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The Mediterranean Diet as a Preventative Measure Against Alzheimer's Disease

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Every 69 seconds, an individual in the United States is diagnosed with Alzheimer's disease, (AD). By the year 2050, the Alzheimer's Association estimates a new diagnosis will occur every 33 seconds (Alzheimer's Association, 2014). AD is defined as one of the most prevalent forms of dementia, a multifactorial disease that can cause memory deficits, inability to reason, disorientation, and mood or behavioral changes (National Institute of Neurological Disorders and Stroke, 2015). While a cure for AD has yet to be found, current research has found that strict adherence to the Mediterranean diet (MeDi) has been associated with primary prevention and slower progression of the cognitive decline that is associated with AD (Solfrizzi & Panza, 2014; Gu, Luchsinger, Stern, & Scarmeas, 2010; Swaminathan, & Jicha, 2014). The proposed 10-year study will employ a sample of adults from the United States who are predisposed to AD and are over the age of 60. This proposal will examine the effect of strict adherence to the MeDi on cognitive decline and the development of AD. Adherence to the MeDi will be assessed according to the *MeDi Adherence Scale* that Singh et al. (2014) employed in their study.

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Dementia is the modern-day term used to describe a collection of symptoms that are associated with cognitive impairment in an individual (National Institute of Neurological Disorders and Stroke, 2015). While dementia can be caused by a number of disorders that affect the brain, those suffering with dementia often have significantly impaired intellectual functioning that may cause memory deficits, inability to solve problems, inability to maintain emotional control, personality changes, and behavioral problems, such as agitation, delusions, and hallucinations (National Institute of Neurological Disorders and Stroke, 2015). Although dementia is common within the aging population, it is not a normal part of the aging process and is often the result of an abnormal underlying condition (Alzheimer's Association, 2014). Alzheimer's disease (AD) is the most common cause of dementia, that accounts for 60 to 80 percent of dementia cases, and affects nearly 5.3 million people in the United States alone (Daviglus et al., 2011). AD is both a progressive and fatal neurodegenerative disease and has increased in prevalence among industrialized nations over the last 30 years (Sofi, Macchi, Abbate, Gensini, & Casini, 2010). AD continues to be a major cause of morbidity and mortality among the aging population and remains a vexing burden on health care systems world-wide (Brookmeyer, Johnson, Ziegler-Graham, & Arrighi, 2007; Swaminathan & Jicha, 2014). It is currently the sixth leading cause of mortality in the U.S. for people over the age of 65 (Kochanek, Murphy, Xu, & Arias, 2014).

Although modern clinicians have extensively searched for definitive ways to make an AD diagnosis, there is no single clinical test that

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can be used to identify the disease. Anatomically, dementia has long been associated with the buildup of amyloid plaque and the development of neurofibrillary tangles within the neural structures of the brain (Gu et al., 2010; Swaminathan, & Jicha, 2014). Accumulations of these deposits are implicated in the loss of neural synapses, death of neurons, and an increase in harmful oxidative stress; all of these are strongly correlated to decreased cognitive and neural functioning in the individual (Jicha & Carr, 2010). Currently, physicians and psychologists use a wide array of assessment measures to diagnose individuals and differentiate between the different types of dementia. Brain scans (i.e., MRI, fMRI, PET scans, CT scans), cognitive and psychological examinations, psychiatric evaluations, laboratory tests, and conductive tests that assess memory, problem solving, attention, counting, and language are all employed in the clinical setting as diagnostic measures (National Institute of Neurological Disorders and Stroke, 2015). While these types of evaluations may provide a diagnosis of possible or probable Alzheimer's with up to 90 percent accuracy, absolute confirmation requires examination of brain tissue upon autopsy (Alzheimer's Association, 2014).

Similar to the uncertainty that accompanies an AD diagnosis, identifiable risk factors that trigger the onset of this disease remain ambiguous, despite the efforts to define these risk factors. The greatest risk factor for the onset of AD appears to be linked to increasing age (Scarmeas, Stern, Tang, Mayeux, & Luchsinger, 2006). According to the Alzheimer's Association (2014), 96 percent of those diagnosed with AD in the United Stated are aged 65 and older. Additional risk factors related to personal medical history have been associated with the onset of AD. Some factors identified are: depression, traumatic head injuries, cardiovascular disease, high cholesterol, obesity, diabetes, and hypertension (Cummings, 2004). Considerable efforts have also been made to identify a genetic marker that would indicate an increased risk of developing AD as one ages. Currently, variations of the APOE gene, located on chromosome 19, have been loosely identified as risk factors for the late onset of AD (Liu et al., 2014). While a blood test can identify which APOE alleles an individual has, it cannot accurately predict who or who will not develop AD due to the many influences that contribute to the development of AD (Liu et al., 2014). In fact, it is unlikely that genetic testing will ever be capable of predicting a condition with absolute certainty since there are numerous variables to account for in multifactorial diseases (Liu et al., 2014).

