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**BILINGUALISM: A WAY TO DELAY THE ONSET OF ALZHEIMER'S DISEASE
AND FIGHT THE GLOBAL BURDEN OF DISEASE IT IMPOSES**

**A thesis submitted to
Regis College
The Honors Program
in partial fulfillment of the requirements
for Graduation with Honors**

by

Abigail G. Wester

May 2021

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I. Preface

Curiosity: inquisitive interest in others' concerns (“Merriam-Webster”). This is the word I would use to explain my relationship with learning and academic pursuits alike. Throughout my time at Regis, I have discovered many things about myself and learned more than I thought possible based upon the Jesuit values that are now instilled in me. As a part of the Honors Program, my thoughts have been challenged in more ways than one, which has pushed me to become a better scholar, but more importantly a better person. Throughout my Jesuit education, I have joined a cohort of people who are just as passionate about their education, but also want to make an impact on the world. Everyone has such a unique discipline and background that allows us to share insight from a basis of mutual respect. This Jesuit education has further enabled me to explore a variety of subjects and double major in Neuroscience and Spanish; two subjects that I absolutely love and have found to be surprisingly connected.

As a Spanish major, I have been driven to travel and explore the world in the context of the language, but also medicine. Through this, my love of the language has only grown and sparked my curiosity to its relation to the brain. Among the many advances we have made regarding the brain, there is still so much left to discover about it! We still have so much to explore, and that unique feature of Neuroscience is what initially piqued my interest. One of the ideas that I pondered over as someone who is dedicated to becoming bilingual, is what does it mean to be bilingual in the aging brain.

Although these topics are relevant to my majors and areas I have focused on a great deal, my thesis theme originally came from personal experience. My grandfather was diagnosed with Vascular Dementia a few years ago and watching that struggle and watching my mother work with various healthcare providers and insurance companies and overall cope with it has really

made me want to learn, study, and explore more about dementia. Furthermore, my grandmother was diagnosed with dementia as well and I have noticed in my conversations with her small changes or repeated conversations. I know I am not unique in my experience with my grandparents and the Neurology Collaborators determined dementia to be the second leading cause of death globally. As I continue to explore what I want to do with my life and how I can make an impact on the world, public health has become a leading focus. Exploring the changes that occur in the aging brain and what it means to be bilingual in different global populations allows me to combine all my passions and interest in a meta-analysis for science going forward. I hope at the end my readers will have a broader understanding of the value of public health and global collaboration, the benefits associated with being bi- or multi-lingual, and the severity and importance of dementia, specifically Alzheimer's Disease, research.

II. Background

We live in a world plagued by disease and hardship, but also driven by innovation and technology. Currently, the global burden of disease (GBD) for non-communicable diseases, specifically neurological disorders, is on the rise and posing a challenge to the sustainability of health care systems (GBD 2016 Neurology Collaborators, 2019; Nichols et al., 2019; Bak & Alladi, 2014). In 2016, neurological disorders were the leading cause of disability-adjusted life-years (DALYs) accounting for 11.6% of global DALYs, and resulted in 16.5% of deaths globally making it the second leading cause of death (GBD 2016 Neurology Collaborators, 2019). More specifically, of these neurological disorders, dementias are responsible for 10.4% of neurological DALYs (GBD 2016 Neurology Collaborators, 2019).

Dementia is a neurodegenerative disorder that results in cognitive decline (e.g., memory, language, orientation, and judgement) and a marked deterioration in the capacity to function independently (Atkinson, 2016; Robinson, Stephan, & Magklara, 2019). The population of individuals with dementia is on the rise and as the global population ages and life expectancy increases, the number of people living with dementia will also increase. The percentage of individuals with dementia inside the population doubles nearly every five years for individuals between 50-80 years old (Nichols et al., 2019). In 1990, there were 20.2 million people diagnosed with dementia, but by 2016, this number had increased 117% to ~50 million. This accounts for ~ 5% of the world elderly population (people over the age of 60) (Nichols et al., 2019; World Health Organization, 2019; Prince et al., 2015). This trend is expected to continue and by 2030, the number of people living with dementia is expected to be 82 million, and by 2050 it's projected to triple to 152 million (World Health Organization, 2019; Robinson, Stephan, & Magklara, 2019).

Dementia is a broad term and will take on many forms and versions. The most common types of dementia include Alzheimer's Disease (AD), Vascular Dementia, Lewy Body dementia, and Parkinson's Dementia (DeTure & Dickson, 2019). AD is the most common type of dementia and is more specifically characterized by amyloid plaques and neurofibrillary tangles (DeTure & Dickson, 2019). Like other dementias, AD is a progressive neurodegenerative disease. It is initially characterized by memory impairment and cognitive decline, but later impacts behavior, speech, visuospatial orientation, and the motor system (DeTure, & Dickinson, 2019).

AD can be found in individuals all over the globe. When looking at the Pacific Islands in particular, we see that the population over the age of sixty is set to quadruple between 2014-2020 (Johnston, Preston, Strivens, Qaloewai, S., & Larkins, 2020). This will lead to a significantly older population. A possible reason for this increase could be due to the global rise in life expectancy. Life expectancy has steadily increased in high income countries (HICs) for decades excluding times of war, famine, or pandemics, although there has been stagnation or decline in groups of people who are poor or marginalized (Kontis, Bennet, Guanquan, Foreman, & Ezzati., 2017). In a study by Kontis, Bennet, Guanquan, Foreman, & Ezzati. (2017), the researchers looked at life expectancy projections in 35 HICs for 2030 based on a Bayesian Model. They included countries from Asia and the Pacific, North America, central Europe and western Europe, and Latin American countries that are members of the Organization for Economic Cooperation and Development (OECD). What they found was that life expectancy is expected to continue to rise and possibly reach over 90 years old for females in South Korea (Kontis, Bennet, Guanquan, Foreman, & Ezzati, 2017). Furthermore, the life expectancy in the United States is lower than that of other HICs and this is thought to be due to the social inequalities that exist

inside the healthcare system (Kontis, Bennet, Guanquan, Foreman, & Ezzati, 2017). As humans are living longer, it is important to understand what this means in regard to life expectancy, but also how it changes health, social services, and pensions that often come after retirement (Kontis, Bennet, Guanquan, Foreman, & Ezzati, 2017). As life expectancy increases, policies need to change to better support aging, education, work, retirement, and social care in order to support longer lives (Kontis, Bennet, Guanquan, Foreman, & Ezzati, 2017).

Not only is dementia one of the leading neurological disorders, it is also the leading cause of dependency and disability worldwide (Atkinson, 2016). As previously mentioned, dementia is characterized by the loss of independence (Robinson, Stephan, & Magklara, 2019). This loss of independence can take a large toll on the family or caregivers in addition to a high economic toll. In the United States, where dementia is a major health concern, the estimated health cost was \$818 million in 2015 alone (Nichols et.al, 2019). This cost is projected to increase and by 2030, the global cost of dementia is expected to exceed 1 trillion dollars annually (Robinson, Stephan, & Megklara, 2019). Sperling et al., (2011), found that a hypothetical delay of AD, the most common type of dementia, by five years would lead to a 57% decrease in the number of patients with AD. Not only would this reduce the number of AD patients, it would also decrease the projected Medicare spending in the US for AD from \$627 billion to \$344 billion, nearly a 50% cut in cost (Sperling et al., 2011; Brini et al., 2019). Similarly, a study by Bialystok, Craik, and Freedman (2007), found that a delay of dementia by four years could translate to a 47% decrease in the prevalence of dementia in the population. As the global population grows and dementia, specifically AD, is on the rise, an increase in understanding the neural mechanisms behind AD and ways to delay and slow the onset of AD are at the forefront of research. One way of doing this is through studying the bilingual brain and how the neuroanatomical changes that occur can

act as a defense to delay AD by upwards of five years. This paper is a meta-analysis exploring what dementia, specifically Alzheimer's Disease is, and what it means to be bilingual. This paper will then further explore how we can use this information to lessen the global burden of disease associated with AD.

III. What is Alzheimer's Disease

a. What we know about AD and Dementia

Dementia is characterized as a neurodegenerative disorder that leads to cognitive decline (e.g. memory, language, orientation, and judgement) and a clear deterioration or complete loss in the capacity to function independently (Atkinson, 2016; Robinson, Sephan, & Magklara, 2019). The most common type of dementia, AD, is progressive, irreversible, and a disabling disease that causes a large socioeconomic burden for communities — particularly families and individuals, as well as the government (Crous-Bou et al., 2017). It is characterized by changes in behavior, speech, visuospatial orientation, and changes in the motor system (DeTure & Dickson, 2019). In the past, researchers have found that the onset of dementia and cognitive decline can be delayed through intellectual and lifestyle factors such as high levels of education, occupation level, and participation in leisure activities (Abutalebi et al., 2015). These factors are thought to lead to higher levels of cognitive function and thus lower the rate of memory decline as an individual ages. Additionally, factors such as playing an instrument, formal school, and even certain video games are thought to improve brain fitness and reduce cognitive decline (Klein, Christie, & Parkvall, 2016). Although these factors may appear to slow cognitive delay, there has been increasing evidence that being bilingual has a major impact on delaying the onset of dementia and AD as it leads to a cognitive reserve, or a maintenance of cognitive function with age through stimulating mental and physical activity (Abutalebi et al., 2015; Atkinson, 2016; Bak &

Alladi, 2014; Bialystok, Craik, and Freedman 2007; Bialstok, Craik, & Luk, 2012; Brini et al., 2019; Crous-Bou et al., 2017; Klein, Christie, & Parkvall, 2016; Schwizer, Craik, & Bialstok, 2013).

