**	**1**	**0.049**	**1.67**	**1.00**	**2.77**
	Dementia family history, no	-0.21	0.22	0.94	1	0.332	0.81	0.53	1.24

Note: R^2=.16 (Cox & Snell), .19 (Negelkerke). Model $\chi 2(20)=75.20$, $p<.001$.
HS=high school; GED=General Equivalency Diploma; MMSE=Mini Mental State Exam; ADRC=Alzheimer Disease Research Center; CCI=Charlson Comorbidity Index

Binary logistic regression for the full sample

Refusers and Avoiders were combined to comprise the Non-Participators group (referent group) and compared to Participators. As in multinomial logistic regression and to account for the potential of multicollinearity between the cognition variables, ADRC diagnosis and MMSE score, two models were run, separating these variables. Model 2a includes ADRC diagnosis as an independent variable while Model 2b includes MMSE score as an independent variable.

Model 2a was statistically significant, $\chi 2$ (11) = 66.45, p<.001 and explained 19% (Nagelkerke R^2) of the variance in amyloid imaging participation (Table 14). Two of the eleven independent variables were statistically significant in modeling. Younger age was significantly related to whether individuals participated in amyloid imaging, b=-0.05, $\chi 2$ (1) = 19.97, p<0.001. With each year of decreased age, participation on amyloid imaging increased by 5% (OR=0.95, 95% CI, 0.93-0.97). Change in cognition diagnosis was also significantly associated with amyloid imaging participation, b=0.67, $\chi 2$ (1) = 3.95, p=0.047. Individuals who had gone through a change in diagnosis were almost two times as likely to participate in amyloid imaging compared to those whose diagnosis remained the same, (OR=1.96; 95% CI, 1.01-3.80).

Table 14. Model 2a: Binary logistic regression of factors associated with participation in amyloid imaging, with ADRC diagnosis included in modeling (N=440)

	Estimate	Std. Error	Wald	df	*p*	Odds Ratio	95% Confidence Interval	
							Lower Bound	Upper Bound
Constant	3.19	0.90	12.68	1	.000	24.23		
Age	**-0.05**	**0.01**	**19.96**	**1**	**.000**	**0.95**	**0.93**	**0.97**
Sex, female	0.26	0.22	1.30	1	.254	1.29	0.83	2.00
Race, white	0.11	0.41	0.08	1	.779	1.12	0.50	2.49
Education, <HS/HS/GED (referent)			2.36	2	.307			
Some college/Associate's/Bachelor's	0.25	0.26	0.92	1	.338	1.28	0.77	2.13
Graduate work/Graduate degree	0.43	0.28	2.34	1	.126	1.53	0.89	2.66
ADRC diagnosis, Normal (referent)			3.99	2	.136			
MCI	0.36	0.34	1.14	1	.286	1.43	0.74	2.78
Dementia	-0.24	0.29	0.71	1	.400	0.79	0.45	1.38
Change in ADRC diagnosis, no	**0.67**	**0.34**	**3.95**	**1**	**.047**	**1.96**	**1.01**	**3.80**
Psychiatric diagnosis, no	-0.31	0.23	1.76	1	.185	0.73	0.46	1.16
Modified CCI, 0	-0.46	0.25	3.21	1	.073	0.63	0.39	1.04
Dementia family history, no	0.28	0.21	1.80	1	.180	1.33	0.88	2.00

Notes: R^2=.14 (Cox & Snell), .19 (Negelkerke). Model $\chi2(11)=66.45$, $p<.001$.
HS=high school; GED=General Equivalency Diploma; ADRC=Alzheimer Disease Research Center; MCI=mild cognitive impairment; CCI=Charlson Comorbidity Index

Model 2b, which includes MMSE score as an independent variable, was statistically significant, $\chi2$ (11) = 68.84, p<.001 and explained 39% (Nagelkerke R^2) of the variance in amyloid imaging participation (Table 15). Three of the eleven biopsychosocial factors were statistically significant in modeling. Age remained significantly associated to whether individuals participated in amyloid imaging, b=-0.05, $\chi2$ (1) = 21.21, p<0.001. With each year of decreased age, participation in amyloid imaging increased by 5% (OR=0.95, 95% CI, 0.93-0.97). Higher MMSE score was significantly associated with amyloid imaging participation, b=0.06, $\chi2$ (1) = 6.18, p=0.013. As MMSE score increased by one, the odds of participating in amyloid imaging increased by 6% (OR=1.06, 95% CI 1.01-1.11). Experiencing a diagnostic change was

also significantly related to amyloid imaging participation, b=.83, $\chi 2$ (1) = 7.65, p=0.006. Individuals who underwent a diagnostic transition were more than twice as likely to participate in amyloid imaging, than not participate (OR=2.30, 95% CI, 1.28-4.16).

Table 15. Model 2b: Binary logistic regression of factors associated with participation in amyloid imaging, with MMSE included in modeling (n=440)

	Estimate	Std. Error	Wald	df	*p*	Odds Ratio	95% Confidence Interval	
							Lower Bound	Upper Bound
Constant	1.816	1.080	2.827	1	.093	6.145		
Age	**-.053**	**.012**	**21.211**	**1**	**.000**	**.948**	**.927**	**.970**
Sex, female	.315	.223	1.991	1	.158	1.370	.885	2.122
Race, white	.112	.407	.076	1	.783	1.119	.503	2.486
Education, <HS/HS/GED (referent)			1.031	2	.597			
Some college/Associate's/Bachelor's	.160	.261	.377	1	.539	1.174	.704	1.957
Graduate work/Graduate degree	.288	.284	1.028	1	.311	1.334	.764	2.330
MMSE Score	**.060**	**.024**	**6.180**	**1**	**.013**	**1.062**	**1.013**	**1.113**
Change in ADRC diagnosis, no	**.834**	**.302**	**7.647**	**1**	**.006**	**2.303**	**1.275**	**4.159**
Psychiatric diagnosis, no	-.282	.232	1.479	1	.224	.754	.479	1.188
Modified CCI, 0	-.458	.251	3.315	1	.069	.633	.387	1.036
Dementia family history, no	.243	.211	1.321	1	.250	1.274	.843	1.927

Notes: R^2=.29 (Cox & Snell), .39 (Negelkerke). Model $\chi 2(10)$=68.84, p<.001.
HS=high school; GED=General Equivalency Diploma; MMSE=Mini Mental State Exam; ADRC=Alzheimer Disease Research Center; CCI=Charlson Comorbidity Index

4.3.3 Summary of findings for full sample

In bivariate analysis, being younger, having more education, less cognitive impairment (according to both ADRC diagnosis and MMSE score), experiencing a change in diagnosis, a

younger age at onset of cognitive symptoms, and no physical comorbidity were all significantly associated with greater interest in amyloid imaging participation, when compared to refusing any contact regarding AI (Refusers) or eventual refusal of AI participation (Avoiders). The same findings held when comparing AI Participators to AI Non-Participators. Participators were significantly younger, had more education, less cognitive impairment, experienced diagnostic transition, were younger at age of onset, and had no physical health comorbidities.

In multinomial logistic regression, younger age, better MMSE score, and the occurrence of a cognition-related diagnostic transition were significantly associated with being a Participator, compared to a Refuser. An absence of physical health comorbidities only emerged as having a significant association with being a Participator in modeling that included MMSE score as a measure of cognition. There were no significant associations with being a Refuser in comparison to an Avoider. Binary logistic regression, comparing Participators to Non-Participators, produced similar findings, with younger age, better MMSE score, and diagnostic transition significantly related to participation in amyloid imaging.

4.4 BIOPSYCHOSOCIAL FACTORS ASSOCIATED WITH AMYLOID IMAGING INTEREST AND PARTICIPATION FOR THE SUBSAMPLE OF INDIVIDUALS WITH DEMENTIA

This section addresses the research aim of examining biopsychosocial factors that are associated with of interest in and participation in amyloid imaging among a subsample of individuals with dementia. As with the full sample, results of bivariate analyses are first described, comparing differences in AI interest groups (Refusers, Avoiders and Participators) for each psychosocial

variable. Next, bivariate findings comparing Participators to Non-Participators (Refusers and Avoiders) are presented. The results of four logistic regression models are presented. The first model (Model 3) applies multinomial logistic regression to examine factors associated with the three amyloid interest groups, with Refusers serving as the referent group. A binomial logistic regression model follows (Model 4), which again compare Participators to Non-Participators (referent group).

This subsample was also limited to African Americans and whites, excluding 1 individual who was Asian and 3 individuals who were Multiracial. Additionally one case (a Refuser) was missing data for dementia family history and a second case was missing comorbidity data, limiting multivariate analysis to N=260.

4.4.1 Bivariate findings for the subsample of individuals with dementia

Bivariate comparisons of Refusers, Avoiders, and Participators

The following table (Table 16) presents findings comparing three amyloid interest groups with each psychosocial variable under investigation. There were significant differences across groups for age, $F(2, 256)=9.836$, $p < .001$, $\eta 2=.071$. Participators ($M = 71.17$, $SE = 1.02$) were significantly younger than both Refusers ($M = 76.89$, $SE = 0.79$), $p<.001$, but not Avoiders ($M = 75.29$, $SE = 1.44$). There was no significant difference in age between Refusers and Avoiders. Addressing normality violations, the distributions of age were also significantly different between groups, $\chi 2\ (2) = 19.78$, $p<.001$. Post hoc analysis also revealed significant differences in age between Participators (mean rank = 102.87) and Refusers (mean rank = 147.65) ($p<.001$), but no significant differences between Participators and Avoiders, or Refusers and Avoiders.

Percentages of males and females were not significantly different across amyloid interest groups, $\chi 2$ (2, 260) = 1.190, p=.552, and comprised approximately half of each group. There were no differences in percentages of African Americans and whites across amyloid interest groups (p=0.718). Due to small numbers of African Americans individuals within the sample, the majority were whites across groups. No significant differences in the three-category group of educational attainment were found across amyloid interest groups, $\chi 2$ (4, N=260) = 2.852, p=.589.

MMSE scores did not significantly differ across groups, F(2, 256)=1.499, p=.225, $\eta 2$=.012, and all fell within the mild dementia range. Non-parametric testing resulted in the same finding; distributions of MMSE score did not significantly differ between groups, $\chi 2$ (2) = 2.33, p=.312. Age at onset of cognitive symptoms significantly differed across interest groups, F(2, 256)=7.947, p <.001, $\eta 2$=.058. Post hoc comparisons revealed that Participators (M=66.97, SE=0.98) were significantly younger at age of onset than Refusers (M=71.87, SE=0.76), p<.001, while there were no differences between Participators and Avoiders (M=70.83, SE=1.88) or Refusers and Avoiders. In non-parametric testing, distributions of age at onset were again significantly different between groups, $\chi 2$ (2) = 14.44, p=.001. This post hoc analysis revealed significant differences in age between Participators (mean rank = 106.41) and Refusers (mean rank = 144.51), p<.001, but no significant differences between Participators and Avoiders, or Refusers and Avoiders.

Psychiatric diagnosis did not significantly differ across amyloid imaging interest groups, $\chi 2$ (2, N=259) =0.789, p=.674. Individuals with a psychiatric diagnosis comprised 32.9% of Refusers, 41.7% of Avoiders, and 35.6% of Participators. Presence of comorbidities did significantly differ across amyloid interest groups, $\chi 2$ (2, N=260)=10.014, p=.007. Participators

(83.3%) had a larger percentage of individuals with no comorbidity, than Refusers (65.1%) or Avoiders (62.5%).

