DOES THE THEORY OF REASONED ACTION INFORM THE WILLINGNESS OF INDIVIDUALS UNDERGOING GENETIC TESTING TO SEEK DISCLOSURE OF INCIDENTAL FINDINGS RELATED TO THE RISK FOR ALZHEIMER DISEASE?

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This research was completed as part of the degree requirements for the Nursing Department at Molloy College.
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By

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A Dissertation Submitted in Partial Fulfillment of the Requirements for the Degree of Doctor of Philosophy at Molloy College

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Abstract

**Background:** In recent years, researchers have increasingly employed genetic testing as a means for understanding and treating diseases like Alzheimer disease, a common progressive disease affecting cognition and behavior. Genetic studies hold the potential for major breakthroughs in treatment of diseases like Alzheimer disease. However, with the increase in the use of genome-wide association, microarray, and whole genome sequencing comes the potential for a greater number of incidental findings in genetic research—findings not central to the aim of a study but nonetheless informative about a participant’s health. Although many studies have documented the ethical implications around disclosure of such findings from the point of view of the researcher, fewer studies have examined the attitudes of genetic research participants to the disclosure of incidental findings.

**Purpose:** It is critical that healthcare professionals and genetic researchers understand genetic research participants’ views so that they may appropriately discuss findings with participants and encourage applicable health measures. The purpose of this study was to assess the willingness of members of the general public who might participate in genetic research to request disclosure of incidental findings indicating a future Alzheimer diagnosis, and to apply the Theory of Reasoned Action to explain their intentions. The Theory of Reasoned Action posits that one can explain a person’s decision on the basis of his or her attitudes toward the object of the decision and subjective norms about that object. The potential for variability in people’s desire for awareness of genetic predispositions for Alzheimer disease makes Alzheimer disease an ideal case example for testing this model and improving our understanding of participants’ views toward incidental findings.
Method: The researcher surveyed an online panel of volunteer participants who have been selected by pre-determined criteria from Survey Monkey to represent responses from adult American men and women asked about a hypothetical genetic testing situation in their lives. The researcher employed the Perceptions Regarding Investigational Screening for Memory in Primary Care (PRISM-PC) questionnaire to assess participants’ beliefs about Alzheimer disease and incidental findings.

Results: The researcher employed one-way ANOVA and ordinal logistic regression to analyze the results. The results indicated that household income and level of education were significant predictors of participants’ attitudes toward Alzheimer screening. The two components of the Theory of Reasoned Action—the Attitudes and Subjective Norms subscales—significantly predicted participants’ likelihood to request incidental findings, confirming the hypothesis. Demographic differences did not demonstrate a predictive impact on the likelihood to request incidental findings.

Conclusions: The research question in this study was “Does the Theory of Reasoned Action predict the likelihood to request results of incidental findings related to Alzheimer disease risk?” The results of the study confirmed the predictiveness of the Theory of Reasoned Action. Participants’ attitudes toward Alzheimer screening and subjective norms toward Alzheimer disease significantly predicted their likelihood to request incidental findings from the hypothetical genetic study. This finding provides important insight to nurses and other healthcare professionals treating patients with possible links to Alzheimer disease.
Dedication

In memory of my husband Neil, without whose support this journey would not have been possible.
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CHAPTER ONE: INTRODUCTION TO RESEARCH PROPOSAL

Introduction

While researchers have long believed that genetics underlie many diseases and disorders, only recently have they had the resources to conduct complex genome sequencing to understand the specifics of those genetic causes (Murdoch & State, 2013). With these newly developed resources, the science of genetics has led healthcare providers to employ “precision medicine” to tailor their treatment of an individual’s disease based upon the information they have gathered from the individual’s genetic code as well as other relevant information (Collins & Varmus, 2015).

One of the most researched diseases in the field of genetics is Alzheimer disease, a common progressive disease affecting cognition and behavior (Chao, Roberts, Marteau, Silliman, Cupples & Green, 2008). Genetic researchers have identified a susceptibility polymorphism, the Apolipoprotein-E (APOE) gene, as well as 31 single nucleotide polymorphisms (SNPs), in connection with Alzheimer development risk (Tan et al., 2017). In recent years, clinical trials have suggested that genetic interventions, such as amyloid-modifying treatments, have been started too late in the disease process to alter its course. Researchers have also concluded that the physiological changes associated with late-onset Alzheimer disease (LOAD) start roughly a decade prior to individuals exhibiting symptoms of dementia (Tan et al., 2017). Some researchers have expressed concerns around “lead time bias,” or the appearance of improved outcomes (e.g., longer periods of survival) simply due to early diagnosis and not due to medical intervention (Bastian, 2014).