Another factor in understanding dementia and AD is pre-existing conditions and/or risk factors associated with dementia. For example, Brini et al. (2019) determined that there was not a delayed onset in bilingual individuals who already had a Mild Cognitive Impairment (MCI), but it did show a 3.3 year delay for dementia, and an even larger delay, 4.7 years, for AD (Brini et al., 2019). Crous-Bou et al. (2017), also found that lifelong bilingualism is thought to delay the onset of dementia by 4.5 years. They found it was able to do this because bilingualism contributes to cognitive reserve and thus protects against neurodegeneration. In confirming the delay due to bilingualism, there was no difference in the severity of the onset of dementia once it was set in (Brini et al., 2019). These statistics suggest the importance of looking for symptoms of cognitive impairment and tracking the changes that take place in the brain as a result of MCI's or other alterations in the brain. MCI's are often seen as a precursor and early symptom of dementia (Brini et al., 2019).

These associations found above can be linked to the risk factors — both modifiable and nonmodifiable. Of the individuals diagnosed with dementia, 22.3% of global DALYs were linked to high body-mass index, high fasting plasma glucose, a diet high in sugar-sweetened beverages, and smoking (Nicols, et al, 2019). These are just a few of the manageable risk factors associated with cognitive decline, or AD, other modifiable risk factors include depression, mental inactivity, physical inactivity and poor diet (Crous-Bou et al., 2017). When looking at education and smoking prevalence in a population aged fifteen and older, there was a large evidence base for dementia risk (Nichols et al., 2019). These risks listed above are referred to as

the manageable risk factors because they can be changed and are in our control. Furthermore, 14% of AD cases are attributed to smoking habits and 19% of AD cases globally are potentially linked to low education (Crous-Bou et al., 2017). Schneider, Murray, Banerjee, & Mann (1999), estimated that if there is a 10% reduction in low education in early life, for hypertension in midlife, and for smoking and diabetes throughout the entire life, then dementia prevalence will drop by 8.3% by 2050 and if there is a 20% reduction in these risk factors, there would be a 15.3% reduction in the global presence of dementia by 2050.

Family history plays a large role in dementia and certain biomarkers can be used to understand dementia. In addition to the three non-modifiable risk factors of AD: old age, genetics, and a family member previously diagnosed, the Apolipoprotein E, APOE, gene has been linked to AD. This gene is also linked to vascular dementia, Lewy Body Dementia, Down's Syndrome, and Traumatic Brain Injury (DeTure & Dickson, 2019). The APOE gene has three forms, e2, e3, and e4, and can result in six possible combinations since a copy of the gene is inherited from each parent, e2/e2, e2/e3, e2/e4, e3/e3, e3/e4 and e4/e4 (Alzheimer's Association, 2020). Research has linked the e4 gene with an increased risk of AD as compared to e3 and e2 as the gene with a decreased risk compared to e3. DeTure & Dickson (2019) noted that an individual who has a single copy of the APOE4 polymorphism has an odds ratio 3x that of a non-carrier and that individuals homozygous for APOE4 have an odds ratio 12x that of non-carriers. This is important in understanding the neuropathology of AD.

Alois Alzheimer first noted the pathology for AD over 100 years ago and it is believed to be very specific. AD is classified by the presence of amyloid plaques and neurofibrillary tangles (DeTure & Dickson, 2019). As dense amyloid and tau positive neurites build up, they are linked to neuronal loss and cognitive decline (DeTure & Dickson, 2019). Neuropathology of AD is

believed to include atrophy, or shrinking, in multimodal association cortices, and limbic lobe structures. In AD patients there is often enlarged sulcal spaces and atrophy of the gyri for the frontal and temporal cortices (see Figure 2) (DeTure & Dickson, 2019). This makes sense when thinking about the function of the frontal and temporal cortices as they play a role in cognitive functioning, memory, and emotion (Gupta, 2017). If there is atrophy in these regions, then cognitive functioning, memory, and emotion will be impacted. Furthermore, AD is linked to atrophy in posterior cortical areas as well as in the amygdala and hippocampus.

As mentioned prior, individuals with the APOE4 gene are much more likely to develop AD throughout their lifetime. This is because the e4 gene is more likely to have a beta-amyloid accumulation (increased diffuse plaques, neuritic plaques, tangles, and cerebral amyloid angiopathy) and was linked to disruption of memory function in rodents (Alzheimer's Association, 2020; Raber, Huang, & Ashford, 2004). If beta-amyloid is accumulated, then microglia are likely to go through and clear out the plaques. Microglia are part of the immune system and work to eliminate toxins and debris of dead/dying cells and when activated due to beta-amyloid accumulation, leads to atrophy of the impacted brain areas (Alzheimer's Association, 2020). A study by Mayeux et al. (1998), found that 65% in 1,770 diagnosed individuals, across 26 different Alzheimer's Disease centers in the United States had at least one copy of the APOE-e4 gene. Not only does the copy of genes play a role in the likelihood of developing dementia, it is linked to the age of onset of AD. Individuals homozygous (2 copies) of the e4 allele are much more likely to have clinical AD by the age of 66, followed by e3/e4 individuals who are likely to have an onset by the age of 73, followed by e3/e3 individuals who are likely to have AD onset by 86 years old (Raber, Huang, & Ahsford, 2004). Individuals with the e4 gene have more atrophy of the brain and therefore have a younger age of onset. This leads

to variation in the age of onset based on allele combination. However, of the individuals diagnosed with AD, 61% have the e3/e3 phenotype, 23% have the e3/e4 phenotype, and only 2% have the e4/e4 phenotype (Raber, Huang, & Ahsford, 2004).

Socioeconomic and cultural factors are also thought to play a role in the incidence of AD. It is suggested that certain ethnic minorities have a higher prevalence of dementia than Caucasian individuals (Brini et al, 2019; Gurland et al., 1999). This is supported by Rajan et al (year), who found that Black/African Americans are more likely to have at least one copy of the APOE-e4 gene compared to European Americans. Older Black/African Americans are 2x as likely to have a dementia diagnosis than older Caucasian individuals (Alzheimer's Association 2020). This statistic is similar in Hispanic/Latino populations inside the United States who are 1.5 times as likely as their caucasian counterparts to have dementia (Alzheimer's Association. 2020).

Not only is there a higher dementia incidence in ethnic minorities, Nichols et al. (2019), found that when age is standardized, females are 1.17 times as likely to have dementia as males. Women also have a higher prevalence for AD and other dementia. A study found that 16% of women over the age of 71 are diagnosed with AD while only 11% of men over the age of 71 have AD or another dementia, but this is thought to be linked to a longer life expectancy (Alzheimer's Association, 2020). Furthermore, the prevalence of dementia only increases with age. Dementia is the second leading cause of death in individuals over the age of 70 and increased 148% between 1990 and 2016. Although there are 1.17 times as many incidents of dementia in women as there are in men, approximately every 5-5.5 years of age between 50-80, the prevalence of dementia doubled (Nichols et al., 2019; Fiest et al., 2016). Although Nichols, et al., standardized age, it is possible that women have a higher prevalence due to their longer life expectancy (Fiest et. al., 2016). Fiest et al., (2016) reported that the incidence of AD dementia

increases in both sexes until 85-90 years old at which point it plateaus for men, but continues to increase in women.

As our population ages, dementia rises as well and the longevity of dementia is 20-30 years long and thus, the number of individuals living with dementia is thought to increase to 100-152 million by 2050 (Nichols et al, 2019; World Health Organization, 2019). AD specifically is on the rise and is projected to reach 7.1 million by 2025, a 22% increase from the 5.8 million diagnosed in 2020 (Alzheimer's Association, 2020). However, when looking at and understanding the development of dementia, it is important to understand that there are three stages to dementia: mild, moderate, and severe, and three levels of YLDs for dementia: CDR1 (mild), CDR2 (moderate), and CDR3, (severe) (Nicholes et al, 2019). Furthermore, AD has three stages: mild, moderate, and severe. In mild AD, individuals can typically function somewhat independently, but once they reach moderate AD, the longest phase, individuals typically lose the ability to do simple tasks such as bathing and dressing, and by the time AD progresses to severe AD, the individual requires constant assistance (Alzheimer's Association, 2020). As Alzheimer's and other dementia progress, it is important to understand the burden of disease, but also the disease and what it entails.