Having at least one first degree relative with dementia did not differ across amyloid imaging interest groups, $\chi 2$ (2, N=259) =.101, p=.964. About half of each group was comprised of individuals with a family history. Care support relationship to the patient did significantly differ across AI interest groups, $\chi 2$ (4, N=260)=15.538, *p*=.004. Participators (74.4%) had a greater percentage of spousal or partner relationships (74.4%), than Refusers (49.3%) or Avoiders (62.5%). Refusers had greater a greater percentage of adult child (41.1%) or other care partners (9.6%) than Avoiders (33.3%; 4.2%) or Participators (23.3%; 2.2%).

Table 16. Bivariate comparisons of Refusers, Avoiders, and Participators for the subsample of individuals with dementia (N=260)

Independent Variables	Refuser (n=146)	Avoider (n=24)	Participator (n=90)
Demographics			
Age, Mean (SE)	76.89 (.79)	75.29 (1.44)	71.17 (1.02)
F(2, 256)=9.836, p <.001, η2=.071			
Sex, n (%)			
Female	82 (56.2)	11 (45.8)	46 (51.1)
Male	64 (43.8)	13 (54.2)	44 (48.9)
χ2 (2, 260)=1.190, *p*=.552			
Race, n (%)			
African American	9 (6.2)	2 (8.7)	4 (4.6)
White	137 (93.8)	21 (91.3)	83 (95.4)
Fisher's Exact Test, p=.718			
Education, n (%)			
Less than HS/HS or GED	63 (43.2)	12 (50.0)	33 (36.7)
Some college/Associate's degree/Bachelor's degree	51 (34.9)	9 (37.5)	33 (36.7)
Graduate work/Graduate degree	32 (21.9)	3 (12.5)	23 (26.7)
χ2 (4, N=260)=2.852, *p*=.589			
Cognition			
MMSE Score, Mean (SE)	21.06 (.37)	20.88 (.92)	22.05 (.48)
F(2, 256)=1.499, p=.225, η2=.012			
Age at Onset of Memory Symptoms, Mean (SE)	71.87 (.76)	70.83 (1.88)	66.97 (.98)
F(2, 256)=7.947, p <.001, η2=.058			
Health			
Psychiatric diagnosis, n (%)	48 (32.9)	10 (41.7)	32 (35.6)
χ2 (2, N=259)=.789, *p*=.674			
Modified CCI Score, n (%)			
0	95 (65.1)	15 (62.5)	75 (83.3)
1+	51 (34.9)	9 (37.5)	15 (16.7)
χ2 (2, N=260)=10.014, *p*=.007			
Family History			
Dementia family history, n (%)	75 (51.4)	11 (47.8)	46 (51.1)
χ2 (2, N=259)=.101, *p*=.964			
Care Support			
Informant Relationship to Patient, n (%)			
Spouse/partner	72 (49.3)	15 (62.5)	67 (74.4)
Child	60 (41.1)	8 (33.3)	21 (23.3)
Other	14 (9.6)	1 (4.2)	2 (2.2)
χ2 (4, N=260)=15.538, *p*=.004			

Notes: CCI: Charlson Comorbidity Index; MCI: Mild cognitive impairment;
MMSE: Mini Mental State Exam; SE: Standard error

Bivariate comparisons of Participators and Non-Participators

Table 17 presents findings comparing Participators and Non-Participators for the subsample of IWDs. Age was again significantly different between Participators and Non-Participators, t(153.57)=4.059, p <.001. Participators were on average five years younger than Non-Participators (M=71.23, SE=1.14; M=76.62, SE=0.68, respectively). Non-parametric testing resulted in the same finding, U = 5,163, z = -4.31, p < .001.

No differences were found between groups by sex, $\chi 2$ (1, 260) = .306, p=.603. Females comprised 51.1% of Participators and 54.7% of Non-Participators. The same was true when comparing African Americans with whites, p=.780. Due to low numbers of African Americans in the sample, the majority of both Participators and Non-Participators were white (95.4% and 93.5%, respectively).

Educational attainment did not significantly differ between Participators and Non-Participators, $\chi 2$ (2, N=260) = 1.776, p=.412. Individuals who completed less than high school, a high school diploma, or GED comprised a greater percentage of Non-Participators (44.1%) than Participators (36.7%). Those with some college or an Associate's or Bachelor's degree had fairly similar percentages represented among Participators (36.7%) and Non-Participators (35.3%). Individuals who completed graduate work or a graduate degree comprised a larger percentage of Participators (26.7%) than Non-Participators (20.6%).

Mini Mental State Exam scores were not significantly different between groups, t(258)=-1.77, p =.078. Mean scores were in the mild dementia range for both Participators (M=22.07, SE=0.44) and Non-Participators (M=21.04, SE=0.35). The same non-significant finding was derived from non-parametric testing, U=8.519, z=1.51, p=.13. Age at onset of cognitive decline did significantly differ between amyloid imaging participation groups, t(156.34)=3.67, p <.001.

Non-parametric testing resulted in the same finding, U = 5,482, z = -3.76, p < .001. Participators were significantly younger at age of onset (M=67.07, SE=1.08) than Non-Participators (M = 71.72, SE = 0.66).

Presence of a psychiatric diagnosis did not differ between amyloid imaging participation groups, $\chi 2$ (2, N=259) = 0.79, p=.674. About one-third of both Participators and Non-Participators were comprised of individuals with a psychiatric diagnosis (35.6% and 34.1%, respectively). Presence of physical health comorbidity significantly differed between groups, $\chi 2$ (1, N=260) = 9.95, p=.002. Participators had a lower percentage of individuals with comorbidity (16.7%) than Non-Participators (35.3%).

There was no significant difference between amyloid imaging participation groups in whether individuals had a first degree relative with dementia, $\chi 2$ (1, N=259)=.001, p=.973. About half of each group was comprised of individuals with a dementia family history (Participators, 51.1%; Non-Participators, 50.9%).

Care support relationship significantly differed between AI participation groups, p=.001. Spousal or partner relationships comprised a greater percentage of Participators (74.4%) than Non-Participators, while adult child and other care partner relationships accounted for greater percentages of Non-Participators (40.0% and 8.8%) than Participators (23.3% and 2.2%).

Table 17. Bivariate comparisons of Participators and Non-Participators for the subsample of individuals with dementia (N=260)

Independent Variables	Non-Participator (n=170)	Participator (n=90)
Demographics		
Age, Mean (Standard Error)	76.62 (0.68)	71.23 (1.14)
U = 5,163, z = -4.31, p < .001		
Sex, n (%)		
Female	93 (54.7)	46 (51.1)
Male	77 (45.3)	44 (48.9)
$\chi 2$ (1, 260)=.306, p=.603		
Race, n (%)		
African American	11 (6.5)	4 (4.6)
White	158 (93.5)	83 (95.4)
Fisher's Exact Test, p=.780		
Education, n (%)		
Less than HS/HS or GED	75 (44.1)	33 (36.7)
Some college/Associate's degree/Bachelor's degree	60 (35.3)	33 (36.7)
Graduate work/Graduate degree	35 (20.6)	24 (26.7)
$\chi 2$ (2, N=260)=1.776, p=.412		
Cognition		
MMSE Score (with WORLD), Mean (SE)	21.04 (0.35)	22.07 (0.44)
U = 8,519, z = 1.51, p = .13		
Age at Onset of Memory Symptoms, Mean (SE)	71.72 (0.66)	67.07 (1.08)
U = 5,482, z = -3.76, p < .001		
Health		
Psychiatric diagnosis, n (%)	58 (34.1)	32 (35.6)
$\chi 2$ (2, N=259)=.789, p=.674		
Modified Charlson Comorbidity Score, n (%)		
0	110 (64.7)	75 (83.3)
1+	60 (35.3)	15 (16.7)
$\chi 2$ (1, N=260)=9.948, p=.002		
Family History		
Dementia family history, n (%)	86 (50.9)	46 (51.1)
$\chi 2$ (1, N=259)=.001, p=.973		
Care Support		
Informant Relationship to Patient, n (%)		
Spouse/partner	87 (51.2)	67 (74.4)
Child	68 (40.0)	21 (23.3)
Other	15 (8.8)	2 (2.2)
$\chi 2$ (1, N=260)=14.076, p<.001		

Notes: CCI: Charlson Comorbidity Index; MCI: Mild cognitive impairment; MMSE: Mini Mental State Exam; SE: Standard error

4.4.2 Multivariate findings for the subsample of individuals with dementia

Multinomial logistic regression for the subsample of individuals with dementia

The multinomial logistic regression model (Model 3, See Table 18), comparing Participators and Avoiders to the referent group, Refusers, was statistically significant, $\chi 2(24)=48.01$, p=.003, and explained 21% (Nagelkerke R^2) of the variance in amyloid imaging interest. Presence of comorbidity was significantly associated with being a Participator compared to a Refuser, *b*=-1.05, $\chi 2(1)=7.91$, *p*=0.005. Individuals with no comorbidity were almost three times more likely to be a Participator, than a Refuser (OR=2.85, 95% CI, 1.37-5.90). Care support relationship to the patient was an additional factor distinguishing Participators from Refusers. Having a spouse or partner in a care support role rather than an adult child or another type of care partner significantly related to participation in amyloid imaging, compared to refusal to any contact regarding imaging (*b*=-0.76, $\chi 2(1)=4.03$, *p*=0.045 and *b*=-2.25, $\chi 2(1)=7.62$, *p*=0.006, respectively). Individuals with an adult child providing care support were half as likely to be a Participator than a Refuser (OR=.47, 95% CI, 0.22-0.98), while individuals with care support other than a spouse/partner or adult child were one-tenth as likely to be a Participator than a Refuser (OR=0.11, 95% CI, 0.02-0.52). No other psychosocial variables differentiated Predictors from Refusers. Additionally, no factors significantly distinguished Avoiders from Refusers.

Table 18. Model 3: Multinomial logistic regression of factors associated with participation in amyloid imaging for the subsample of individuals with dementia (N=255)

AI Interest Group		Estimate	Std. Error	Wald	df	*p*	Odds Ratio	95% Confidence Interval	
								Lower Bound	Upper Bound
Avoider	Constant	1.12	2.52	0.20	1	0.657			
	Age	-0.08	0.08	0.91	1	0.341	0.93	0.79	1.08
	MMSE score	0.00	0.05	0.00	1	0.993	1.00	0.90	1.11
	Age at onset of cognitive decline	0.06	0.08	0.57	1	0.449	1.06	0.91	1.24
	Sex, female	0.50	0.55	0.84	1	0.361	0.61	0.21	1.77
	Race, white	0.97	0.90	1.17	1	0.279	0.38	0.07	2.20
	Education, Less than HS/HS/GED (referent)								
	Some college/Associate's/Bachelor's	-0.05	0.51	0.01	1	0.916	0.95	0.35	2.59
	Graduate work/Graduate degree	-1.34	0.83	2.59	1	0.108	0.26	0.05	1.34
	Age at onset of cognitive decline	0.06	0.08	0.57	1	0.449	1.06	0.91	1.24
	Psychiatric diagnosis, no	0.59	0.49	1.44	1	0.231	0.56	0.21	1.45
	Modified CCI, 0	-0.29	0.53	0.29	1	0.591	1.33	0.47	3.80
	Dementia family history, no	-0.23	0.48	0.23	1	0.635	1.25	0.49	3.19
	Care Support Relationship, Spouse/partner (referent)								
	Adult child	-0.12	0.59	0.04	1	0.837	0.89	0.28	2.83
	Other	-1.36	1.14	1.43	1	0.232	0.26	0.03	2.39
Participator	Constant	1.81	1.64	1.22	1	0.270			
	Age	-0.05	0.05	1.12	1	0.289	0.95	0.86	1.05
	MMSE score	0.06	0.04	2.86	1	0.091	1.06	0.99	1.14
	Age at onset of cognitive decline	0.01	0.05	0.02	1	0.903	1.01	0.91	1.11
	Sex, female	-0.08	0.34	0.06	1	0.809	1.09	0.56	2.10
	Race, white	0.56	0.68	0.66	1	0.415	0.57	0.15	2.19
	Education, Less than HS/HS/GED (referent)								
	Some college/Associate's/Bachelor's	-0.05	0.35	0.02	1	0.890	0.95	0.48	1.91
	Graduate work/Graduate degree	-0.08	0.40	0.04	1	0.849	0.93	0.42	2.03
	Psychiatric diagnosis, no	0.01	0.32	0.00	1	0.983	0.99	0.53	1.86
	Modified CCI, 0	**-1.05**	**0.37**	**7.91**	**1**	**0.005**	**2.85**	**1.37**	**5.90**
	Dementia family history, no	-0.06	0.30	0.03	1	0.856	1.06	0.59	1.90
	Care Support Relationship, Spouse/partner (referent)								
	Adult child	**-0.76**	**0.38**	**4.03**	**1**	**0.045**	**0.47**	**0.22**	**0.98**
	Other	**-2.25**	**0.82**	**7.62**	**1**	**0.006**	**0.11**	**0.02**	**0.52**