Despite the prevalence and current awareness, there is a clear lack of disease-modifying therapy for this condition (Voisin & Vella, 2009). While current pharmaceutical approaches are designed to manage the symptoms of AD, many clinicians agree that the treatment options are not substantial enough (Voisin & Vella, 2009). While modern medicine has yet to find a cure for this disease, AD researchers have been prompted to follow a divergent approach, away from curative medicine, and have focused more on the prevention of this disease. This approach has examined additional risk factors, specifically, the association between dietary habits and the onset of dementia (Luchsinger & Mayeux, 2004).

Nutritional approaches to prevent or slow the onset of a disease have become promising strategies under recent exploration (Swaminathan & Jicha, 2014). Gillette-Guyonnet et al, (2013) suggests that nutritional intake may influence the development and progression of AD. One nutritional guideline that has been under recent examination for its disease prevention capabilities is the Mediterranean diet (MeDi). The MeDi is widely recognized as a healthy eating model because of its correlation with low morbidity and low mortality for many chronic diseases (Roman, Carta, Martínez-González, & Serra-Majem, 2008). Individuals living in the Mediterranean region, including Naples and the neighboring parts of Italy, has been found to have the longest life expectancies in the world, in addition to a very low prevalence of AD among the aging population (Swaminathan & Jicha, 2014). Scarmeas et al. (2006) have also suggested that strict adherence to the MeDi was associated with a lower risk of developing AD.

The MeDi is fundamentally different from other dietary plans that entail a great measure of structure and rigidity. Rather, this diet is a collection of flexible eating habits followed by people of various countries that border the Mediterranean Sea (Sofi et al., 2010). The diet consists of a high consumption of vegetables, legumes, cereals, fruits, unsaturated fats (e.g., olive oil), moderate to high consumption of fish, low to moderate consumption of dairy products, low consumption of meats and fats, and a regular to moderate drinking of alcohol (Solfrizzi & Panza, 2014). The benefits of the MeDi have been shown to promote a satisfactory health status and a better quality of life by increasing the intake of antioxidant vitamins, monounsaturated fats, polyunsaturated fats, and other beneficial nutrients for the prevention of chronic degenerative diseases (Sofi, Cesari, Abbate, Gensini, & Casini, 2008). Physiologically, these nutrient components have been suggested to regulate the cellular health processes that have been associated with increasing a patient's risk for AD (Swaminathan & Jicha, 2014). Such cellular

health processes are inflammatory mediators and oxidative stress-induced reactions within the brain (Swaminathan & Jicha, 2014). By moderating these harmful variables within the body that contribute to dementia-like deficits, strict adherence to the MeDi has thus been correlated with the primary prevention and slower progression of cognitive decline and specifically Alzheimer's disease (Solfrizzi & Panza, 2014).

While this emerging evidence presents a bright outlook to the ongoing epidemic of AD, results are still interpreted with caution due to the limited number of studies completed. Currently, the best available data for dietary influences in the prevention of AD come from retrospective cohort and epidemiological studies rather than present clinical trials (Swaminathan & Jicha, 2014). Given the complexity of diet regulation as an implemented plan among patients, clinical trials have not been sought out by researchers (Swaminathan & Jicha, 2014). Only additional research will be able show greater connection to the prevention of neurodegenerative disease among the many confounds that are characteristic to total dietary regulation. With greater causality shown between diet and the prevention of AD, a clinical trial could be implemented in the future, and could potentially bring about a new approach to preventing or delaying a disease that we cannot definitively treat in the United States (Swaminathan & Jicha, 2014).

In conclusion, Alzheimer's disease continues to be a debilitating illness that is currently affecting over 5.3 million Americans (Thies & Blieler, 2013). While treatment options are often deemed ineffective, a nutritional approach to prevent or slow disease progression has been widely investigated. Recent studies have suggested that strict adherence to a Mediterranean diet might prevent or slow cognitive decline and avert the diminished quality of life associated with neurodegenerative disease (Solfrizzi & Panza, 2014; Gu et al., 2010; Swaminathan, & Jicha, 2014). Additional research is needed to better establish the correlation of the MeDi as a preventative measure and to introduce a benchmark clinical trial. This proposed longitudinal study will aim to further examine the relationship between the MeDi and the prevention of AD in the aging population (> 60 years). It is hypothesized that individuals of at least 60 years of age that are at risk for developing Alzheimer's disease will show reduced or slower cognitive decline with sustained, strict adherence to the Mediterranean diet over the course of the longitudinal study.

PROPOSED METHOD

Study Design

We will conduct a ten year longitudinal study which will evaluate the effectiveness of the Mediterranean diet as a preventative measure against Alzheimer's disease.