Screening for and diagnosing dementia can be done in a variety of ways. Currently methods include a neuropsychological assessment battery, which is a comprehensive test battery that assesses the five cognitive domains: Attention, Language, Memory, Spatial, and Executive Functions, automated cognitive measures that comprise computerized versions of traditional or newly developed tests, and functioning scales for daily activities (Robinson, Sephan, & Magklara, 2019; Zgaljardic & Temple, 2010). In addition to these measures, new cognitive instruments such as The Dementia Screening battery 100 (DES-100, Tunisia), The NIMHANS

Neuropsychological Battery for Elderly (NNB-E, India), The Dementia Assessment by Rapid Test (DART, India), The Cognitive State Test (COST, Turkey), The Identification and Intervention for Dementia in Elderly Africans (IDEA, Sub-Saharan Africa including Tanzania and Nigeria) have been developed in specific LMIC countries (as listed next to the name) to take into account cultural, literacy, and educational biases that might exist when using the HIC screening and diagnostic methods. Furthermore, specific AD screening exists. Although the criteria for dementia is often determined using the Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM IV), AD is often determined using the National Institute on Neurological and Communicative Disorders and Stroke and the Alzheimer Disease and Related Disorders Association (NINCDS-ADRDA) criteria originally proposed in 1984 (Deb, Thornton, Sambamoorthi, & Innes, 2017).

Inside the United States, there are 5.8 million individuals living with AD in 2020. This can be broken down into three age categories: 65-74 years old (17%), 75-84 years old (47%), and 85+ years old (36%). Based on estimates, 14.7% of all people over age 70 in the United States have some type of dementia (Hurd, Martorell, Delavande, Mullen, & Langa, 2013).

b. Financial and Familial Burden of AD

Given the longevity associated with dementia, a high financial burden falls upon families and caregivers. This is particularly true in HICs such as the United States where the direct cost of care for individuals with AD and related dementias was estimated to be \$236 billion (Deb, Thornton, Sambamoorthi, & Innes, 2017). This number is only set to rise and is expected to be \$1 trillion annually in the US by 2050 (Deb, Thornton, Sambamoorthi, & Innes, 2017). A similar study by Ferri et al. (2005)., determined that 0.6% of the UK GDP goes towards taking care of the elderly with cognitive impairment. Since dementia is the leading cause of disability and

dependence, the financial and physical burden associated with dementia often falls on a family member. In a study that looked at AD in particular, the researchers found that women typically become the primary caretaker and that it is usually a daughter or wife who accepts the burden (Alzheimer's Association, 2020). Inside the United States, family members, friends, or other unpaid caregivers are thought to account for 75% - 83% of caregivers (Deb, Thornton, Sambamoorthi, & Innes, 2017; Alzheimer's Association, 2020).

The role of caregiver takes on a physically and financially demanding responsibility. Deb, Thornton, Sambamoorthi, and Innes (2017) found that unpaid caregivers provide approximately 18.1 billion hours of assistance, with their care valued at \$221.3 billion annually. This type of care is known as informal. Conversely, formal care exists and involves hired caregivers through an agency or through a direct hire individual (Hurd, Martorell, Delavande, Mullen, & Langa, 2013). Either through formal or informal care, this is a heavy burden and extremely costly for families. Furthermore, in 2019, the lifetime care estimate for an individual with dementia was \$357,297. This takes a toll on the family and caregivers to provide adequate and good care. When surveyed, caregivers gave three main reasons for accepting the financial and personal burden for a person with dementia. The first and main reason (65%) is the desire to keep a family member or friend at home, followed by forty-eight percent who responded they accepted in order to be close to the to the person with dementia, and finally, the caregiver felt obligated to take care of the individual with dementia (38%) (Alzheimer's Association, 2020).

Since many family members take on the toll of caring for an individual with dementia, it is important to understand how to properly provide for their needs. This trend is not only occurring in the United States. A study conducted by Giebel et al. (2019)., looked at individuals in the UK who have dementia and the care they are given. Interestingly enough, they determined

that the cost of informal care was relatively similar to the cost of paid care by a professional staff. Similar to the statistics above for individuals living in the US with dementia, there are 850,000 people living with dementia in the UK and two thirds of which live in their own homes (Giebel et al., 2019). Because of this, it is important to understand and explore the balance of formal and informal health care especially as the population with AD and related dementia increases.

Cost of AD and related dementias can be grouped into direct and indirect costs. There are both direct medical, hospital visits, physician visits, emergency department visits, pharmacy, and short term nursing facility care, and nonmedical causes, transportation, and the cost of necessary changes such as diet or home modification (Deb, Thornton, Sambamoorthi, & Innes, 2017). Inside the United States where there is a private healthcare system, 68% of the total direct health care for AD and other dementia related disorders are covered by Medicare and Medicaid — our form of public health insurance. Although Medicare and Medicaid pick up a large part of the direct health care cost, it is estimated that patients with AD and other related dementias and their families spend an average of \$10,495 out of pocket (Deb, Thornton, Sambamoorthi, & Innes, 2017). This number increases to up to six times as much for people with AD and other related dementias who reside in long-term care facilities or assisted living facilities (Deb, Thornton, Sambamoorthi, & Innes, 2017). Additionally, individuals living in the community over the age of 65 with AD and related dementias spend 44% more on health-care related costs than their counterparts without AD or a related dementia (Deb, Thornton, Sambamoorthi, & Innes, 2017). This is also true when looking at Medicaid spending. In AD individuals, the overall expenditure of Medicaid was 13% higher than NonAD patients (\$101,810 vs. \$89,835) (Deb, Thornton, Sambamoorthi, & Innes, 2017).

Additionally, when addressing the financial burden of AD, there are two typical approaches: the “replacement cost” and “foregone wage.” The “replacement cost” takes the cost of an equivalent service purchases in the market through a home health agency while the “foregone wage” approaches care by looking at the value on the labor-market income foregone because of caregiving (Hurd, Martorell, Delavande, Mullen, & Langa, 2013). However, when using these mechanisms, it is important to address that many of the caregivers would already be retired. Because of this, the costs were adjusted as a means to estimate the loss of income and productive services (Hurd, Martorell, Delavande, Mullen, & Langa, 2013). With adjustments, the estimated cost of dementia care using the “foregone wage” method was \$41,689 while the value used for the “replacement cost” method was \$56,290 (Hurd, Martorell, Delavande, Mullen, & Langa, 2013) (see Table 2 for yearly adjusted costs). This number is only set to increase total societal costs by 80% by the year 2040 (Hurd, Martorell, Delavande, Mullen, & Langa, 2013). In 2010, the estimated monetary cost for AD alone was \$172 billion however, with adjustment Hurd, Martorell, Delavande, Mullen, & Langa (2013) predicted it to be closer to \$109 billion. If this cost is set to increase by 80% over 30 years, it becomes increasingly important to understand and address AD and other dementias.

c. Dementia Across the Globe

Dementia impacts individuals in every part of the world. Currently Low Income Countries (LIC) tend to have a reduced prevalence, but between 2015 and 2050, the number of people with dementia in LIC is set to rise 264%. Similarly, in Low and Middle Income Countries (LMIC), dementia will rise 227% in between 2015 and 2050, 223% in Middle Income Countries (MIC), and 116% in HIC (Prince et al., 2015). Furthermore, LMIC carries the highest burden of dementia and accounts for 58% of all global cases and this percentage is predicted to increase to

68% of all global cases by 2050. As of 2015, East Asia has the largest population of individuals living with dementia at 9.8 million, followed by Western Europe with 7.8 million, South Asia is next with 5.1 million, and finally North America has 4.8 million (Prince et al., 2015). These numbers are incredibly high and with the prediction to rise by upwards of 264%, dementia impacts the entire globe. In Western Europe alone, the number of individuals living with dementia is set to nearly double by 2050 and go from 7.5 million people to 14.3 million people impacted (Prince et al., 2015). These numbers have already grown exponentially from the 2005 study by Ferri et al., where the prevalence in China/Western Pacific Countries was 6 million, followed by Western Europe with 4.9 million, and North America with 3.4 million. Global cases are expected to double every twenty years (Ferri et al., 2005). With global dementia cases on the rise, and AD accounting for 60-80% of all cases, it is important to understand what these mean for each country, the globe, and ultimately testing and preventative methods (DeTure & Dickson, 2019).

In their study, Ferri et al., (2005), used a Delphi consensus approach to look at the prevalence of dementia from around the world. In the study, the researchers focused on dementia prevalence in all 14 regions of the world and broke down five-year age bands for individuals aged 60-84 and then a final group of individuals 85+ years old. The fourteen regions were based on WHO guidelines and included AMRO [Americas], EURO [Europe], EMRO [north Africa and the middle east], AFRO [Africa], SEARO [south Asia], and WPRO [western Pacific]). Globally, there are roughly 4.6 million new dementia cases every year (Ferri et al., 2005). If broken down, this is about 1 new case every 7 seconds (Ferri et al., 2005). What they determined was that developed countries will experience a steady increase in dementia cases over the next forty years while Latin American and African countries will have a rapid increase in the number of

individuals living with dementia and India, China, South Asian, and Western Pacific countries will have a rise in their already high prevalence (Ferri et al., 2005). They also predict that by 2040, the number of individuals living with dementia in North America will be the same as individuals living with dementia in Latin America (Ferri et al., 2005). This is a staggering increase because Latin America currently has about half as many individuals living with dementia as North America.