Note: R^2=.17 (Cox & Snell), .21 (Negelkerke). Model $\chi 2(24)$=48.01, p=.003.
HS=high school; GED=General Equivalency Diploma; MMSE=Mini Mental State Exam; CCI=Charlson Comorbidity Index

Binomial logistic regression for the subsample of individuals with dementia

The final binomial logistic regression model (Model 4, See Table 19) comparing Participators to Non-Participators (referent group) was also statistically significant, $\chi 2(12)=39.39$, $p<.001$, and explained 20% (Nagelkerke R^2) of the variance in amyloid imaging participation. Presence of medical comorbidity significantly related to being a Participator compared to a Non-Participator, b=-1.01, $\chi 2$ (1)=7.65, p=0.006. Having no comorbidity meant individuals were more than two and a half times more likely to participate in amyloid imaging than not participate (OR=2.74, 95% CI 1.34-5.59). As in multinomial modeling, care support relationship was significantly associated with participation in amyloid imaging when comparing adult child supports to spousal/partner or other supports (b=-.75, $\chi 2(1)=4.06$, p=0.009), or spousal/partner and adult child supports to other supports (b=-2.09, $\chi 2(1)=6.72$, p=0.010). Individuals with adult children care supports were half as likely to be Participators as individuals with spousal/partner or other care support relationships (OR=0.47, 95% CI, 0.23-0.98). Individuals with other care relationships were about one-tenth as likely to be Participators as individuals with spousal/partner or adult child relationships (OR=0.12, 95% CI, 0.03-0.60).

Table 19.Model 4: Binary logistic regression of factors associated with participation in amyloid imaging for the subsample of individuals with dementia (N=255)

	Estimate	Std. Error	Wald	df	*p*	Odds Ratio	95% Confidence Interval	
							Lower Bound	Upper Bound
Constant	1.17	1.58	0.55	1	0.459	3.22		
Age	-0.04	0.05	0.76	1	0.385	0.96	0.87	1.06
Sex, female	-0.16	0.33	0.25	1	0.620	1.18	0.62	2.23
Race, white	0.41	0.66	0.38	1	0.535	0.66	0.18	2.43
Education, <HS/HS/GED (referent)			0.11	2	0.945			
Some college/Associate's/Bachelor's	-0.04	0.34	0.01	1	0.907	0.96	0.49	1.88
Graduate work/Graduate degree	0.09	0.39	0.05	1	0.820	1.09	0.51	2.35
MMSE score	0.06	0.04	3.04	1	0.082	1.06	0.99	1.14
Age at onset of cognitive decline	0.00	0.05	0.00	1	0.968	1.00	0.90	1.10
Psychiatric diagnosis, no	-0.09	0.31	0.08	1	0.780	1.09	0.59	2.01
Modified CCI, 0	**-1.01**	**0.36**	**7.65**	**1**	**0.006**	**2.74**	**1.34**	**5.59**
Dementia family history, no	-0.02	0.29	0.01	1	0.943	1.02	0.58	1.81
Care support relationship, Spouse/partner (referent)			**9.40**	**2**	**0.009**			
Adult child	**-0.75**	**0.37**	**4.06**	**1**	**0.044**	**0.47**	**0.23**	**0.98**
Other	**-2.09**	**0.81**	**6.72**	**1**	**0.010**	**0.12**	**0.03**	**0.60**

Notes: R2=.14 (Cox & Snell), .20 (Negelkerke). Model $\chi 2(12)=39.39$, $p<.001$.
HS=high school; GED=General Equivalency Diploma; MMSE=Mini Mental State Exam; CCI=Charlson Comorbidity Index

4.4.3 Summary of findings for the subsample with individuals with dementia

In bivariate analysis, being younger, younger age at onset of cognitive symptoms, no physical comorbidity, and care support relationship were all significantly associated with greater interest in amyloid imaging participation, when compared to refusing any contact regarding AI or eventual refusal of AI participation. The same findings held when comparing AI Participators to AI Non-Participators.

In multivariate analysis, both in multinomial and binomial logistic regression modeling, biopsychosocial factors that were significantly associated with being a Participators were absence of comorbidity and a spousal/partner care support relationship. There were no factors that significantly distinguished Refusers from Avoiders.

4.5 RESULTS SUMMARY

In summary and for the full sample, significant factors associated with interest in amyloid imaging were younger age, better scoring on cognitive testing, and the experience of a change in cognition diagnosis. These findings held upon examination of biopsychosocial factors related to participation in AI. When examining the subset of IWDs, absence of comorbidity and having a spousal or partner care support relationship was significantly related to both interest and participation in AI. The following chapter will discuss these findings within the context of current research on participation in dementia screening, genetic testing and diagnostic assessment, as well as current work exploring engagement in dementia research studies.

5.0 DISCUSSION

Early detection of Alzheimer's disease (AD) allows patients and families extended time to care plan for the future and amyloid imaging (AI) is developing into a primary tool for gaining insight regarding cognitive status. This study aimed to identify the patients that are being included in these research advances and who may be missing out on participation in AI. Results from a sample of individuals who were followed at an Alzheimer Disease Center, and were queried regarding their willingness to participate in amyloid imaging studies, may also provide some first steps for social workers to understand what biopsychosocial factors may boost, or impede, participation in amyloid imaging research. To summarize, significant factors associated with interest in AI were younger age, scoring better on cognitive testing, and experiencing a change in cognitive diagnosis. The same findings resulted when examining factors related to AI research participation. Individuals with dementia were more likely to participate and express interest in amyloid imaging if they had no medical comorbidities and had spousal or partner care support. These findings lay the groundwork for understanding how AI may be adopted in clinical practice, and given the growing availability for testing that may detect AD pathology before symptoms arise, point to a clear need for clinicians to have discussions about dementia and dementia testing earlier in their care relationships. Limitations of the study and implications for practice and research are also discussed.

5.1 FACTORS ASSOCIATED WITH INTEREST AND PARTICIPATION IN AMYLOID IMAGING

5.1.1 Experiencing cognitive diagnostic change

Experiencing a change in cognition diagnosis from the Alzheimer Disease Research Center (ADRC) was significantly related to participation in amyloid imaging research, and this association held throughout modeling for the full sample. The presence of a change in diagnosis incorporated a range of diagnostic experiences, although all had the shared experience of meeting with a social worker and clinician to discuss the diagnosis and consider treatment and care plan options. Most individuals were told of a cognitive impairment diagnosis and a progression in illness process, whether it was a diagnosis of mild cognitive impairment (MCI) or dementia. In light of a diagnostic transition, individuals may feel that an uncertainty in diagnostic status exists, and AI participation provides an action that can be taken to address this uncertainty.

Much has been written about the experience of diagnostic disclosure, either of mild cognitive impairment or dementia, predominantly within studies using qualitative methods (Bamford et al., 2004; Robinson et al., 2011). Reviews of work point to a wide characterization of experiences, with negative and positive consequences resulting from diagnostic disclosure, as well as high variability in beliefs and attitudes corresponding to the diagnostic revelation (Bamford et al., 2004). All of which points to the weighty, transformative nature of cognitive diagnosis. Beard (2004) identified diagnosis as a “defining moment” for patients with early AD or a hallmark in the illness trajectory, especially in the absence of any ability to change the treatment process. A follow-up study (Beard & Fox, 2008) of individuals with early-stage AD or MCI reported a strong patient interest in being proactive following a diagnosis and seeking

adjustments that would benefit well-being. One quantitative study found positive, AD-related health behavior change (e.g. taking medications, changes to diet or exercise) was a significant occurrence one year after the receipt of information regarding a positive AD genetic susceptibility status for individuals with an immediate family history of AD (Chao et al., 2008). This proactive post diagnosis behavior could certainly extend to amyloid testing where, as in the current sample, individuals receiving a cognitive impairment diagnosis positively view the pursuit of AI as a means to engage in meaningful activity that might result in a health benefit.

Social workers play an especially pronounced role at this critical moment in the care continuum. All participants receiving a change in diagnosis had additional time with social work staff for discussion focused on understanding and processing diagnostic findings, care planning, and considering strategies to cope with and compensate for memory loss. Patient and family discussions with the social worker are weighty. They may focus on the how to support patient engagement in meaningful activity in the face of memory loss or balancing an increasing need for support with patient independence. Given the depth and magnitude of the discussion, there is no doubt that a therapeutic alliance is likely formed among discussion members - an enriched relationship between the patient, family, and clinicians. Equal partnerships within this alliance are considered to be the ideal, with a client-centered approach to care decision-making (Dupuis et al., 2012). While diagnostic experiences varying on the ideal were more likely, social work facilitation to attain a supportive, patient-centered, authentic relationship may have led patients and families to seek a continuing contact with the ADRC, via participation in AI. As social workers are also one of the first in-person contacts with memory clinic staff, a first source of information regarding AI studies, and an ongoing point of contact for the patient-family dyad, a natural link between social work and AI involvement occurs, and may facilitate AI participation.

5.1.2 Younger age and amyloid imaging

For the full sample, younger age was significantly associated with AI interest and participation, notably when controlling for physical comorbidity and dementia status. As noted in the literature review, the same finding was reported in studies examining participation in AD genetic testing (Demirovic et al., 2003) and intent to participate in cognitive assessment (Boustani et al., 2006; Dale et al., 2008; Demirovic et al., 2003; Fowler et al., 2012).

As this sample was predominantly comprised of older adults (3.4% were <55 years), it may be that the "young-old" have the greatest interest in testing. A multi-country study of interest in preclinical testing for Alzheimer's disease reported that individuals who expressed high interest in testing were in the 50-64 and 65-74 age ranges, rather than older (75-85+ years) and younger (30-49 years) age groups (Wikler, Blendon, & Benson, 2013). It may be that the development of cognitive symptoms are believed to be closer at hand than for young adults, while the opportunity to change health behaviors and care plan may be viewed as more viable, with more potential for positive outcomes, than for their older counterparts. Previous work has also shown that the "old-old" have greater negative health behavior changes, compared to the "young-old" (Zanjani, Schaie, & Willis, 2006).