Although genetic studies hold the potential for major breakthroughs in treatment (or even prevention) of diseases like Alzheimer disease, with the increase in the use of genome-wide
association, microarray, and whole genome sequencing comes the potential for an increase in the
count of incidental findings in genetic research (Downing, Williams, Daack-Hirsch,
Driessnack, & Simon, 2012). Incidental findings are “findings that were not the direct object of
the study” (Clayton, 2008, p. 287), or, as Miller, Mello and Joffe (2008) described them,
“findings concerning an individual research participant that have potential health or reproductive
importance and are discovered in the course of conducting research but are beyond the aims of
the study” (p. 271). While “incidental findings” are most often associated with genomics
research, and thus are sometimes referred to as “genomic incidental findings” or “GIFs,” by
definition they can arise in any type of biomedical research study. Synonymous with incidental
findings are “serendipitous” and “iatrogenic” findings, “non-incidental secondary findings,”
“unanticipated findings,” and “off-target results” (Lohn, Adam, Birch, & Friedman, 2014, p.
464).

Additionally, as large data samples from genome-wide association studies and whole
genome sequencing (WGS) are being archived and stored in biobanks for usage by researchers
now and in the future, there is an increased likelihood that incidental findings will be discovered
(Wolf et al., 2008). Indeed, according to Wolf (2013), the American College of Medical Genetics
and Genomics (ACMG) in 2012 acknowledged that with respect to genetic studies, “incidental
findings are highly likely, if not inevitable” (p. 571). The group identified the need to establish
preliminary guidelines to ensure homogeneity in the clinical laboratory with respect to disclosure
of incidental findings (Roche & Berg, 2015). In some cases, the disclosure of these findings
could potentially provide life-saving information to participants. However, as Miller, Mello, and
Joffe (2008) point out, investigators have to be concerned about two types of errors in assessing
incidental findings: “(1) the false-positive error of reporting a finding that turns out to be of no
clinical significance and (2) the false-negative error or failing to report a finding linked to a serious health problem” (p. 277). And despite the growing likelihood of the discovery of incidental findings in research, many researchers have not yet experienced the dilemma around whether to disclose these findings. In Williams et al. (2012), 53 researchers or IRB chairs reported that they had little experience in the actual disclosure of genomic incidental findings. In fact, only 3 researchers and 2 IRB chairs reported ever having made a decision regarding the disclosure of incidental findings.

**Background**

**Incidental Findings and Researcher Responsibilities**

In all cases, there is much debate about whether researchers should disclose the findings since the incidental findings are not the principal aim of the study. Because procedures and statistical methods used for analysis of whole genome sequences differ from one laboratory to another, it may be difficult for researchers to confirm one another’s findings. Indeed, in a recent review, Wyres et al. (2014) noted “the bioinformatic challenges associated with the application of whole genome sequencing data in clinical settings, highlighting the need for standardization, appropriate management of computing resources, data integration and storage” (p. 452).

What is more, even when there exist known associations between variants and disease, it is not a given that individuals with those variants will in fact develop the disease. As Krier and Green (2013) noted, “the penetrance and expressivity of variants discovered by screening have not been ascertained for most variants and are almost universally unknown” (p. 14). The accuracy by which a certain finding predicts the “presence or absence of the underlying condition” is known as clinical validity (Shkedi-Rafid, Dheensa, Crawford, Fenwick, & Lucassen, 2014, p. 719). For example, a phenotype may appear to be completely normal, but
there may be a deletion in the gene, making the clinical validity very difficult to determine. Genetics and environment also factor into whether or not the variant is expressed in the development of a disease. “The absence of population-based data on the range of effects of specific variants on health and disease makes interpretation difficult” (Williams, Cashion, & Veenstra, 2015, p. 49).

In light of these complexities, recently, researchers have voiced a preference for genetic healthcare professionals to absorb the responsibility for disclosure (Dheensa et al., 2016). This can prove problematic, since clinicians are unlikely to be part of research teams (Dheensa et al., 2016). According to the Centers for Medicare and Medicaid Services (CMS) (2014), a clinical laboratory is defined as a laboratory that examines “materials derived from the human body for the purpose of providing information for the diagnosis, prevention, or treatment of any disease or impairment of, or the assessment of the health of, human beings.” These laboratories are regulated by the Clinical Laboratory Improvement Amendments of 1988 (CLIA). When disclosing results to individuals, regardless of whether they are symptomatic or asymptomatic, the clinics have a definitive responsibility to establish and follow clear, specific guidelines around disclosure of findings and communication with patients (Wolf, 2013, p. 571).

Some studies have focused explicitly on genetic testing for disease and disclosing that information to participants. For instance, the Risk Evaluation and Education for Alzheimer's Disease (REVEAL) study is a multi-phase study focused on the psychological and behavioral impacts of disclosure of information regarding participants’ Alzheimer risk (Besser et al., 2015; Chao et al., 2008). REVEAL’s primary focus is the genetic testing and disclosure of Alzheimer risk to participants, who received education regarding Alzheimer disease and were aware of its centrality to the study. However, many other research studies do not provide individual-level
results. Indeed, research laboratories that do not provide individual patients with results are exempt from CLIA regulation (Centers for Medicare and Medicaid Services, 2014). As such, an ethical dilemma results: should researchers whose studies do not intend to provide patients with individual health results be responsible for disclosing incidental findings that pertain to individuals’ health?