To further support the points above, the prevalence of dementia increases exponentially with age, but doubles at different rates (Schneider, Murray, Banerjee, & Mann, 1999). Dementia doubles in 5.5 year increments of age in North America, 5.7 year increments in Asia Pacific, 5.9 year increments in Latin America, in 6.3 year increments in East Asia, in 6.5 year increments in West and Central Europe, in 6.6 year increments in South Asia, every 6.9 years in Australasia, in 7.2 year increments in the Caribbean and SSA, and finally, in 10.6 year increments in South East Asia (Schneider, Murray, Banerjee, & Mann, 1999).

AD rates are on the rise as well. Making up 60-80% of all dementia cases, it is estimated that there will be 106 million cases worldwide compared to the 30 million in 2010 (Norton, Matthews, Barnes, Yaffe, & Brayne, 2014). This is ~3.5x as many cases over 40 years. However, many of the risks are modifiable and Norton, Matthews, Barnes, Yaffe, and Brayne (2014) determined that combined, the seven risk factors considered account for half of the cases of AD worldwide. The risk factors included in the study were diabetes, midlife hypertension, midlife obesity, physical inactivity, smoking, depression and educational attainment (Norton, Matthews, Barnes, Yaffe, & Brayne, 2014). By addressing these risk factors, by 2050 we could reduce the worldwide prevalence of AD by 8%-15% or by 8.8 to 16.2 million cases (Norton, Matthews, Barnes, Yaffe, & Brayne, 2014). Given that AD accounts for the largest percentage of dementia,

reducing the prevalence by 8%-15% would significantly lower the burden associated with dementia (see Figure 1).

d. Neuroanatomical Changes associated with AD and related dementia

A healthy adult brain will have ~100 billion neurons and create 100 trillion synapses (Alzheimer's Association, 2020). However, as the brain changes and ages, this can change. Aging is a normal human process that everyone experiences. With age, the brain has both structural and functional changes that lead to a normal amount of cognitive decline (Abutalebi et al., 2015). As individuals age, they naturally lose grey matter in the anterior regions of the brain and they lose white matter between the anterior and posterior cortical regions. Changes in the brain associated with Alzheimer's begin to take place at least 20 years before symptoms start to appear (Alzheimer's Association, 2020). In AD specifically, the accumulation of beta-amyloid plaques, or beta-amyloid protein fragments, on the outside of the neuron, and accumulation of tau tangles, an abnormal form of the protein tau, builds up inside the neuron (Alzheimer's Association, 2020). These changes in neuroanatomy, lead to an activation of microglia. Microglia are responsible for clean-up of toxic proteins and dead or dying cells. Since the tau tangles and beta-amyloid plaques are toxic changes, the microglia are activated and signaled to go through and clear out the toxic tangles and plaques and thus, leads to atrophy, or shrinkage of the brain (Alzheimer's Association, 2020). Atrophy of the brain is one of the most noticeable changes that results from AD.

White matter changes are frequently found in dementia patients. A study by Lind, Jonsson, Karlsson, Sjögren, Wallin & Edman et al. (2006), involved participants with AD, Frontotemporal Dementia, Vascular Dementia, and a mixture of Alzheimer's/Vascular Dementia. White matter consists of myelinated nerve fibers (axons) and get their color from

myelin lipids. If myelin is reduced, it has been associated with white matter changes. Not only is it important to look at the physical structural changes, it is also important to take into account the personality and psychological changes that typically take place in individuals with dementia. Behavioral changes in individuals with AD have been linked to structural changes and degeneration in the frontotemporal lobe (Mahoney, Rohrer, Omaar, Rossor, & Warren, 2011).

AD in particular has a very specific neuropathology, but is not normally confirmed until a post-mortem analysis. However, the pathology includes cortical atrophy throughout the brain, but most obvious in the multimodal association cortices and the limbic lobe structures (DeTure & Dickson, 2019). The limbic systems structures are involved in learning, memory, and emotion (Gupta, 2017). The limbic lobe is a ring of cortex located on the medial part of the cerebral hemisphere. The limbic lobe includes the cingulate gyrus, the parahippocampal gyrus, and septal cortex (Gupta, 2017). Atrophy is also common in other parts of the brain. The frontal and temporal cortices often have atrophied gyri and enlarged sulcal spaces. This is often accompanied by medial temporal atrophy in regions of the amygdala and hippocampus — two brain structures involved in memory and emotion (DeTure & Dickson, 2019). Not only are temporal and frontal regions of the brain impacted, AD has two main types of lesions: amyloid plaques and neurofibrillary tangles (Jouanne, Rault, & Voisin-Chiret, 2017). Dysfunction of the tau and beta-amyloid proteins lead to this build up and lead to neuronal loss and cognitive decline common in AD (Jouanne, Rault, & Voisin-Chiret, 2017; DeTure & Dickson, 2019).

IV. What does it mean to be bilingual and how does that help us?

a. Definition

Bilingualism is a hard concept to describe because a definition can easily be too narrow or too broad and thus leave out a large group of people or include too many. Albert Costa (2019)

said “bilingualism is a window into the study of human cognition,” but what does this mean? A bilingual individual processes information in two languages and has to be able to process the different phonetic and phonological breakdowns in order to produce the correct sounds (Costa, 2019). However, bilingual studies have had varying results in whether or not being bilingual is beneficial or harmful to an individual. The benefits are vast and thought to be greater than the negatives associated with bilingualism. To begin, it is believed that there is joint activation of both languages even when only speaking one language (Bialystok, Craik, & Luk, 2012). They are thought to have better executive control and thus have outperformed monolingual participants in naming the font color in a Stroop task, have smaller costs in task switching, and have an increased ability to maintain a task set in an attention task (Atkinson, 2016; Bialystok, Craik, & Luk, 2012). The Stroop Test is a commonly used neuropsychological test that assesses the participant’s ability to inhibit cognitive inference. This is done while a specific stimulus feature impedes the processing of a second, simultaneous stimulus (Scarpina & Tahini, 2017). Furthermore, when looking at bilingual children, researchers found that bilingual and monolingual children solve non-verbal tasks differently (Bialystok, Craik, & Luk, 2012). They found that bilingual children outperformed their monolingual counterparts in non-verbal tasks, but bilingual and monolingual children performed the same on tasks that did not include distracting perceptual information.

Interestingly, the bilingual advantage appears to be found in older adults rather than younger adults, but there is still an advantage for young adults on tasks that are deemed difficult (Bialystok, Craik, & Luk, 2012). Given bilingual individuals are learning two languages at the same time, they often have a smaller vocabulary than monolinguals. This is because bilingual individuals are thought to be slower to comprehend and produce words. Since bilingual

individuals are able to comprehend and process two languages, their brain has to register which language is being spoken and respond accurately (Bialystok, Craik, & Luk, 2012). This causes them to be more susceptible to negative priming, and this is thought to be because of greater inhibition (Bialystok, Craik, & Luk, 2012). However an increase in the grey matter density in the most medial part of the lobule VIIA of the right cerebellum predicted a bilingual person's ability to resist speech interference from their first language while comprehending something in their second language (Green & Abutalebi, 2016). This ease is something monolinguals do not have.

When looking at and defining protocol for analyzing bilingual differences, García-Pentón, García, Costello, Duñabeitia, & Carreiras (2016), said there needs to be a more consistent and sophisticated method through combining behavioral and brain measures, more complex but standardized procedures, and larger and more thoroughly characterized samples.

b. Bilingualism Across the Globe

Bialystok, Craik, and Luk, (2012) state that roughly fifty percent of the global population is thought to be bilingual compared to twenty percent of the population in the United States and Canada, two English speaking countries. In the past few decades there has been increased mobility throughout European Union (EU) countries due to immigration and rapid growth in the number of refugees (Dockrell et al., 2021). Because of this, multilingual classrooms have become the norm where many children have different first languages. In the EU (including the United Kingdom (UK) and Ireland), there are 23 officially recognized languages, 60 indigenous regional and minority languages, and many non-indigenous languages spoken by migrant communities (“Europeans and their Languages,” 2012). A long-term goal of the EU is that every citizen has enough language skills in at least two foreign languages, but this is not yet feasible in all countries. They found that 54% of Europeans are able to hold a conversation in at least one

additional language, 25% could speak at least two additional languages, and 10% could speak at least three additional languages (“Europeans and their Languages,” 2012). Over 90% of the respondents in Luxembourg, Latvia, the Netherlands, Malta, Slovenia, Lithuania, and Sweden speak at least two languages (“Europeans and their Languages,” 2012). Inside the EU, English is the most widely spoken foreign language. This is interesting because the UK and Ireland were among the countries least likely to have citizens able to speak a second language. Given that English is considered the *lingua franca*, and is spoken in the United States, Canada, the UK, and Ireland, this might be why they fall behind in bi- and multi-lingual speakers.

c. Neuroanatomical Changes associated with Bilingualism

The lifelong use of two or more languages is thought to produce neuroprotective effects and the changes that ensue are more likely to reflect the neural response to increased demand of neural connections in the brain (Green & Abutalebi, 2016). It is important to note that when studying bilingualism, that it is not something that can just be reduced to structural neural plasticity (García-Pentón, García, Costello, Duñabeitia, & Carreiras, 2016). This is because neural plasticity does not necessarily point to a bilingual advantage (García-Pentón, García, Costello, Duñabeitia, & Carreiras, 2016). However, the benefit of being bilingual has long been studied with cognitive benefits detected as early as seven months old (Bak & Alladi, 2014). This ability to detect a cognitive benefit so young has led some researchers to consider evidence that shows that being bilingual might even be the human norm rather than the exception (Bak & Alladi, 2014). To further explore what it means to be bilingual in the aging brain, researchers have looked at neuroanatomical differences and the changes that take place in response to bilingualism. Bilingualism has been linked to changes in the left inferior parietal lobe, the anterior cingulate cortex (ACC), the dorsal ACC in particular, and the subcortical areas of the

left caudate and putamen (Abutalebi et al., 2015; Green & Abutalebi, 2016). Aging bilinguals have increased grey matter densities in the temporal pole and orbito-frontal complex (Abutalebi et al., 2015). This is valuable when looking at the negative correlation often found between age and grey matter because young bilinguals with increased grey matter maintain it throughout their lifetime (Abutalebi et al., 2015; Green & Abutalebi, 2016).