Planning for the future may in fact be primarily on the minds of the "young-old," particularly those seeking information about their cognitive status. Researchers examining the completion of advance directives in a sample derived from the same setting as for this dissertation reported that ADRC participants younger than age 65 were significantly more likely to have an advance directive in place than individuals age 65 and older (Garand, Dew, Lingler, & DeKosky, 2011). A survey using a representative sample of older adults (age 55+) in Allegheny County, Pennsylvania reported that from the age groups of 55-64 to 65-74, a large jump occurs

in the percentage of older adults that have a living will (34% to 58%) or health care power of attorney (35% to 60%; University Center for Social and Urban Research, 2014). "Local" percentages are similar to those based on a nationally representative mail panel survey (Rao, Anderson, Lin, & Laux, 2014), in which percentages of advance directive completion significantly differed between ages 35-54, 55-65, and ≥65 years, and increased with age groups (19.2%, 29.3%, and 51.2%, respectively).

While the "young-old" may be those first seeking access to tools that may better delineate disease status, those who are older may in fact be getting left out. A systematic review of studies examining variations in medical care provision for individuals with dementia reported high variation in the use of diagnostic tools, including memory testing and imaging (Sivananthan, Puyat, & McGrail, 2013). A follow-up, population-based study examining variation in the application of dementia care guidelines in primary care practices reported that older age of patients with dementia were significantly associated with less adherence to guideline-consistent clinical care (Sivananthan, Lavergne, & McGrail, 2015). The authors attributed the difference to a lessened inclination among physicians to complete imaging when it may create a hardship for the patient. Older individuals may also perceive that cognitive impairment is an inevitability in older age (Ayalon & Areán, 2004), with little utility gained from pursuing confirmatory testing. Further exploration of these age differences, to tease out whether underlying motivations do in fact differ by age groups, is warranted. Additionally, from a clinical perspective, amyloid imaging counseling protocols may need to particularly address the concerns of the older-old regarding the potential hardships imposed by AI, and the potential value gained.

5.1.3 Better cognition associated with participation

Although diagnostic status was not a factor associated with of amyloid imaging interest or participation in regression modeling, as hypothesized, a higher Mini Mental State Exam (MMSE) score did relate to both interest and participation. While this dissertation unfortunately was not able to examine the patient's subjective perception of memory status, less impairment may imply greater patient decisional ability to make a determination regarding AI. And, when decisional impairment does exist, family members or decision-making proxies may be more hesitant to enroll the patient in something that may be difficult for the patient to understand or viewed as onerous. Studies examining the reasons that individuals do participate in dementia research often cite altruism as a key motivator (Jefferson et al., 2011); when another individual is making the decision, altruism may play a lessor role. Older adults queried about their views on surrogate decision-making for dementia studies using a range of protocols (e.g. lumbar puncture, vaccine, randomized controlled trial, gene-transfer neurosurgical study) reported that comfort with surrogate decision-making participation was not absolute (Kim et al., 2009). Therefore, the conservative route, in which AI participation is not pursued, may be more common when patient decisional ability is in question.

5.1.4 Education was not associated with participation

While educational attainment was initially significant in bivariate comparisons for the full sample as hypothesized, it did not remain significant in multivariate analysis. Education levels of the sample were higher than for individuals age 60 and over residing in the Pittsburgh Metropolitan Statistical Area (MSA; U.S. Census Bureau, 2014). This may mean that any self-

selection bias related to education has already occurred when individuals elected to participate in a memory research clinic, and was washed out as a significant variable related to AI involvement; or a differing, non-significant relationship between education and AI participation may simply exist than that noted between education and dementia research participation.

5.2 FACTORS ASSOCIATED WITH INTEREST AND PARTICIPATION IN AMYLOID IMAGING FOR INDIVIDUALS WITH DEMENTIA

At the time of data collection when studies were being conducted using amyloid imaging, individuals with dementia (IWDs) were the focus of research. AI was most widely utilized by this group. There now are firmer recommendations regarding who should complete AI in the clinical setting (Johnson et al., 2013) and most work is focusing on the implementation of appropriate use criteria (AUC) that include early-onset, atypical, and mixed presentations of dementia as diagnoses of interest (Zakaid, 2015). However an examination of IWDs, separate from the full sample, does help tease out who participates given this constellation of symptoms and progression and findings are likely applicable to individuals with dementia, who also meet the AUC recommendations.

5.2.1 Absence of medical comorbidity

The relationship between health comorbidity and AI participation differed from what had been hypothesized. However, a previous study finding that comorbidity was related to interest in memory screening used a sample of community-dwelling older adults with varying subjective

report of memory problems (Boustani et al., 2003). The current, differing finding in this dissertation may be specific to IWDs for which ongoing health concerns, in addition to a dementia diagnosis, may already require significant health care use that is more highly prioritized over further diagnostic testing for dementia. As AI may not be viewed to lead to a change in treatment protocol or health status in comparison to the ongoing monitoring and treating of other chronic health conditions, its import may have less weight. Comorbidity in this sample was lower than that reported in a community-based sample of people with AD (Doraiswamy, Leon, Cummings, Marin, & Neumann, 2002). Alternatively, good physical health may also mean participants are more available and inclined to be active participants in their health. Good physical health may in turn imply no functional impairments that would make it difficult to complete imaging or create health-related concerns.

Physical health problems, including associated medication regimens, may also impact cognition and neurodegeneration, possibly making it all the more important to better tease out the underlying condition causing cognitive impairment. Comorbid conditions commonly co-occur with cognitive impairment and correlate with greater cognitive impairment (Doraiswamy et al., 2002). Additionally, appropriate use criteria recommends the use of AI in instances when individuals present with dementia of mixed etiology, including cerebrovascular disease or another medical condition (Johnson et al., 2013). Pre-test counseling protocols, not only tailored to diagnostic status, but also incorporating health history, may better reach those who could most benefit from amyloid imaging. Compared to adults with no dementia diagnosis, IWDs experience more potentially avoidable hospitalizations due to complications related to comorbid conditions, predominantly diabetes and hypertension (Lin, Fillit, Cohen, & Neumann, 2013).

Focusing on these health conditions, in the context of a dementia diagnosis, is therefore critical and should take precedence.

5.2.2 Spousal or partner care support

Although individuals with dementia have an interest in being involved in their care decisions (von Kutzleben, Schmid, Halek, Holle, & Bartholomeyczik, 2012), qualitative work has characterized varied modes of discussion occurring between IWDs, family members, and care managers to elicit care preferences, and noted that family preferences do play a pivotal role in determining care outcomes (Österholm, Taghizadeh Larsson, & Olaison, 2015). As hypothesized and supported by previous research (Cary et al., 2015), spousal and partner care support relationships significantly related to AI interest and participation. Greater time availability in retirement and more overall interest in meaningful activity for the person with dementia may be driving this relationship. Secondary data analysis using the National Alzheimer's Coordinating Center Uniform Data Set (NACC UDS) found that participation in clinical trials was less common for patients with adult children as study partners than spousal study partners due to the patient's age, poorer health, poor cognition and the inability of the adult child study partner to allocate time for clinical trial visits (Grill, Monsell, & Karlawish, 2012). Adult children experience greater role conflicts between caregiving and work that inhibit participation (Pinquart and Sorensen, 2007). Social work counseling protocols need to explore ways to support care dyads when care partner time limits related to work and family obligations inhibit participation. One option would be to identify additional sources of care support for the patient who may have an interest in facilitating AI involvement. Better employer support and greater societal acceptance of family leave programs might additionally free adult children to apply more time to

care roles and responsibilities. For care supports comprising the "other" group, further delineation of those care support relationships that comprise this group is needed. It may be that "secondary" relationships may result in a hesitancy to make decisions about AI participation and may signify a need for additional support in understanding the process and implications of AI.

5.3 LIMITATIONS

Several limitations are worth noting for this dissertation, primarily related to the study sample. First, it is important to reiterate that the individuals who completed amyloid imaging in this sample did not receive the results of testing. The key difference primarily relates to differing risks and benefits that arise when completing a clinical, versus a research, scan. Since a research scan does not conclude with disclosure of test results, the main risks relate to the amyloid imaging procedure, including exposure to a radioactive tracer and a lengthened time of immobility. In fact, one might view there to be less risk associated with a research scan than with a clinical scan. In addition to procedural risks, a clinical scan results in findings placed in the patient's medical record, and, although confidential, may be a potential source of discrimination related to employment, health insurance, or long-term care insurance. Currently there are no legal protections for the patient against such discrimination, however a federal law that prohibits health insurance and employment discrimination related to genetic information (The Genetic Information Nondiscrimination Act of 2008) provides a template for future legislation.

Given the provision of results that come with a clinical scan, counseling regarding the risks and benefits would hypothetically occur in conjunction with imaging, and also address the interpretation of results, emotional response of the patient and family, and its impact on

treatment and health outcomes. One study examining interest in research results disclosure within a sample of cognitively normal individuals, who had participated in a longitudinal cognitive assessment study based in an Alzheimer Disease Center, reported significantly lower interest in disclosure following the receipt of an educational session numerating the risks and benefits related to receiving test results (Gooblar et al., 2015). Further examination of the same biopsychosocial factors within a similar substantially sized sample of individuals who have been approached regarding the completion of a clinical scan is certainly warranted.

Second, a small number of Avoiders (9.4%, n=42), individuals who first expressed interest, yet never actually participated in AI was derived from the categorization process for AI interest groupings. This may have limited the comparisons made between Avoiders and the other interest groups, Refusers and Participators. However, these groupings were derived from ten years of ADRC registry participation and provided a fairly accurate snapshot of the overall prevalence of AI interest and participation.

Third, the sample was derived from a research-focused Alzheimer's Disease Center, and may differ in motivation levels regarding dementia research participation and overall interest in cognitive assessment from the general population. The dissertation sample did, however, share some similarities with demographic reports from U.S. Census data for *individuals age 60 and older* residing in the Pittsburgh Metropolitan Statistical Area (MSA; U.S. Census Bureau, 2014). Median age was higher than that reported in Census data (75 years versus 70 years). However, similar percentages of males and females were evident when comparing the study sample to U.S. Census estimates (53.7% female/46.3% male versus 55.8% female/44.2% male, respectively). Racial composition was also similar, with the study sample comprised of slightly more African Americans than the Pittsburgh MSA (7.3% versus 5.8% African American). Educational

attainment for the sample was higher; almost half of the current sample (47.4%) had completed at least a Bachelor's degree, while the same was true for just 23.4% of the older cohort from the Pittsburgh MSA. While generalization to other populations may be limited, the value of using this sample, including a set of variables derived from standardized measurement tools, is a critical first step to understanding who may first the first adopters of such technology.

As hypothesized, being African American was not significantly related to being a Participator. The lack of racial diversity in the sample (7.3%, n=33) does limit findings and makes it difficult to draw firm conclusions from analysis. Many challenges to recruiting African Americans for study participation exist and share similarities with the challenges African Americans face in accessing care (Ballard, Gwyther, & Edmonds, 2010). Addressing low research participation for African Americans and access to care may go hand-in-hand, especially as results of amyloid imaging in the research setting become available. Outreach approaches for cognitive assessment and AD research participation recruitment continue to place focus on African Americans, as well as other people of color. Sharing information about the advances related to amyloid imaging and the growing potential for receiving results, as well as understanding how such a diagnostic tool is perceived by underrepresented groups is a needed addition to existing outreach programming and research. Social workers bring a unique expertise in reducing barriers to care for individuals who historically and currently have experienced medical disenfranchisement, and may offer intervention approaches for improving participation from these underrepresented groups.

5.4 IMPLICATIONS FOR SOCIAL WORK PRACTICE

Several implications for social work practice resulted from this dissertation that support the inclusion of social work practitioners in dementia care teams employing amyloid testing and enrich the content of amyloid imaging counseling protocols, as well as diagnostic disclosure protocols. In these roles, social workers may also employ advocacy skills to address the tension between patient and clinician views regarding the utility of amyloid imaging.