Participants

This study will consist of 5,000 men and woman from various ethnic backgrounds, who reside within the U.S., and are over the age of 60. Participants must have a predisposition to develop AD but cannot have any other preexisting conditions that would attribute to cognitive decline or memory loss. Predisposition will be defined as having an immediate family member diagnosed with AD.

Measures

The MeDi score is a 9-point scale in which a value of zero or one is assigned to the nine components of the Mediterranean diet (Singh et al., 2014). These nine components are defined as; fats, alcohol, legumes, cereals and breads, fruits, vegetables, dairy products, meat and poultry, and fish (Singh et al., 2014). Beneficial components such as vegetables, legumes, fruits, cereal, and fish all receive a value of 1, and meat, dairy products, and foods high in saturated fats receive a value of 0 (Singh et al., 2014). The total MeDi score ranges from 0 (minimal adherence) to 9 (maximal adherence) and totals are categorized into three statistics according to adherence: MeDi scores 0–3 (low), 4–5 (middle), and 6–9 (higher) (Singh et al., 2014).

Procedure

Participants will be recruited from the physician offices of general practitioners from various regions of the U.S. Physicians will be contacted by the researchers and given the necessary information to inform patients that fit the criteria. Once the sample is selected and participants have given informed consent, participants will be randomly assigned and split evenly into either the experimental or control group. The experimental group will receive bi-monthly home deliveries of Mediterranean diet components that may then be prepared into meals by the participants. Each participant in the experimental group will receive a MeDi cookbook that informs the participants of cooking recipes and meal options. Experimental group participants will also complete monthly food journals in which they evaluate their meals using the *MeDi Adherence scale* system that Singh et al.

(2014) employed in their study. Each subject will be given enough food components to prepare three MeDi meals per day for the duration of the study. Participants will also be given guidelines on how to assess their meals according to the scale and how to keep a food log. Participants in the control group will not be given any MeDi meals. However, they will be required to submit monthly food journals that track their regular eating habits at the end of every month. The control group will receive specific, in home instructions at the beginning of the study on how to properly keep a food log, similar to the experimental group. All participants in the study will take part in bi-annual cognitive health evaluations conducted by either a primary care physician or a neurologist. The bi-annual evaluations will be first performed on a randomly selected day and subsequently six months after until the completion of the ten year study. Each subject will be evaluated on their cognitive and neural health during the bi-annual evaluations with the aid of diagnostic screening techniques such as CT scans, fMRI scans, PET scans, and MRI scans. These brain scans are capable to show signs of cognitive decline when interpreted by medical professionals. Laboratory tests and conductive tests that assess memory, problem solving, attention, counting, and language will also be used to assess the mental health of participants during the bi-annual evaluations. Physicians will report their assessments of each patients' mental health to the researchers after each evaluation. This data will then be compiled and analyzed at the outset of the study. Ultimately, cognitive decline, as interpreted by the physicians, will be compared to the degree of adherence to the Mediterranean diet over the course of time. Both the experimental and control group participants will receive $500 reimbursement for each year they participate in the study. This compensation is designed to offset the cost of travel expenses and the physical exams. Compensations will be discontinued for those who drop out over the course of the study.

CONCLUDING REMARKS

Significance

The proposed study will be the first of its kind in implementing a clinical trial and longitudinal study on subjects that are placed on the Mediterranean diet and are guided to adhere to the regimented dietary schedule. Researchers hypothesized that the participants who strictly adhere to the MeDi will show greater cognitive health and a slower neurological decline, and investigated this hypothesis through a 10-year longitudinal study. By pioneering the first clinical trial to study the effects of the MeDi in relation to the onset and progression of AD, this study will require the allocation of numerous resources and financial subsidiaries. However, the potential of affirming the most effective preventative plan against AD would be an unprecedented breakthrough in our treatment of the abnormal aging process. In fact, the greatest benefit may be seen in the improvements to our health care system if we can drastically limit the number of new AD diagnoses per year. When there is no treatment yet available, the best solution would appear to be prevention. Therefore, this study sets out to solidify a benchmark prevention method and create a standard that future research may follow, in the treatment and prevention of AD.

Limitations

Some limitations should be noted for this proposed study. Our most pressing concern is the financial allocations that would be required. A longitudinal study for a ten year duration will require countless deliveries of MeDi food components, numerous physical assessments, data analysis resources, and compensation for all participants who continue the study. Any study for an extended duration will also incur a high number of participant dropouts. These will occur among the aging population as participants move, morbidity rates increase, and mortality rates increase. There may also be a general loss of interest as a contributing factor to dropping out of the study. The study will also limit itself by using a convenience sample from only the U.S, making the results non-generalizable. Although participants will be instructed on how to obey to the MeDi and document their adherence, the study will rely on the subjective data that each participant will report. There will be a variance among different participants, and there is a possibility that some may not provide full disclosure of their dietary consumption.

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