When looking at German-French bilinguals, Chinese-English bilinguals, and Spanish-English bilinguals, Bialystok, Craik, and Luk (2012) found that the involvement of various brain areas was extremely widespread in language activation. They found that when a participant switched languages, there was distributed activation of the bilateral frontal and precentral areas, bilateral caudate, bilateral (or midline) pre-supplementary areas (pre-SMA), and bilateral temporal regions (Bialystok, Craik, & Luk, 2012). This bilateral activation is particularly interesting because it implies strong neuronal connections between both lobes of the brain. In Japanese-English bilinguals, in particular, there was a connection between the left inferior frontal lobe and the left middle temporal gyrus (Bialystok, Craik, & Luk, 2012). Additionally, when switching languages, Broca's area which is in charge of speech production, the Dorsolateral Prefrontal Cortex (DLPFC), and the left front area are activated (Bialystok, Craik, & Luk, 2012). These areas of the brain are often associated with executive control which is thought to be better trained in bilinguals than in monolinguals (Abutalebi et al., 2015; Atkinson, 2016; Bialystok, Craik, Luk, 2012). By processing and speaking two languages, the brain creates stronger cognitive networks to allow for enhanced cognitive performance throughout a lifetime. This leads to the idea of joint activation whereby bilingual speakers have some activation of both languages when speaking (Bialystok, Craik, Luk, 2012). This connects to the idea of bilingualism as a more holistic notion because of the different sounds and grammatical concepts

that in turn, lead to more executive control (Bak & Alladi, 2014) The increased executive control portrayed by bilinguals is thought to be one of the factors that leads to the delay in the onset of dementia. This bilingual benefit was found in frontotemporal dementia, AD, and vascular dementia in particular (Bak & Alladi, 2014).

The cognitive benefits of bilingualism can be detected in babies as young as seven months old (Bak & Alladi, 2014). Furthermore, the ability for babies to detect language differences as young as seven months connects to the idea of bilingualism as a more holistic skill due to the variety of sounds and grammatical concepts that bilingual speakers acquire (Bak & Alladi, 2014). This varied language could lead to differences in brain region activation. Biaylstok, Craik, & Luk, (2012) found that fMRI studies show that monolingual participants had increased activation of the right inferior frontal gyrus whereas bilinguals have increased activity in the left inferior frontal gyrus when measuring reaction time of switch costs.

V. Global Burden of Disease

a. Global Health Overview: Understanding Burden of Disease

Public and Global Health professionals dedicate their life to studying and understanding health in our local and global communities. This focus on population health allows the globe to stay connected and follow trends and patterns between and among countries. One way to do this is by looking at the GBD for a specific disease. The concept was first developed in the 1990s by Harvard's School of Public Health, the World Bank (a source of financial and technological assistance for developing countries globally), and the World Health Organization as a way to describe the death and loss of health as a result of injury, diseases, and other risk factors globally (World Health Organization "Burden of disease"). The GBD is calculated by looking at the Years of Life Lost (YLL) as a result of an early death and the number of Years of Life Lived

with Disability (YLD) as calculated by the number of years a person lives with disability (Whitefor, Ferrari, Degenhardt, Feigin, & Vos, 2015). These two values are then added together to determine the Disability Adjusted Life Year (DALY), and thus the burden of disease imposed (Chen, Jacobsen, & Deshmukh, 2015). The ability to determine the GBD for each disease in different regions of the world is essential to improving global and community health. This measure has been used to determine the DALY and burden of disease for more than 130 different causes of death or disability (World Health Organization, 2019). By using data from many countries, we can look into environmental factors and clustered risk (Nichols et al., 2019).

b. Who is most impacted?

Dementia currently impacts 50 million people worldwide (~five percent) of the elderly population (World Health Organization, 2019; Robinson, Sephan, & Magklara, 2019). However, of the individuals impacted, dementia disproportionately impacts individuals in LMIC and indigenous people (Johnston, Preston, Strivens, Qaloewai, S., & Larkins, 2020). Currently, 58-60% of individuals diagnosed with dementia live in LMIC, but most of the trials for dementia are being conducted in HICs such as the United States (Johnston, Preston, Strivens, Qaloewai, and Larkins, 2020; World Health Organization, 2019; Robinson, Sephan, & Magklara, 2019). Furthermore, 67% of the individuals living with dementia in Africa and 63% of the individuals living with dementia in South East Asia said their symptoms were joked about by others (Alzheimer's Association, 2020). This stigma, along with inadequate screening causes dementia to impact LMIC countries in particular. Screening for dementia in LMIC has been adapted from HIC methods. Given these tools are not always adapted properly to the given country, it can lead to education, literacy, and cultural bias (Robinson, Sephan, & Magklara, 2019). If an individual is illiterate, it is possible that a specific battery or cognitive test will not function in the same way

for that individual. Specifically cultural bias can appear when using HIC adapted tools to screen indigenous groups in LMIC.

A major problem with adopting HIC screening tools is that it does not always adapt for language and cultural norms. For example, if a culture does not follow the Western calendar, asking someone who is taking the test what day it is would not provide fair or accurate results (Robinson, Stephan, & Magklara, 2019). This leads to biases due to language and culture. Furthermore, many screening tools used in LMIC countries are done to address AD and test recall (Paddick et al., 2017). Although AD is the most prevalent dementia, screening tools need to be more inclusive for all types of dementia. This can lead to under representation and misrepresentation of dementia globally.

A meta-analysis by Fiest et al., (2016), looked at the prevalence of AD across 44 European, 36 Asian, 32 North American, 5 South American, 2 African, and 2 Australian studies. When looking at the estimated age, sex, diagnostic criteria, location, and time of incidence and prevalence, they found that there is a higher estimated prevalence of AD in North Africa than in Asia or Europe and found a higher prevalence in North America as compared to Asia (Fiest et al., 2016).

As previously mentioned, dementia is a growing health concern in Indigenous individuals in particular (Johnston, Preston, Strivens, Qaloewai, S., & Larkins, 2020). In Indigenous communities, there is limited experience and formal care. This limited diagnosis is based in the perception of dementia in the communities. Dementia was defined in the context of aging, mental illness, traditional cultural beliefs, and the trauma of colonization (Johnston, Preston, Strivens, Qaloewai, S., & Larkins, 2020). Cognitive decline is perceived as a social construct that is inevitable with aging rather than something pathological (Johnston, Preston, Strivens,

Qaloewai, S., & Larkins, 2020). Similarly, when reviewing a study that looked at Japanese individuals, the idea of “boke” continued to appear. “Boke” is a cultural concept that is characterized by various signs that are typical of AD. “Boke” was defined as an individual who is perceived to be “spacing out” or disconnected from social interactions and it is a social responsibility to prevent “boke” (Johnston, Preston, Strivens, Qaloewai, S., & Larkins, 2020).

As individuals progress into later stages of dementia, it falls upon the family to be the primary caregiver (Alzheimer’s Association, 2020; Kasper, Freedman, Spillman, & Wolff, 2015). In a study looking at AD, researchers found that 59% of caregivers rated their emotional stress levels as high or very high, 30-40% reported feelings of depression, 38% indicate the physical stress as high to very high (Alzheimer’s Association, 2020; Sallim, Sayampanathan, Cuttilan, & Chun-Man, 2015; Collins & Kishita, 2019). These statistics further enforce the burden of AD and the harsh reality it imposes on both the family/caregiver and the individual diagnosed. This makes it hard to find a positive outlook on the future of dementia research, but the narrative is changing. In an analysis of AD, the Alzheimer’s Association (2020), compared typical age-related changes compared to signs of dementia or AD. A normal age related change would be occasionally forgetting names or appointments, but later remembering them, but a sign of AD or another dementia would be memory loss that disrupts life such as forgetting important dates or events or repeatedly asking for the same information over and over again. Another normal change in aging is developing a routine and becoming irritated when it is disrupted, but an individual with AD or a different dementia, has a noticeable mood or personality change and has become increasingly confused, suspicious, depressed, fearful or anxious (Alzheimer’s Association, 2020).

c. Why is there such a large burden?