5.4.1 Supporting and informing social work roles in amyloid imaging counseling protocols

The current findings provide social workers with a first look at the biopsychosocial factors that impact who pursues diagnostic testing for dementia and who may be left out. These findings in turn inform content of AI pre- and post-counseling protocols, allowing for some insight regarding the factors that may be driving personal motivations or hesitancies related to testing. As biomarker testing including AI advances, a range of health care settings with social workers on staff are likely to be involved in implementing such testing. Research centers will continue to be a home base for AI testing, as study participants begin to gain access to test results. Other likely environs are geriatric clinics and primary care clinics serving significant numbers of older adults (Sommers, Marton, Barbaccia, & Randolph, 2000). Emerging sites for biomarker testing may fall under the medical home model, either adapted to focus on dementia assessment and care (Boustani et al., 2005) or through partnerships between primary care practices and memory clinics (Callahan et al., 2006). The primary objectives of these emerging care settings are to

improve access to screening, diagnosis, and treatment in the primary care setting, via multidisciplinary memory care staff, inclusive of social workers.

Physician practices serving older adults with dementia are clearly in need of in-house social work for ongoing counseling and care coordination; and justification for multidisciplinary approaches is marked, including from the physician perspective. A study of primary care physicians (PCPs) serving older adults with dementia reported a lack of physician connections and knowledge regarding social service agencies serving IWDs and their families (Hinton et al., 2007). One salient quote from a PCP via semi-structured interviews summarized the problem stating, "I am not a licensed clinical social worker" (Hinton et al., 2007, p. 1490). Cross-training physicians in an expertise already covered by social work practitioners becomes an inefficient approach, particularly when social workers are already well equipped to assess biopsychosocial factors that may inhibit or enhance participation in diagnostic testing, and can provide supportive counseling and care coordination post testing. Sharing care responsibilities across a multidisciplinary team, via in-house and collaborative models, will offer the best approach to care.

Appropriate use criteria for AI (Johnson et al., 2013) will be a significant driver of the physician referral process for amyloid imaging and it will be important during counseling to ensure patients understand their diagnostic status and the related rationale for referral, including the potential medical benefit. Counseling should also incorporate a biopsychosocial model to explore medical, psychological, and social aspects of the individual that may impact, and be impacted by, the completion of AI. For instance, based on dissertation findings, AI protocols should specifically address concerns of more *aged* adults at the point of the pre-counseling stage and efforts should be taken to ensure that counseling approaches are not biased toward specific

age groups. More *impaired cognition* may be excluding individuals from pursuing testing. Social work-inclusive counseling protocols need to include supportive approaches for individuals with memory impairment throughout the decision-making process, applying tools that aid and assess understanding of discussion content. For individuals with amnestic impairments, visual aids, including written summaries of discussion material and providing examples of PET imaging, may improve understanding, as well as checks to clarify content and address questions or concerns (Lingler et al., 2015). Guiding familial support throughout this process will additionally aid in patient understanding of the decision at hand.

A recent qualitative pilot study using a focus group to examine reactions to a hypothetical protocol for delivering AI results to individuals with MCI and their care partner, reported that participants were satisfied with the disclosure process (Lingler et al., 2015). Participants and specifically felt that pre-test counseling and follow-up via phone calls after receiving test results would enhance understanding and experience. Within the care settings noted above, social workers are likely to be key staff in counseling and follow-up contacts, and gaining perspective on factors impacting process and content for such care protocols will enhance their roles.

5.4.2 Diagnostic transition and testing

Participation in amyloid imaging may also be inherently tied to contact with social work clinicians, as change in cognitive diagnosis was significantly related to AI involvement. As noted previously, social workers play a primary role in the diagnostic disclosure meeting and follow-up care coordination. Diagnostic change can be a significant care transition for older adults and their families. A key tenet of social work acknowledges that patients and families experiencing care transitions require support and social workers have a unique and critical expertise to meet this

need (Herman, 2009). Health transitions put individuals at risk for additional health and psychosocial problems (Tahan, 2007) and acknowledging that diagnosis can present challenges may aid the process of identifying support needs for the patient and care partner and include a discussion about the utility of additional diagnostic testing. Understanding the potential implications of biopsychosocial factors that impact patient views on utility of testing enriches the conversation regarding the diagnostic change. As models of care may be moving to a merging of cognitive impairment disclosure, or even disclosure of the risk of cognitive impairment, with counseling on biomarker testing, social work roles will be of particular import.

5.4.3 Addressing tension between personal and clinical utility

Age at onset of memory symptoms was not a significantly associated with AI involvement, although individuals with early onset dementia are considered those likely to benefit from testing and are currently in the recommended group according to appropriate use criteria (Johnson et al., 2013). While this dissertation did not tease out differences according to dementia diagnosis, where possible (not probable) AD or an atypical dementia presentation might also lead to AI interest - and may muddy the above finding - it does point to a potential mismatch between current recommendations and patient preferences.

Tensions between the clinical and personal utilities derived from amyloid imaging do exist for AI (Lingler et al., 2015), and have been noted for other AD biomarkers (Roberts & Tersegno, 2010). Patients and families may view a benefit to be derived from completing testing, or personal utility even when clinical evidence recommends against testing, because testing is believed to lead to no medical benefit, such as a change in treatment or care management protocols. As a key social work value is to uphold the self-determination of the patient in care

decision-making (National Association of Social Workers, 2008), it naturally falls in social work's purview when facilitating the AI decision-making processes to specifically advocate for patient preference and ensure that the patient's views regarding testing have weight. Yet, do we advocate for the patient whose goal is to pursue testing when clinical utility is not believed to exist? Maybe we do, and our role as patient advocator may mark one of the key reasons that social workers need to be included in counseling processes for AI. Clinical recommendations are going to be in continuous change, resulting from ongoing research on the utility of AI. It may make a clinical difference to complete AI testing, even when current recommendations do not indicate one.

Work examining the reasons individuals with first degree relatives who have AD pursue susceptibility genotyping for Alzheimer's disease point to many motives that uphold personal utility, primarily related to planning for the future (Roberts et al., 2003). Planning for the future included arrangement of personal affairs and long-term care, preparing family members for the potential of illness, and the opportunity to complete certain activities sooner than planned (Roberts et al., 2003). Hence there was a clear belief that pertinent and life-altering information could be derived from testing beyond medical care, all of which could benefit from supportive counseling and care management from social workers.

5.5 SUGGESTIONS FOR FUTURE RESEARCH

This area is ripe for further investigation, including qualitative examinations of the motivations underlying AI participation, the roles of social workers in discussions related to AI testing, and inclusive of individuals who receive AI results. Further examination of specific cognitive

diagnosis, as well as varied measures of age, cognition, and health are also warranted. Recruitment and counseling protocols for intervention study may also be informed by the current findings.

5.5.1 Qualitative investigation

Applying qualitative methods to future research exploring interest in amyloid imaging is definitely warranted. A first step might include semi-structured interviews with individuals (and their care partners) from the current sample, and drawn from each AI interest grouping. To inform social work practice in particular and build from the findings of this study, interview guide content could focus on question structures exploring underlying motivations, and aspects of personal and clinical utility attached to participation. Triangulation with data from the current study could explore thematic links to biopsychosocial factors.

As there is a growing group of patients who have completed amyloid imaging and received results from testing at the ADRC, a mixed methods study derived from this group could include qualitative interviews with patients and care partners. The study sample should include individuals who elected to complete AI, and a sample of individuals who declined. Data extraction from the ADRC could pair interviews with biopsychosocial factors to explore thematic links and better inform social work practice. This work might also reveal any potential differences that exist between willingness to complete testing and willingness to receive results. Longitudinal follow-up with patients and families, via interviewing and ADRC data extraction, could aid in our understanding of whether the personal and clinical utilities anticipated to be derived from AI participation, come to fruition, in comparison to those who decline AI testing.

Finally, those experiencing diagnostic change were more likely to participate in AI. Qualitative investigation of the content of discussions during diagnostic meetings, often facilitated by a social worker and clinician, and inclusive of patients and one more or more family member(s), might further inform our understanding of motivations related to AI participation. The voiced discussion content of diagnostic disclosure meetings for cognitive impairment has not been well examined and has primarily focused on emotional response to diagnosis (Aminzadeh, Byszewski, Molnar, & Eisner, 2007), rather than care planning and health care use following disclosure, or the roles of clinical staff in such meetings. This qualitative approach may also enrich our understanding of the roles that social workers play in facilitating decision-making related to AI testing.

5.5.2 Diagnostic and AD family history groupings

As this dissertation provided an initial look at how participation in AI research, examining whether diagnostic grouping was significantly associated with AI interest and participation was important to include. Individuals with dementia were examined separately as they comprise the diagnostic group that has historically been the focus of AI testing. From a clinical perspective, understanding how significant factors differ by diagnosis offers a pathway to more nuanced discussions with patients, that take into account diagnostic status and related factors that may be important. ADRC diagnosis significantly differed between AI interest groups, yet this significant relationship did not hold in multivariate analysis. Individuals with dementia had higher percentages of Refusers than Participators, while those diagnosed with MCI had more representation among Participators than in the Refusers or Avoiders groups. Interestingly, individuals with no cognitive impairment represented a greater proportion of Avoiders, than

Participators or Refusers. Future work should examine the relationship between diagnostic grouping and AI interest particularly among subsamples of individuals with MCI or no cognitive impairment. Both groups had greater percentages of Participators overall, and, as was noted for IWDs, the biopsychosocial factors driving AI interest and participation are likely to differ from the current sample that included varying cognitive diagnoses. For example, in the current sample and the subset of IWDs, presence of a psychiatric diagnosis was not related to AI interest, as hypothesized. However, completing similar multivariate modeling with a sample diagnosed with MCI may present a different picture because, although psychiatric symptoms more commonly co-occur with dementia rather than MCI (Lyketsos et al., 2002), psychiatric diagnosis may be predictive of progression to dementia from MCI (Palmer et al., 2007), and may enhance interest in AI testing that elucidates the underlying disease process.

Additionally, drilling down to more specified diagnoses is warranted, and should focus on the diagnostic groups specified by appropriate use criteria. AUC points to several recommended diagnostic groups: 1) individuals with persistent or progressive unexplained MCI; 2) individuals diagnosed with possible AD (rather than probable AD) with an atypical course or a mixed presentation; and 3) individuals with early onset dementia (age 65 years or younger at onset) (Johnson et al., 2013). This would likely require a larger sample than that used for this dissertation, and could be derived from multiple Alzheimer Disease Centers, improving generalizability. For comparison, an analysis of diagnoses for which there is no recommendation would aid in characterizing who may still view a utility to be gained from testing, when no medical benefit is present.

Having a first degree relative with dementia was not significantly related to AI interest and participation. Alternative measures of dementia family history, such as AD genetic

susceptibility status or number of family members with dementia (Lautenschlager et al., 1996), may serve as better indicators of AI involvement. As with cognitive diagnostic groupings, examining whether biopsychosocial factors related to AI participation differ by presence or absence of dementia family history might also tease out differences between groups.

5.5.3 Further examination of age, race, cognition, and health

Several significant factors, age, cognition, and physical health comorbidity, identified in this dissertation warrant further examination via alternative measurement approaches. Modeling age groups may further demarcate the age range most associated with AI, or a cutpoint at which age becomes significantly related to amyloid testing. Expanding sampling to the national UDS dataset may allow for better representation of people of color. The NACC UDS includes a detailed question structure to gain data on race and ethnicity, allowing for a deeper dive into this examination. The cognition measure used in this dissertation, Mini Mental State Exam score, is a generalized measure; more specified, single-domain neuropsychological measures of memory or executive functioning, among others, might better tease out what aspects of cognitive functioning may be impacting decision-making related to AI. Lastly, measurement of medical comorbidity was limited by data available from the ADRC, via the NACC UDS. More detailed examination of health status, including medical comorbidities also considered risk factors for dementia (e.g. diabetes, cardiovascular disease) and health behaviors (e.g. smoking, alcohol use, exercise, advance care planning) that might relate to AI interest, might further characterize who is seeking testing. These more delineated characterizations will better inform pre and post-counseling approaches for AI.