In 2016, dementia was the leading cause of Disability Adjusted Life Years (DALYs) and second leading cause of death for neurological disorders globally. Dementias account for 10.4% of neurological DALYs (GBD 2016 Neurology Collaborators, 2019). Combined Neurological Disorders are responsible for 276 million DALYs across the globe. Dementia alone accounts for roughly 30 million DALYs for which the greatest number of DALYs due to dementia is in individuals between the ages of 80 and 89 years old (GBD 2016 Neurology Collaborators, 2019). When looking at noncommunicable diseases, dementia accounts for 11.9% of YLDs (World Health Organization, 2019). These statistics cause many individuals to believe that they will inevitably develop dementia. As the global burden of disease shifts more from communicable (transmittable) to non-communicable diseases, it is important to be aware of the increasing numbers and challenge to sustainable health neurological disorders in particular (World Health Organization, 2019; Peters et al., 2019).

Another factor to take into account is the increasing life expectancy. Currently, there is a reduced prevalence of dementia in LICs specifically due to the lower life expectancy (Prince et al., 2015). As access to healthcare continues to grow and we transition from communicable to non-communicable diseases as the leading causes of death, there is an increase in global life expectancy. Although HICs still lead in life expectancy, there is an overall global increase. Interestingly enough, the United States is behind based on its life expectancy compared to other HICs. A study by Kontis, Bennet, Guanquan, Foreman, & Ezzati (2017), looked at 35 industrialized countries (HICs in Asia and the Pacific, North America, central Europe and western Europe, and Latin American countries that are member of the OECD) and predicted age-specific mortality up to 2030. They found that life expectancy has steadily increased for decades except for in times of war, famine, or infectious outbreaks in high income countries, but that this

trend does not hold true for the marginalized groups (Kontis, Bennet, Guanquan, Foreman, & Ezzati, 2017).

Marginalized and poor groups will not have the same access to healthy foods, healthcare, or clean water in the same way that other, wealthier groups do and will not have the same increase in life expectancy because there are higher levels of young adult deaths, risk for major chronic diseases, and less effective health systems. Where social inequalities are higher, there tends to be a lower life expectancy (Kontis, Bennet, Guanquan, Foreman, & Ezzati, 2017). This might be the reason that the United States lags behind other high income countries. The United States is the only OECD country without universal health care and this in turn leads to poor healthcare due to the financial burden (Kontis, Bennet, Guanquan, Foreman, & Ezzati, 2017). The study draws attention to the United States because they have the highest child and maternal mortality, homicide rate, and body-mass index of any HIC (Kontis, Bennet, Guanquan, Foreman, & Ezzati, 2017). With high and rising health inequalities, the USA's life expectancy is set to stagnate or even decline for certain populations (Kontis, Bennet, Guanquan, Foreman, & Ezzati, 2017).

By using the Bayesian model approach to mortality and life expectancy, life expectancy is set to increase in all industrialized countries, particularly South Korea where the female life expectancy is set to break 90 by 2030 (Kontis, Bennet, Guanquan, Foreman, & Ezzati, 2017). Currently, life expectancy is lower in men because there is a greater correlation to death by external causes such as injuries, but this gap between men and women is projected to decrease in all of the countries except Mexico by 2030 (Kontis, Bennet, Guanquan, Foreman, & Ezzati, 2017). However, when looking at life expectancy, it is important to take into account the life expectancy of an individual living with dementia. Inside the United States, once an individual is

diagnosed with AD, they live an average of four to eight years, but some people live up to twenty years with the disease (Alzheimer's Association, 2020). The burden of AD in the US is huge, where it is the sixth leading cause of death and the fifth leading cause of death in individuals 65 and older. In the United States alone, ~14.7% of individuals over the age of 70 have dementia and as the population ages and individuals move into the risk category, the burden of AD and other dementias will only increase (Hurd, Martorell, Dellavande, Mullen & Langa, 2013). In order to combat this, the focus of preventative methods and a long term cure becomes even more important.

When addressing the burden of AD and dementia, it is important to look at the role they take on in LMIC countries. In LMIC countries in particular, there is a large stigma around dementia and the symptoms that come along with it. In China, Tanzania, and India, symptoms of dementia have traditionally been included inside the cultural conceptualization of aging (Johnston, Preston, Strivens, Qaloewai, S., & Larkins, 2020). In China in particular, early symptoms are believed to be a part of normal aging, but as the symptoms progress and worsen, this often leads to social isolation of the individual with dementia. This study by Johnston, Preston, Strivens, Qaloewai, S., & Larkins (2020) evaluated nineteen publications and of those nineteen studies, fifteen were set in LMIC countries and three involved First Nations in Canada and the Aboriginal Torres Strait Islander populations in Australia. A common theme they found throughout the various communities was the belief that dementia arose as a part of natural aging rather than as the development of a disease, or as a result from a hard life (Johnston, Preston, Strivens, Qaloewai, S., & Larkins, 2020). Other common beliefs for dementia-like symptoms included stress, death of a loved one, neglect by family, abuse, loneliness, various physiological diseases, malaria, faking or deliberate misbehavior, weakness, poverty, curses, a growing

connection with the spiritual world, colonization, witchcraft, or as a form of punishment from your ancestors (Johnston, Preston, Strivens, Qaloewai, S., & Larkins, 2020). This false characterization makes it hard to diagnose.

Moreover, in the First Nations Community, there has been a shift in the stigma associated with dementia. It was once viewed as a way of being closer to the creator and the spiritual world, but now memory loss, a common symptom of dementia, is associated with the impact of colonization and is something to be feared (Johnston, Preston, Strivens, Qaloewai, S., & Larkins, 2020). As mentioned earlier with the screening techniques, low or no formal education plays a role in bias. In addition to improving screening technique, public health education around AD and dementia is equally as important to improving the quality of life and presentation of the disease.

d. Solutions

AD and other dementias are debilitating and life altering diseases that we have not figured out how to prevent or slow. In order to reduce the cost of dementia care and the burden of disease that comes with it, there needs to be more, and better screening for earlier intervention and more screening in high risk groups (Robinson, Sephan, & Magklara, 2019). By placing an emphasis on these two screening practices, individuals can maintain more of a functional independence, but also be more aware of their dementia. Currently, scientists are looking into the benefit of playing a musical instrument, formal schooling, and even playing certain video games on improving brain fitness and as ways to reduce cognitive decline (Klein, Christie, Parkvall, 2016). Similarly, bilingualism is thought to produce similar neural structural changes. The increase in cognitive reserve is thought to leave indelible marks on the brain similar to those created by highly specialized skills such as musical expertise and navigational experience (Baum

& Titone, 2014). Additionally, they found that countries with a higher literacy had a lower incidence of AD (Klein, Christie, Parkvall, 2016). Alzheimer's Association (2020), determined that brain health is closely linked to an individual's access to medical care and medical treatment. Although researchers are still searching for a cure and successful prevention method for dementia, they have looked into different modifiable risk factors and found ways to limit the risk associated with modifiable risk factors.

In addition to avoiding social isolation and cognitive inactivity, there are varying levels of recommendations. Strong recommendations for modifiable risk factors include physical activity, stopping the use of tobacco, social interaction, and management of hypertension and diabetes (World Health Organization, 2019; Edwards III, Gamez, Escobedo Jr., Calderon, & Moreno-Gonzalez, 2019). Physical activity in particular is recommended for individuals to reduce the risk of cognitive decline in people with normal cognition, but is only a conditional recommendation in individuals who already have an MCI (World Health Organization, 2019). Other recommendations include eating a healthy, balanced diet, eating a mediterranean-like diet, cognitive training, interventions to reduce obesity, and management of hypertension/diabetes. Furthermore, individuals with normal cognition or mild impairment should reduce harmful drinking (World Health Organization, 2019; Edwards III, Gamez, Escobedo Jr., Calderon, & Moreno-Gonzalez, 2019). However, it is important to note that The World Health Organization does not recommend Vitamins B and E, or polyunsaturated fatty acids and multi-complex supplementation as a way to protect cognition.

Another possible avenue of research includes drug therapy. Currently, there are five FDA approved drugs to treat AD. These five drugs are rivastigmine, galantamine, donepezil, memantine, and memantine combined with donepezil (Alzheimer's Association, 2020).

Excluding memantine, all of the drugs temporarily improve cognitive symptoms by increasing the amount of neurotransmitter. Additionally, researchers have found that the use of antipsychotics in individuals with dementia leads to an increased risk of stroke (Alzheimer's Association, 2020).

Another critical step in managing dementia is by drawing on cultural and individual beliefs to provide the best and most holistic care. This is particularly important in LMIC countries where more stigmas and notions exist around dementia. Dementia stigma is a major problem and can lead to individuals being turned away from residential care or excluded from the hospital (Ferri et al., 2005). The key to de-stigmatizing dementia is education. Many individuals do not necessarily know they need help or if they do, will not seek out help. If a person does seek out help, health care providers will not necessarily tend to their needs. As prevalence increases, we need to improve medical and social care through public health awareness and education (Ferri et al., 2005). All of these platforms involve education and to do this we need to incorporate more in day-to-day life.

VI. Connecting the dots between AD and Bilingualism

Various studies have looked into how bilingualism delays the onset of dementia and they have shown that being bilingual delays the onset of dementia anywhere from 3.2 to 6 years (Abutalebi et al., 2015; Atkinson, 2016; Bak & Alladi, 2014; Bialystok, Craik, and Freedman 2007; Brini et al., 2019; Schwizer, Craik, & Bialstok, 2013). Not only is the diagnosis of dementia delayed in bilingual speakers, the onset of symptoms reported is an average of 5.1 years after monolingual individuals (Askinson, 2016). If the onset of dementia can be delayed by 4 years, the prevalence of dementia is reduced by 47% (Bialystok, Craik, & Freedman, 2007).

When looking at the delay of dementia in the bilingual community, it is important to remember how diverse of a community it is and take into account other factors such as socioeconomic status, education level, immigration, and employment status (Bak & Alladi, 2014). When looking at these factors there have been mixed results in their role in the delayed onset. Bialystok, Craik, and Freedman (2007), took into account cultural differences, immigration, formal education, and employment status, but none of this could deny that being bilingual delayed the onset. However, another study found that dementia is higher in ethnic minorities than in Caucasian individuals suggesting that there are socioeconomic and cultural factors that may play a role in the relationship between bilingualism and dementia (Brini et al., 2019). Furthermore, a study that took place in Canada looked at the role of immigration in the delayed onset of AD and the authors found that the bilingual benefit was not only seen in immigrants, but also native born bilingual speakers (Schwizer, Craik, & Bialstok, 2013). Although they did not see this trend in bilingual individuals whose first language was English, a delay of 3.2 years occurred in non-immigrant bilinguals whose first language was French. They further found that the delay of AD in the immigrant bilingual population was 5.1 years (Schwizer, Craik, & Bialstok, 2013). This finding showed the same functional organization of neural responses for both immigrant and nonimmigrant bilingual individuals (Schwizer, Craik, & Bialstok, 2013). These neural responses differed from their monolingual counterparts (Schwizer, Craik, & Bialstok, 2013). Interestingly enough, there is evidence to affirm the delay of dementia in the bilingual brain because no differences are found between monolinguals and bilinguals on the severity of dementia upon diagnosis (Brini et al., 2019). Had the bilingual speaker delayed going to the doctor for cultural differences, the researchers would have expected further cognitive decline. This suggests that being bilingual somehow better preserves the

neurocognitive function and alters the brain so that it has enhanced cognitive function and executive control (Atkinson, 2016).

A factor that could influence the delay in dementia onset associated with bilingualism is the level of proficiency in each language. When choosing participants for a study involving bilingual individuals, it is extremely important that there are clear guidelines for the definition of bilingualism rather than a loose, liberal definition for bilingualism (Atkinson, 2016). This idea is supported by better performance on the Stroop Test by individuals who consistently use both languages (Atkinson, 2016; Bialystok, Craik, & Luk, 2012). Studies have found that individuals who become bilingual during adulthood or who do not frequently speak the second language do not have the same protection against dementia as individuals who learn a language from birth or consistently speak both (Atkinson, 2016). The reasons behind these brain differences and what they mean on the bilingual and aging brain are areas that are currently being studied. Discovering the underlying mechanisms of bilingualism will provide researchers further insight into the benefits of bilingualism for the onset of dementia. Bialystok, Craik, and Freedman (2007), said that increased resting phosphocreatine levels, synapses and arborized dendrites, increased generation of neurons, and functional reorganization of the brain network are among the plausible underlying mechanisms to understanding what it means to be bilingual.

When returning to neuroanatomy, there is actually a lot of overlap between the neuroanatomical changes that take place in a bilingual brain and in a brain with AD or a related dementia. In bilingual individuals, there is an increase in grey matter in the temporal pole and orbitofrontal complex (Abutalebi et al., 2015). Abutalebi et al. (2015) found this in aging individuals in particular. This increase in grey matter creates a defense for the brain as it ages because a common neuroanatomical change of dementia is loss of grey matter (Alzheimer's

Association, 2020). Furthermore, the increase in the temporal pole and orbitofrontal complex can combat the degeneration of the frontotemporal lobe that is common of dementia, and the atrophy of the frontal lobe and the temporal lobe that is a common trait of AD. Finally, bilingualism leads to changes of the anterior cingulate gyrus which includes the cingulate gyrus, an area impacted by AD. By speaking a second language, you strengthen neural connections and create a defense to aging.

VII. Discussion and Conclusion

a. My Opinion

After seven years of language learning in the United States I have always wanted to be bilingual and I wish that I had learned a foreign language as a young child, rather than as a high school student. My introduction to and love of language was not immediate and it was not until I started college that I decided to further pursue Spanish. I am so thankful I did and hope to be a lifelong learner of the language. Between my love of language, neuroscience, and my grandparent's living with dementia, this topic is very important to me.

The United States has coined the term "The Melting Pot" to refer to the various cultures, countries, and individuals that make up our country. However, this term is also backed by a desire to be individual and make a way for yourself. Unlike individuals I met in other countries throughout my travels abroad, inside the US learning a second language does not begin until high school rather than as a young child. As I discussed earlier in the text, being a lifelong learner of the language and early development change the way the brain develops. There is even evidence to suggest that the bilingual brain, and not the monolingual brain is the human norm (Bak & Alladi, 2014).

This then poses the question of “why don’t we offer language at a younger age,” but also “why is bilingualism discouraged in the United States?.” English is the current *lingua franca*, but that does not mean learning other languages is any less important. The United States is thought to be a place to follow and achieve the “American Dream.” However, I wonder if the American Dream might actually be perpetuating monolingualism. The United States is a very polarized country and filled with a very racist history. I wonder if the close-mindedness of many people inside the United States fuels the lack of language diversity and lack of empathy towards other cultures. I know this does not apply to everyone, but a study by Bialystok, Craik, and Luk (2012) determined that fifty percent of the world’s population is thought to be bilingual whereas only twenty percent of the population in the United States is believed to be bilingual. This is really an interesting statistic to reflect on given the number of people who immigrate to the US. Furthermore in regard to dementia, 14.7% of people over the age of 70 in the US are living with dementia and this number is only set to increase (Hurd, Martorell, Delavande, Mullen, & Langa, 2013). As more individuals move into the 65+ age group, I think as a country we need to look at the culture we perpetuate and evaluate the mindset of the “American Dream” and instead of driving the use of only English, we can create a more culturally accepting, and empathetic community. Language acquisition is not an easy feat, but starting at a young age will not only benefit our brain, but also our language skills.

In a study looking at second language acquisition in Alberta, Canada, Archibald et al., (2006) found that exposure to multiple languages enhances cultural awareness. When a student is exposed to another language, they also learn about the culture and gain a respect for it. This has great long term implications and is potentially linked to creating a more empathetic, inclusive,

and anti-racist community (Archibald et al., 2006). Translating this practice into the United States could prove to be extremely helpful to fostering empathy.

b. Future Implications

I reviewed studies in regard to global health and the lifetime benefit of bilingualism while tying it all into the delay of dementia, but more specifically AD. As the general population ages, we need to find ways to combat AD and related dementias. The research overwhelmingly points in favor of bilingualism as a way to do this. In order for bilingualism to combat and delay the onset of dementia, specifically AD, we need to understand the basis of bilingualism and have a better encompassing definition. Additionally, there needs to be more access to and studies done on a global level to analyze the number of bilingual and multilingual speakers. In my research, I was only able to find scientific information on multilingualism in Europe. By comparing the number of bi/multilingual speakers in Latin America, Europe, North America, Asia, Oceania, and Africa to the number of monolingual speakers, researchers would gain insight into language in different cultures. Furthermore, this data could then be used to look at AD prevalence and dementia in each country as a global marker.

The brain is vital to human survival and we are constantly learning new information about it. This makes me wonder if the term bilingual could be extended to individuals who write and understand code. When you write in code, you are writing in a computer language. I think this would be a really interesting avenue to explore in the future, but especially with the Millennial and Gen Z generations as it is much more of a norm to be able to code. Additionally, American Sign Language (ASL) is a different form of language that is widely used inside the community. A future avenue would be to explore what neuroanatomical changes take place in the brain structures of individuals who work with code and who speak ASL.

Another future avenue would involve looking into bilingualism on the global scale to understand the real presence of it. Furthermore, it would be really interesting to delve into the role of genetics and environment in dementia development. Inside the United States, Black/African American and Latino populations are 2x and 1.5x as likely to have a dementia diagnosis compared to older, Caucasian adults (Alzheimer's Association, 2020). This is a really important statistic to explore because Stewart, Boyle, James, Yu, Han, and Bennet (2018) found that the APOE-e4 gene had a higher prevalence in individuals with a lower financial, health, and total literacy. APOE-e4 is a key marker of Clinical AD (Stewart, Boyle, James, Yu, Han, & Bennet, 2018). This returns to the modifiable risk factors discussed earlier and how education can help prevent the onset of AD. This leads me to wonder why the APOE-e4 gene is more common in individuals with lower literacy rates. My research about the APOE-e4 gene involved individuals in the United States. Our education system needs reform and improvement because socioeconomic status plays a large role in the resources, funding, and the overall experience a student has while in school. Although this is a genetic trait, I want to explore more about the role of the environment and whether rates really are higher in lower literacy areas and if institutional racism plays a role in the likelihood of developing AD. These are questions that we need to explore and understand in order to progress in dementia research. Other future avenues include looking into the mediterranean diet, whether or not being monolingual is actually a disadvantage, and if our brains are actually designed to be bilingual. If our brains are designed to be bilingual, this could really be a changing point in bilingual research. AD is a progressive and neurodegenerative disease and finding ways to prevent it through limiting modifiable risks and using language to strengthen the brain could lead to a big breakthrough in treatment, delay, and prevention.