5.5.4 Intervention studies

Work is underway to test approaches for disclosing amyloid imaging results to individuals with no cognitive impairment (Harkins et al., 2015; Karlawish et al., 2013), and individuals diagnosed with MCI (Lingler, Roberts, Schulz, & Klunk, 2012; Lingler et al., 2015), in research settings. A large, multi-site study will begin in 2016 to examine whether a medical benefit is derived from AI testing adapted to clinical practice for individuals meeting AUC (Zakaid, 2015). Tailoring study recruitment protocols, for example using sampling quotas to address a potentially low yield of certain subgroups (i.e. the older old), and incorporating intervention materials to be tested to address biopsychosocial factors that impact personal utility related to AI may aid in improving study outcomes.

5.6 CONCLUSIONS

This study examined biopsychosocial factors related to interest and participation in amyloid imaging for the diagnosis of dementia. A second set of analyses examined factors associated with amyloid imaging interest and participation for a subsample of individuals with dementia. For the full sample, younger age, better cognition, and experience of cognitive diagnostic change were related to both AI interest and participation when controlling for sex, race, education, medical comorbidity, psychiatric diagnosis and dementia family history. For the subsample of IWDs, absence of medical comorbidity and having a spousal or partner relationship providing informal care support were associated with AI interest and participation, when controlling for demographics (age, sex, race, and education level), cognition, age at onset of cognitive

symptoms, psychiatric diagnosis, and dementia family history. The significance of experiencing a cognitive diagnostic transition points to the importance of social workers in facilitating amyloid imaging participation. The finding that the "younger-old" were more likely to agree to AI than the "older-old" may relate to a greater interest among "young-older" adults to be more active participants in their health, yet points to a need for social workers to address participation among the "older-old". Better cognition, potentially a proxy for better decisional ability, implies a need for social workers to ensure counseling protocols for AI are easily understandable for individuals with memory impairment, or that supportive decision-making is provided by family members. For individuals with dementia, medical comorbidity and related health concerns may create a barrier to seeking AI, while the significance of spousal and partner care relationships intimates that these care partners have more time and interest to devote to amyloid imaging. These findings support social work roles in multidisciplinary dementia care teams using amyloid imaging, as well as other biomarker tests for AD, and enrich the content of AI counseling protocols by identifying factors impacting motivations to participate in AI.

BIBLIOGRAPHY

Abley, C., Manthorpe, J., Bond, J., Keady, J., Samsi, K., Campbell, S., . . . Robinson, L. (2013). Patients' and carers' views on communication and information provision when undergoing assessments in memory services. *Journal of Health Services Research & Policy, 18*(3), 167-173.

Aizenstein, H. J., Nebes, R. D., Saxton, J. A., Price, J. C., Mathis, C. A., Tsopelas, N. D., . . . Klunk, W. E. (2008). Frequent amyloid deposition without significant cognitive impairment among the elderly. *Archives of Neurology, 65*(11), 1509-1517.

Alzheimer's Association. (2011). Early Diagnosis: The Value of Knowing. Retrieved from http://www.alz.org/documents_custom/public-health/value_of_knowing.pdf

Alzheimer's Association. (2012). 2012 Alzheimer's disease facts and figures. *Alzheimer's and Dementia: The Journal of the Alzheimer's Association, 8,* 131-168.

Alzheimer's Association. (2015). 2015 Alzheimer's disease facts and figures. *Alzheimer's & Dementia: The Journal of the Alzheimer's Association, 11*(3), 332-384.

American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders: DSM-5. 5th ed.* Washington, DC: American Psychiatric Association.

Aminzadeh, F., Byszewski, A., Molnar, F. J., & Eisner, M. (2007). Emotional impact of dementia diagnosis: exploring persons with dementia and caregivers' perspectives. *Aging & Mental Health, 11*(3), 281-290.

Ayalon, L., & Areán, P. A. (2004). Knowledge of Alzheimer's disease in four ethnic groups of older adults. *International Journal of Geriatric Psychiatry, 19*(1), 51-57.

Ballard, E. L., Gwyther, L. P., & Edmonds, H. L. (2010). Challenges and Opportunities: Recruitment and Retention of African Americans for Alzheimer's disease Research: Lessons Learned. *Alzheimer Disease & Associated Disorders, 24*(0), S19-S23.

Bamford, C., Lamont, S., Eccles, M., Robinson, L., May, C., & Bond, J. (2004). Disclosing a diagnosis of dementia: a systematic review. *International Journal of Geriatric Psychiatry, 19*(2), 151-169.

Barthel, H., Gertz, H.-J., Dresel, S., Peters, O., Bartenstein, P., Buerger, K., . . . Sabri, O. (2011). Cerebral amyloid-β PET with florbetaben (18F) in patients with Alzheimer's disease and healthy controls: a multicentre phase 2 diagnostic study. *The Lancet Neurology, 10*(5), 424-435.

Beard, R. L. (2004). In their voices: Identity preservation and experiences of Alzheimer's disease. *Journal of Aging Studies, 18*(4), 415-428.

Beard, R. L., & Fox, P. J. (2008). Resisting social disenfranchisement: Negotiating collective identities and everyday life with memory loss. *Social Science & Medicine, 66*(7), 1509-1520.

Blendon, R. J., Benson, J. M., Wikler, E. M., Weldon, K. J., Georges, J., Baumgart, M., & Kallmyer, B. A. (2012). The impact of experience with a family member with Alzheimer's disease on views about the disease across five countries. *International Journal of Alzheimer's Disease,* 9.

Bodenheimer, T., Wagner, E. H., & Grumbach, K. (2002). Improving primary care for patients with chronic illness. *JAMA: The Journal of the American Medical Association, 288*(14), 1775-1779.

Boustani, M., Callahan, C. M., Unverzagt, F. W., Austrom, M. G., Perkins, A. J., Fultz, B. A., . . . Hendrie, H. C. (2005). Implementing a screening and diagnosis program for dementia in primary care. *Journal of General Internal Medicine, 20*(7), 572-577.

Boustani, M., Perkins, A. J., Fox, C., Unverzagt, F., Austrom, M. G., Fultz, B., . . . Hendrie, H. C. (2006). Who refuses the diagnostic assessment for dementia in primary care? *International Journal of Geriatric Psychiatry, 21*(6), 556-563.

Boustani, M., Watson, L., Fultz, B., Perkins, A. J., & Druckenbrod, R. (2003). Acceptance of dementia screening in continuous care retirement communities: a mailed survey. *International Journal of Geriatric Psychiatry, 18*(9), 780-786.

Boustani, M. A., Justiss, M. D., Frame, A., Austrom, M. G., Perkins, A. J., Cai, X., . . . Hendrie, H. C. (2011). Caregiver and noncaregiver attitudes toward dementia screening. *Journal of the American Geriatrics Society, 59*(4), 681-686.

Broadstock, M., Michie, S., & Marteau, T. (2000). Psychological consequences of predictive genetic testing: a systematic review. *European Journal of Human Genetics, 8*(10), 731-738.

Bunn, F., Goodman, C., Sworn, K., Rait, G., Brayne, C., Robinson, L., . . . Iliffe, S. (2012). Psychosocial factors that shape patient and carer experiences of dementia diagnosis and treatment: a systematic review of qualitative studies. *PLoS Med, 9*(10).

Callahan, C. M., Boustani, M. A., Unverzagt, F. W., Austrom, M. G., Damush, T. M., Perkins, A. J., . . . Hendrie, H. C. (2006). Effectiveness of collaborative care for older adults with Alzheimer disease in primary care: a randomized controlled trial. *JAMA: The Journal of the American Medical Association, 295*(18), 2148-2157.

Callahan, C. M., Boustani, M. A., Weiner, M., Beck, R. A., Livin, L. R., Kellams, J. J., . . . Hendrie, H. C. (2011). Implementing dementia care models in primary care settings: The Aging Brain Care Medical Home. *Aging & Mental Health, 15*(1), 5-12.

Carpenter, B. D., Xiong, C., Porensky, E. K., Lee, M. M., Brown, P. J., Coats, M., . . . Morris, J. C. (2008). Reaction to a dementia diagnosis in individuals with Alzheimer's disease and mild cognitive impairment. *Journal of the American Geriatrics Society, 56*(3), 405-412.

Cary, M. S., Rubright, J. D., Grill, J. D., & Karlawish, J. (2015). Why are spousal caregivers more prevalent than nonspousal caregivers as study Partners in AD dementia clinical trials? *Alzheimer Disease & Associated Disorders, 29*(1), 70-74.

Centers for Medicare and Medicaid Services. (2013, January 30, 2013). MEDCAC Meeting 1/30/2013 - Beta Amyloid Positron Emission Tomography (PET) in Dementia and Neurodegenerative Disease Retrieved from http://www.cms.gov/medicare-coverage-database/details/medcac-meeting-details.aspx?MEDCACId=66&year=2013&bc=AgAIAAAAAAAAAA%3d%3d&

Chao, S., Roberts, J. S., Marteau, T. M., Silliman, R., Cupples, L. A., & Green, R. C. (2008). Health behavior changes after genetic risk assessment for Alzheimer disease: The REVEAL Study. *Alzheimer Disease & Associated Disorders, 22*(1), 94-97

Charlson, M. E., Pompei, P., Ales, K. L., & MacKenzie, C. R. (1987). A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *Journal of Chronic Disease, 40*(5), 373-383.

Clark, C. M., Schneider, J. A., Bedell, B. J., Beach, T. G., Bilker, W. B., Mintun, M. A., . . . Group, A.-A. S. (2011). USe of florbetapir-pet for imaging β-amyloid pathology. *JAMA: The Journal of the American Medical Association, 305*(3), 275-283.

Cotrell, V., & Schulz, R. (1993). The perspective of the patient with Alzheimer's disease: a neglected dimension of dementia research. *The Gerontologist, 33*(2), 205-211.

Cutler, S. J., & Hodgson, L. G. (2003). To test or not to test: Interest in genetic testing for Alzheimer's disease among middle-aged adults. *American Journal of Alzheimer's Disease and Other Dementias, 18*(1), 9-20.

Dale, W., Hemmerich, J., Hill, E. K., Hougham, G. W., & Sachs, G. A. (2008). What Correlates With the Intention to be Tested for Mild Cognitive Impairment (MCI) in Healthy Older Adults? *Alzheimer Disease & Associated Disorders, 22*(2), 144-152.

Dale, W., Hougham, G. W., Hill, E. K., & Sachs, G. A. (2006). High interest in screening and treatment for mild cognitive impairment in older adults: A pilot study. *Journal of the American Geriatrics Society, 54*(9), 1388-1394.

Dean, K., Jenkinson, C., Wilcock, G., & Walker, Z. (2014). Exploring the experiences of people with mild cognitive impairment and their caregivers with particular reference to healthcare - a qualitative study. *International Psychogeriatrics, 26*(3), 475-485.

Demirovic, J., Prineas, R., Loewenstein, D., Bean, J., Duara, R., Sevush, S., & Szapocznik, J. (2003). Prevalence of dementia in three ethnic groups: The South Florida Program on Aging and Health. *Annals of Epidemiology, 13*(6), 472-478.