Finally, as Neurological disorders are the leading cause of disability worldwide, understanding the financial burden is extremely important. In future studies I think it would be really valuable to look at the financial, physical, and mental toll AD and dementia take on caregivers. I also think it would be really interesting to delve deeper into the differences between informal and formal care.

c. Concluding Remarks and Acknowledgments

As I conclude my thesis, I am so thankful for the help and support that has been provided along the way from my incredible honors professors, Dr. Howe and Dr. Narcisi, as well as Dr. Fricks-Gleason my thesis advisor, and Dr. Carrión, my thesis reader. Furthermore, I want to thank my writing group, Danielle Beckman, Lorenzo Patti, Sarah Smacz, and Moriah Weir for holding me accountable and providing me with much needed thesis support. Finally, I cannot thank my friends and family for their unending support and reassurance throughout college, but specifically my thesis process. This is not the end of the question and something I hope will continue to be studied. Who knows, science changes every day and new advances are constantly being made, so that in 30-40-80 years, there might be a cure to AD and dementias. My hope is that we begin to foster more bilingual communities and education systems. As Archibaldt et al. (2006) found, understanding and learning about another culture promotes empathy and that is something we all could use a little bit more of in our lives.

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IX. FIGURES AND TABLE

FIGURE 1. PROJECTED NUMBER OF AD CASES PREVENTED, CORRESPONDING TO 10 OR 20% REDUCTIONS PER DECADE IN EACH RISK FACTOR

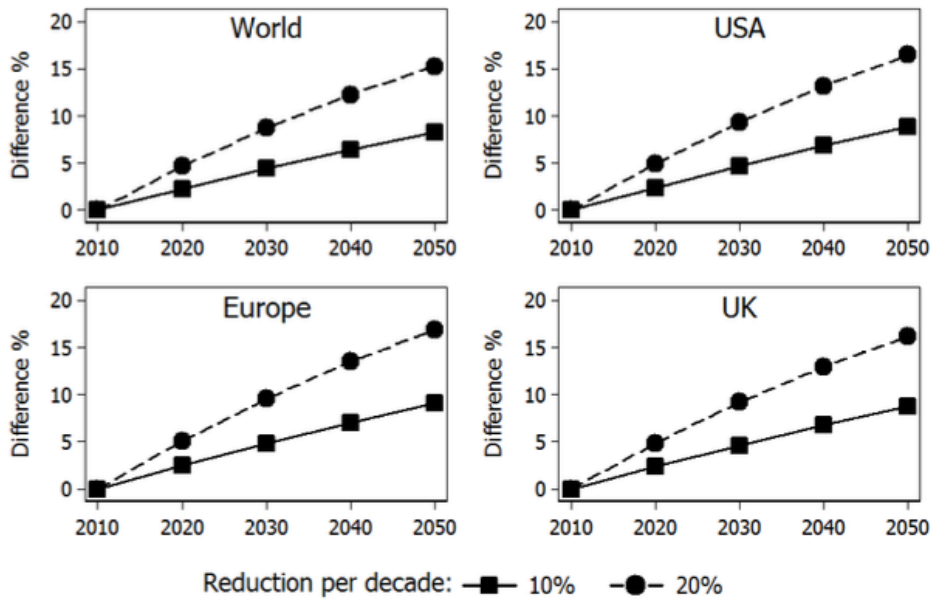


Figure 1. Projected Number of AD Cases Prevented, Corresponding to 10 or 20% Reductions per Decade in Each Risk Factor. Taken from Norton, S., Matthews, F. E., Barnes, D. E., Yaffe, K., & Brayne, C. (2014). Potential for primary prevention of Alzheimer's disease: an analysis of population-based data. *The Lancet. Neurology*, 13(8), 788–794. [https://doi.org/10.1016/S1474-4422\(14\)70136-X](https://doi.org/10.1016/S1474-4422(14)70136-X)

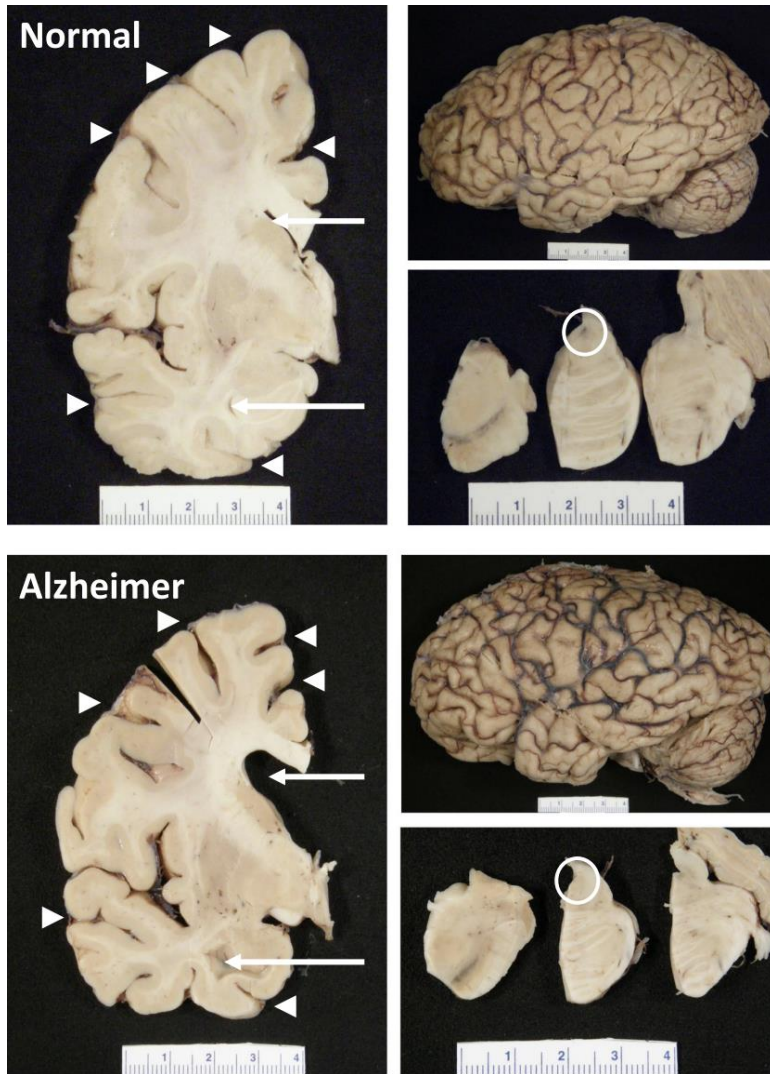


Figure. 2 Gross Anatomy of Alzheimer's Brain. Lateral view of an Alzheimer's brain can show widening of sulcal spaces and narrowing of gyri compared to a normal brain. This may be more readily observed in coronal sections as indicated by the arrowheads, and this atrophy is often accompanied by enlargement of the frontal and temporal horns of the lateral ventricles as highlighted by the arrows. Additionally, loss of pigmented neurons in the locus coeruleus is commonly observed in the pontine tegmentum as shown with the open circle. None of these features is exclusive to Alzheimer's disease. Taken from DeTure, M. A., & Dickson, D. W. (2019). The neuropathological diagnosis of Alzheimer's disease. *Molecular neurodegeneration*, 14(1), 32. <https://doi.org/10.1186/s13024-019-0333-5>

Yearly Cost per Person Attributed to Dementia, in 2010 Dollars.

Variable	Yearly Cost per Person (95% CI)	
	Unadjusted	Adjusted for Demographic Characteristics and Coexisting Conditions
		<i>dollars</i>
Care purchased in marketplace		
Total out-of-pocket spending	6,838 (4,854–8,821)	6,194 (4,522–7,866)
Total Medicare spending	5,226 (3,086–7,365)	2,752 (1,116–4,389)
Net formal home care	6,888 (4,775–9,000)	5,678 (3,739–7,618)
Nursing home care (excluding payments by Medicare and out-of-pocket spending)	14,377 (10,016–18,739)	13,876 (9,769–17,983)
Total	33,329 (24,223–42,434)	28,501 (20,881–36,122)
Informal home care		
Caregiving time valued according to replacement cost	30,839 (23,578–38,099)	27,789 (21,112–34,466)
Caregiving time valued according to cost of forgone wages	14,591 (10,910–18,273)	13,188 (9,636–16,740)
Grand total		
Care purchased in marketplace plus caregiving time valued according to replacement cost	64,168 (48,406–79,928)	56,290 (42,746–69,834)
Care purchased in marketplace plus caregiving time valued according to cost of forgone wages	47,920 (35,433–60,406)	41,689 (31,017–52,362)

Table 2 Yearly Cost per Person Attributed to Dementia, in 2010 Dollars. Taken from Hurd, M. D., Martorell, P., Delavande, A., Mullen, K. J., & Langa, K. M. (2013). Monetary costs of dementia in the United States. *The New England journal of medicine*, 368(14), 1326–1334. <https://doi.org/10.1056/NEJMsa1204629>