Doraiswamy, P. M., Leon, J., Cummings, J. L., Marin, D., & Neumann, P. J. (2002). Prevalence and impact of medical comorbidity in Alzheimer's disease. *The Journals of Gerontology Series A: Biological Sciences and Medical Sciences, 57*(3), M173-M177.

Dubois, B., Feldman, H. H., Jacova, C., DeKosky, S. T., Barberger-Gateau, P., Cummings, J., . . . Scheltens, P. (2007). Research criteria for the diagnosis of Alzheimer's disease: Revising the NINCDS/ADRDA criteria. *The Lancet Neurology, 6*(8), 734-746.

Dupuis, S. L., Gillies, J., Carson, J., Whyte, C., Genoe, R., Loiselle, L., & Sadler, L. (2012). Moving beyond patient and client approaches: Mobilizing 'authentic partnerships' in dementia care, support and services. *Dementia, 11*(4), 427-452.

Engel, G. L. (1977). The need for a new medical model: a challenge for biomedicine. *Science, 196*(4286), 129-136.

Fisk, J. D., Beattie, B. L., Donnelly, M., Byszewski, A., & Molnar, F. J. (2007). Disclosure of the diagnosis of dementia. *Alzheimer's & Dementia, 3*(4), 404-410.

Folstein, M. F., Folstein, S. E., & McHugh, P. R. (1975). "Mini-mental state" : A practical method for grading the cognitive state of patients for the clinician. *Journal of Psychiatric Research, 12*(3), 189-198.

Fowler, N. R., Boustani, M. A., Frame, A., Perkins, A. J., Monahan, P., Gao, S., . . . Hendrie, H. C. (2012). Effect of patient perceptions on dementia screening in primary care. *Journal of the American Geriatrics Society, 60*(6), 1037-1043.

Ganguli, M., Dodge, H. H., Shen, C., & DeKosky, S. T. (2004). Mild cognitive impairment, amnestic type: an epidemiologic study. *Neurology, 63*(1), 115-121.

Garand, L., Dew, M. A., Lingler, J. H., & DeKosky, S. T. (2011). Incidence and predictors of advance care planning among persons with cognitive impairment. *The American Journal of Geriatric Psychiatry, 19*(8), 712-720.

The Genetic Information Nondiscrimination Act of 2008, Pub. L. No. 110-233, 881 Stat. 122 (2008).

Geslani, D. M., Tierney, M. C., Herrmann, N., & Szalai, J. P. (2005). Mild cognitive impairment: an operational definition and its conversion rate to Alzheimer's disease. *Dementia & Geriatric Cognitive Disorders, 19*(5-6), 383-389.

Gill, D. P., Koepsell, T. D., Hubbard, R. A., & Kukull, W. A. (2011). Risk of decline in functional activities in dementia with Lewy bodies and Alzheimer disease. *Alzheimer Disease & Associated Disorders, 25*(1), 17-23.

Gooblar, J., Roe, C. M., Selsor, N. J., Gabel, M. J., & Morris, J. C. (2015). Attitudes of research participants and the general public regarding disclosure of Alzheimer disease research results. *JAMA Neurology*, 1-7.

Green, R. C., Clarke, V. C., Thompson, N. J., Woodard, J. L., & Letz, R. (1997). Early detection of Alzheimer disease: methods, markers, and misgivings. *Alzheimer Disease & Associated Disorders, 11 Suppl 5*, S1-5; discussion S37-39.

Green, R. C., Cupples, L. A., Go, R., Benke, K. S., Edeki, T., Griffith, P. A., . . . Group, M. S. (2002). Risk of dementia among white and African American relatives of patients with Alzheimer Disease. *JAMA: The Journal of the American Medical Association, 287*(3), 329-336.

Green, R. C., Roberts, J. S., Cupples, L. A., Relkin, N. R., Whitehouse, P. J., Brown, T., . . . Farrer, L. A. (2009). Disclosure of APOE genotype for risk of Alzheimer's disease. *New England Journal of Medicine, 361*(3), 245-254.

Greene, R. R. (2011). *Social work with the aged and their families* (Vol. 1): AldineTransaction.

Grill, J. D., Monsell, S., & Karlawish, J. (2012). Are patients whose study partners are spouses more likely to be eligible for Alzheimer's disease clinical trials? *Dementia & Geriatric Cognitive Disorders, 33*(5), 334-340.

Gurland, B. J., Wilder, D. E., Lantigua, R., Stern, Y., Chen, J., Killeffer, E. H., & Mayeux, R. (1999). Rates of dementia in three ethnoracial groups. *Interntaional Journal of Geriatric Psychiatry, 14*(6), 481-493.

Hardy, J., & Selkoe, D. J. (2002). The amyloid hypothesis of Alzheimer's disease: Progress and problems on the road to therapeutics. *Science, 297*(5580), 353-356.

Harkins, K., Sankar, P., Sperling, R., Grill, J., Green, R., Johnson, K., . . . Karlawish, J. (2015). Development of a process to disclose amyloid imaging results to cognitively normal older adult research participants. *Alzheimer's Research & Therapy, 7*(1), 1-9.

Hebert, L. E., Scherr, P. A., McCann, J. J., Beckett, L. A., & Evans, D. A. (2001). Is the risk of developing Alzheimer's disease greater for women than for men? *American Journal of Epidemiology, 153*(2), 132-136.

Hebert, L. E., Weuve, J., Scherr, P. A., & Evans, D. A. (2013). Alzheimer disease in the United States (2010-2050) estimated using the 2010 census. *Neurology, 80*(19), 1778-1783.

Herman, C. (2009). Aging Practice Update: Social Work and Transitions of Care. Retrieved from https://www.socialworkers.org/practice/aging/2009/Social%20Work%20and%20Transitions%20of%20Care.pdf

Hinton, L., Franz, C. E., Reddy, G., Flores, Y., Kravitz, R. L., & Barker, J. C. (2007). Practice constraints, behavioral problems, and dementia care: Primary care physicians' perspectives. *Journal of General Internal Medicine, 22*(11), 1487-1492.

Hipps, Y. G., Roberts, J. S., Farrer, L. A., & Green, R. C. (2003). Differences between African Americans and Whites in their attitudes toward genetic testing for Alzheimer's disease. *Genet Test, 7*(1), 39-44.

Holroyd, S., Turnbull, Q., & Wolf, A. M. (2002). What are patients and their families told about the diagnosis of dementia? Results of a family survey. *Int J Geriatr Psychiatry, 17*(3), 218-221.

Hurt, C. S., Burns, A., Brown, R. G., & Barrowclough, C. (2012). Why don't older adults with subjective memory complaints seek help? *International Journal of Geriatric Psychiatry, 27*(4), 394-400.

IDEAS Study. (2015). Imaging Dementia - Evidence for Amyloid Scanning. Retrieved from http://www.ideas-study.org/

Jefferson, A. L., Lambe, S., Chaisson, C., Palmisano, J., Horvath, K. J., & Karlawish, J. (2011). Clinical research participation among aging adults enrolled in an Alzheimer's Disease Center research registry. *Journal of Alzheimer's disease, 23*(3), 443-452.

Johnson, K. A., Minoshima, S., Bohnen, N. I., Donohoe, K. J., Foster, N. L., Herscovitch, P., . . . Thies, W. H. (2013). Appropriate use criteria for amyloid PET: a report of the Amyloid Imaging Task Force, the Society of Nuclear Medicine and Molecular Imaging, and the Alzheimer's Association. *Alzheimer's & Dementia: The Journal of the Alzheimer's Association, 9*(1), e-1-16.

Kaplan, D. B., & Andersen, T. C. (2013). The transformative potential of social work's evolving practice in dementia care. *Journal of Gerontological Social Work, 56*(2), 164-176.

Karlawish, J., Harkins, K., Sankar, P., Sperling, R., Grill, J., & Green, R. C. (2013). Development of a process to disclose amyloid imaging results to cognitively normal older adult research participants. *Alzheimer's & Dementia: The Journal of the Alzheimer's Association, 10*(4), P808.

Keady, J., Jones, L., Ward, R., Koch, S., Swarbrick, C., Hellström, I., . . . Williams, S. (2013). Introducing the bio-psycho-social-physical model of dementia through a collective case study design. *Journal of Clinical Nursing, 22*(19-20), 2768-2777.

Kim, S. Y., Cox, C., & Caine, E. D. (2002). Impaired decision-making ability in subjects with Alzheimer's disease and willingness to participate in research. *American Journal of Psychiatry, 159*(5), 797-802.

Kim, S. Y., Kim, H. M., Langa, K. M., Karlawish, J. H., Knopman, D. S., & Appelbaum, P. S. (2009). Surrogate consent for dementia research: a national survey of older Americans. *Neurology, 72*(2), 149-155.

Klunk, W. E., Engler, H., Nordberg, A., Wang, Y., Blomqvist, G., Holt, D. P., . . . Langstrom, B. (2004). Imaging brain amyloid in Alzheimer's disease with Pittsburgh Compound-B. *Annals of Neurology, 55*(3), 306-319.

Kukull, W. A., & Ganguli, M. (2012). Generalizability: The trees, the forest, and the low-hanging fruit. *Neurology, 78*(23), 1886-1891.

Landau, S. M., Breault, C., Joshi, A. D., Pontecorvo, M., Mathis, C. A., Jagust, W. J., . . . Initiative, f. t. A. s. D. N. (2013). Amyloid-β imaging with Pittsburgh Compound B and Florbetapir: Comparing radiotracers and quantification methods. *Journal of Nuclear Medicine*.

Lautenschlager, N. T., Cupples, L. A., Rao, V. S., Auerbach, S. A., Becker, R., Burke, J., . . . Farrer, L. A. (1996). Risk of dementia among relatives of Alzheimer's disease patients in the MIRAGE study: What is in store for the oldest old? *Neurology, 46*(3), 641-650.

Lilly, U., LLC. (2013). Amyvid (TM) (Florbetapir F18 Injection). Retrieved from http://www.amyvid.com/pages/index.aspx?oldUrl=http://www.amyvid.com/pages/home.aspx

Lim, W. S., Rubin, E. H., Coats, M., & Morris, J. C. (2005). Early-stage Alzheimer disease represents increased suicidal risk in relation to later stages. *Alzheimer Disease & Associated Disorders, 19*(4), 214-219.

Lin, P.-J., Fillit, H. M., Cohen, J. T., & Neumann, P. J. (2013). Potentially avoidable hospitalizations among Medicare beneficiaries with Alzheimer's disease and related disorders. *Alzheimer's & Dementia: The Journal of the Alzheimer's Association, 9*(1), 30-38.

Lingler, J., Roberts, S., Schulz, R., & Klunk, W. (2012). Development of a standardized approach to disclosing amyloid imaging results in MCI. *Alzheimer's & Dementia: The Journal of the Alzheimer's Association, 8*(4, Supplement), P422.

Lingler, J. H., Butters, M. A., Gentry, A. L., Hu, L., Hunsaker, A. E., Klunk, W. E., . . . Shulz, R. (2015). *Development of a Standardized Approach to Disclosing Amyloid Imaging Research Results in Mild Cognitive Impairment*. Manuscript in preparation.

Lingler, J. H., & Klunk, W. (2013). Disclosure of amyloid imaging results to research participants: Has the time come? *Alzheimer's & Dementia: The Journal of the Alzheimer's Association, 9*(6), 741-744.

Lingler, J. H., Rubin, D., & Saxton, J. A. (2010). Temporal stability of receptiveness to clinical research on Alzheimer's disease. *Alzheimer Disease & Associated Disorders, 24*(Suppl), S30-S34.

Lumley, T., Diehr, P., Emerson, S., & Chen, L. (2002). The importance of the normality assumption in large public health data sets. *Annual Review of Public Health, 23*, 151-169.

Lyketsos, C. G., Lopez, O., Jones, B., Fitzpatrick, A. L., Breitner, J., & DeKosky, S. (2002). Prevalence of neuropsychiatric symptoms in dementia and mild cognitive impairment: Results from the cardiovascular health study. *JAMA: The Journal of the American Medical Association, 288*(12), 1475-1483.

Lyman, K. A. (1989). Bringing the social back in: a critique of the biomedicalization of dementia. *Gerontologist, 29*(5), 597-605.

Magin, P., Juratowitch, L., Dunbabin, J., McElduff, P., Goode, S., Tapley, A., & Pond, D. (2015). Attitudes to Alzheimer's disease testing of Australian general practice patients: a cross-sectional questionnaire-based study. *International Journal of Geriatric Psychiatry*, doi: 10.1002/gps.4335

McInnis-Dittrich, K. (2005). *Social work with elders: A biopsychosocial approach to assessment and intervention*: Allyn & Bacon.

Mintun, M. A., LaRossa, G. N., Sheline, Y. I., Dence, C. S., Lee, S. Y., Mach, R. H., . . . Morris, J. C. (2006). [11C]PIB in a nondemented population: Potential antecedent marker of Alzheimer disease. *Neurology, 67*(3), 446-452.

Morris, J. C., Roe, C. M., Grant, E. A., & et al. (2009). Pittsburgh Compound B imaging and prediction of progression from cognitive normality to symptomatic Alzheimer disease. *Archives of Neurology, 66*(12), 1469-1475.

Mueller, S. G., Weiner, M. W., Thal, L. J., Petersen, R. C., Jack, C. R., Jagust, W., . . . Beckett, L. (2005). Ways toward an early diagnosis in Alzheimer's disease: The Alzheimer's Disease Neuroimaging Initiative (ADNI). *Alzheimer's & Dementia: The Journal of the Alzheimer's Association, 1*(1), 55-66.

National Association of Social Workers. (2008). Code of Ethics of the National Association of Social Workers. Retrieved from https://www.socialworkers.org/pubs/code/code.asp

Neumann, P. J., Hammitt, J. K., Mueller, C., Fillit, H. M., Hill, J., Tetteh, N. A., & Kosik, K. S. (2001). Public attitudes about genetic testing for Alzheimer's disease. *Health Affairs (Millwood), 20*(5), 252-264.

Österholm, J. H., Taghizadeh Larsson, A., & Olaison, A. (2015). Handling the dilemma of self-determination and dementia: A study of case managers' discursive strategies in assessment meetings. *Journal of Gerontological Social Work, 58*(6), 613-636.

Palmer, K., Berger, A. K., Monastero, R., Winblad, B., Bäckman, L., & Fratiglioni, L. (2007). Predictors of progression from mild cognitive impairment to Alzheimer disease. *Neurology, 68*(19), 1596-1602.

Parker, J., & Penhale, B. (1998). *Forgotten people: Positive approaches to dementia care*. Aldershot: Ashgate.

Pinquart, M., & Sörensen, S. (2006). Helping caregivers of persons with dementia: which interventions work and how large are their effects? *International Psychogeriatrics, 18*(04), 577-595.

Plassman, B. L., Langa, K. M., Fisher, G. G., Heeringa, S. G., Weir, D. R., Ofstedal, M. B., . . . Wallace, R. B. (2007). Prevalence of dementia in the United States: the aging, demographics, and memory study. *Neuroepidemiology, 29*(1-2), 125-132.

Rao, J. K., Anderson, L. A., Lin, F.-C., & Laux, J. P. (2014). Completion of advance directives among U.S. consumers. *American Journal of Preventive Medicine, 46*(1), 65-70.

Rinne, J. O., Brooks, D. J., Rossor, M. N., Fox, N. C., Bullock, R., Klunk, W. E., . . . Grundman, M. (2010). 11C-PiB PET assessment of change in fibrillar amyloid-β load in patients with Alzheimer's disease treated with bapineuzumab: a phase 2, double-blind, placebo-controlled, ascending-dose study. *The Lancet Neurology, 9*(4), 363-372.

Roberts, J. S. (2000). Anticipating response to predictive genetic testing for Alzheimer's disease: a survey of first-degree relatives. *Gerontologist, 40*(1), 43-52.

Roberts, J. S., Barber, M., Brown, T. M., Cupples, L. A., Farrer, L. A., Larusse, S. A., . . . Green, R. C. (2004). Who seeks genetic susceptibility testing for Alzheimer's disease? Findings from a multisite, randomized clinical trial. *Genetics in Medicine, 6*(4), 197-203.

Roberts, J. S., Dunn, L. B., & Rabinovici, G. D. (2013). Amyloid imaging, risk disclosure and Alzheimer's disease: ethical and practical issues. *Neurodegenerative Disease Management, 3*(3), 219-229.

Roberts, J. S., LaRusse, S. A., Katzen, H., Whitehouse, P. J., Barber, M., Post, S. G., . . . Green, R. C. (2003). Reasons for seeking genetic susceptibility testing among first-degree relatives of people with Alzheimer disease. *Alzheimer Disease & Associated Disorders, 17*(2), 86-93.

Roberts, J. S., & Tersegno, S. M. (2010). Estimating and disclosing the risk of developing Alzheimer's disease: challenges, controversies and future directions. *Future Neurology, 5*(4), 501-517.

Robinson, L., Gemski, A., Abley, C., Bond, J., Keady, J., Campbell, S., . . . Manthorpe, J. (2011). The transition to dementia--individual and family experiences of receiving a diagnosis: a review. *International Psychogeriatrics, 23*(7), 1026-1043.

Schmider, E., Ziegler, M., Danay, E., Beyer, L., & Bühner, M. (2015). Is it really robust? *Methodology, 6*, 147-151.

Sivananthan, S. N., Lavergne, M. R., & McGrail, K. M. (2015). Caring for dementia: a population-based study examining variations in guideline-consistent medical care. *Alzheimer's & Dementia: The Journal of the Alzheimer's Association, 11*(8), 906-916.

Sivananthan, S. N., Puyat, J. H., & McGrail, K. M. (2013). Variations in self-reported practice of physicians providing clinical care to individuals with dementia: a systematic review. *Journal of the American Geriatrics Society, 61*(8), 1277-1285.

Sommers, L. S., Marton, K. I., Barbaccia, J. C., & Randolph, J. (2000). Physician, nurse, and social worker collaboration in primary care for chronically ill seniors. *Archives of Internal Medicine, 160*(12), 1825-1833.

Spector, A., & Orrell, M. (2010). Using a biopsychosocial model of dementia as a tool to guide clinical practice. *International Psychogeriatrics, 22*(6), 957-965.

Steeman, E., De Casterlé, B. D., Godderis, J., & Grypdonck, M. (2006). Living with early-stage dementia: a review of qualitative studies. *Journal of Advanced Nursing, 54*(6), 722-738.

Steinberg, M., Sheppard, J. M., Tschanz, J. T., Norton, M. C., Steffens, D. C., Breitner, J. C., & Lyketsos, C. G. (2003). The incidence of mental and behavioral disturbances in dementia: the cache county study. *Journal of Neuropsychiatry & Clinical Neurosciences, 15*(3), 340-345.

Tahan, H. A. (2007). One patient, numerous healthcare providers, and multiple care settings: addressing the concerns of care transitions through case management. *Professional Case Management, 12*(1), 37-46.

Thies, W., & Bleiler, L. (2011). 2011 Alzheimer's disease facts and figures. *Alzheimer's & Dementia: The Journal of the Alzheimer's Association, 7*(2), 208-244.

Tombaugh, T. N., & McIntyre, N. J. (1992). The mini-mental state examination: a comprehensive review. *Journal of the American Geriatrics Society, 40*(9), 922-935.

U.S. Census Bureau. (2014). 2014 American Community Survey 1-Year Estimates. Retrieved from http://factfinder.census.gov/faces/tableservices/jsf/pages/productview.xhtml?pid=ACS_14_1YR_S0102&prodType=table

U.S. Food and Drug Administration. (2012). FDA approves imaging drug Amyvid. Retrieved from http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm299678.htm

University Center for Social and Urban Research. (2014). *The State of Aging in Allegheny County*. Retrieved from http://pittsburghtoday.org/specialreports/state-of-aging-age.pdf

van den Dungen, P., van Kuijk, L., van Marwijk, H., van der Wouden, J., Moll van Charante, E., van der Horst, H., & van Hout, H. (2014). Preferences regarding disclosure of a diagnosis of dementia: a systematic review. *International Psychogeriatrics, 26*(10), 1603-1618.

Vandenberghe, R., Van Laere, K., Ivanoiu, A., Salmon, E., Bastin, C., Triau, E., . . . Brooks, D. J. (2010). 18F-flutemetamol amyloid imaging in Alzheimer disease and mild cognitive impairment: A phase 2 trial. *Annals of Neurology, 68*(3), 319-329.

Vickrey, B. G., Mittman, B. S., Connor, K. I., Pearson, M. L., Della Penna, R. D., Ganiats, T. G., . . . Lee, M. (2006). The effect of a disease management intervention on quality and outcomes of dementia care: A randomized, controlled trial. *Annals of Internal Medicine, 145*(10), 713-726.

Von Bertalanffy, L. (1950). An outline of general system theory. *British Journal for the Philosophy of Science*.

Von Bertalanffy, L., & Sutherland, J. W. (1974). General systems theory: Foundations, developments, applications. *IEEE Transactions on Systems, Man and Cybernetics, 4*(6), 592-592.

von Kutzleben, M., Schmid, W., Halek, M., Holle, B., & Bartholomeyczik, S. (2012). Community-dwelling persons with dementia: what do they need? What do they demand? What do they do? A systematic review on the subjective experiences of persons with dementia. *Aging & Mental Health, 16*(3), 378-390.

Werner, P. (2003). Factors influencing intentions to seek a cognitive status examination: a study based on the Health Belief Model. *International Journal of Geriatric Psychiatry, 18*(9), 787-794.

Werner, P., & Heinik, J. (2004). Intentions of first-degree relatives of patients with Alzheimer's disease to seek a cognitive status examination. *International Journal of Geriatric Psychiatry, 19*(5), 479-486.

Werner, P., Stein-Shvachman, I., & Korczyn, A. D. (2009). Early onset dementia: clinical and social aspects. *International Psychogeriatrics, 21*(04), 631-636.

Wikler, E. M., Blendon, R. J., & Benson, J. M. (2013). Would you want to know? Public attitudes on early diagnostic testing for Alzheimer's disease. *Alzheimer's Research & Therapy, 5*(5), 43.

Williams, C. L., Tappen, R. M., Rosselli, M., Keane, F., & Newlin, K. (2010). Willingness to be screened and tested for cognitive impairment: cross-cultural comparison. *American Journal of Alzheimer's Disease & Other Dementias, 25*(2), 160-166.

Wolk, D. A., Zhang, Z., Boudhar, S., Clark, C. M., Pontecorvo, M. J., & Arnold, S. E. (2012). Amyloid imaging in Alzheimer's disease: comparison of florbetapir and Pittsburgh compound-B positron emission tomography. *Journal of Neurology, Neurosurgery & Psychiatry, 83*(9), 923-926.

Zakaid, G. D. (2015). $100M IDEAS: CMS Blesses Study to Evaluate Amyloid Scans in Clinical Practice. Retrieved from http://www.alzforum.org/news/community-news/100m-ideas-cms-blesses-study-evaluate-amyloid-scans-clinical-practice

Zanjani, F. A., Schaie, K. W., & Willis, S. L. (2006). Age group and health status effects on health behavior change. *Behavial Medicine, 32*(2), 36-46.