**Potential Recipients’ Views Toward Incidental Findings**

When it comes to understanding the motivations and attitudes of genetic research participants—the potential recipients of information regarding incidental findings—fewer articles have been published. As reflected in Wolf et al. (2008), most studies examine the disclosure issue from the perspective of ethics and the researcher, not the participant. For instance, authors in one study noted that the offer to return research results to participants has been increasingly recognized as a “moral obligation found in the principle of respect for persons” (Fernandez, Kodish, & Weijer, 2003, p. 12). In another study, authors wrote: “the return of research results to a large number of participants may have the beneficial effect of improving a general public understanding of the essential role of research in health care, accuracy of what health research finds, and public commitment to investment in ongoing research” (Fernandez & Weijer, 2006, p. 45). Though it expresses concern for their welfare, such a statement does not truly consider the participants’ points of view.

Some more recent studies have indicated that participants prefer the disclosure of findings “regardless of clinical actionability, including results with no or unclear clinical utility and variants of uncertain significance” (Wynn et al., 2017, p. 842). In one study, researchers found that there were a number of factors that contributed to whether individuals wanted receipt of said findings. These included a certain curiosity, a desire to contribute to the body of research, a
belief in the true value of the information yielded by the secondary results, and the ability to utilize the information toward the prevention of future disease (Wynn et al., 2017).

Understanding research participants’ motivations regarding reports of incidental findings is critical in a research environment in which such incidental findings are increasingly prevalent. With early disease detection, we may improve health care outcomes and reduce health care costs, but if participants are unwilling to receive this information—or unwilling to act upon the receipt of the information—such preventive care is not possible. How can researchers improve their understanding of participants’ attitudes toward incidental findings to encourage participants to learn about prognoses and proceed with preventive care or other preparations, while understanding both the potential usefulness and limitations of these findings?

**The Theory of Reasoned Action**

In this study, the researcher explored the role that the Theory of Reasoned Action (TRA) plays in explaining whether potential genetic research participants express intention to obtain reports of incidental findings regarding possible genetic links to Alzheimer disease (Fishbein, 1967). The TRA, developed by Martin Fishbein and Icek Ajzen in 1967, posits that one can explain a person’s decision on the basis of his or her attitudes toward the object of the decision and beliefs about social (subjective) norms about that object (Ajzen & Fishbein, 1980). The attitude is a function of a person’s evaluation of the behavior’s consequences and the strength of his or her belief that performing the behavior will lead to the given consequence (Ajzen & Fishbein, 1980, p. 67). The subjective norm is defined to be the “perception that important others desire the performance or nonperformance of a specific behavior” (Ajzen & Fishbein, 1980, p. 57). In other words, the subjective norm is how one believes the important figures in his or her life view the behavior in question. Thus, one’s own views about a behavior (attitude) and
the perceived views of important people in one’s life about the behavior (subjective norm) determine the “intention” to perform or not perform the behavior. The TRA has “been used successfully to predict and explain a wide range of health behaviors and intentions, including smoking, drinking, health services utilization, exercise, sun protection, breastfeeding, substance use, HIV/STD-prevention behaviors and use of contraceptives, mammography, safety helmets, and seatbelts” (Montaño & Kasprzyk, 2008, p. 68).

In order to properly examine the intention to receive incidental findings, it is necessary to focus this study’s attention on a disease that meets two principal criteria. First, there must be a known genetic predisposition for developing the disease. Second, there must exist a potential benefit to being made aware of said genetic predisposition. Although no cure for the disease exists, recent advances in our understanding of Alzheimer disease warning signs and promising treatments to slow symptoms indicate that Alzheimer disease fits the criteria and is an appropriate choice for use in this study (Sperling et al., 2014).

**Neuro-Generative Causes of Late-Onset Alzheimer Disease**

Seen as the most pervasive form of dementia in the elderly, Alzheimer disease is thought to be a result of neuro-generative changes caused by an imbalance in the production and subsequent clearance of amyloid-B (AB) peptides and an accumulation in the cerebral cortex and hippocampus of tau proteins. It is estimated that between 10 and 30% of the world population age 65 or over is afflicted with Alzheimer disease, with women suffering more from dementia than men (Manrique de Lara, Nunez-Acosta, Saruwatari-Zavala, Soto-Gomez & Renteria, 2018). The most common form of Alzheimer disease is late-onset Alzheimer disease (LOAD), found in individuals over 65 and involving interactions between a variety of environmental and genetic factors; this is in contrast to early-onset Alzheimer disease, the familial type that only makes up
less than 1% of all Alzheimer cases (Liu, Kanekiyo, Xu & Bu, 2013). As this study focused on the value of incidental findings in informing lifestyle and treatment choices in the years before Alzheimer symptoms occur, the researcher focused on LOAD—the form of Alzheimer that emerges later in one’s life.

Recent research has found that a key genetic risk factor for Alzheimer disease is the presence of the e4 allele of Apolipoprotein E (APOE) gene in an individual’s genetic makeup (Alzheimer’s Drug Discovery Foundation, 2016). As explained by Liu et al. (2013), “Apolipoprotein E (APOE) is a major cholesterol carrier that supports lipid transport and injury repair in the brain” (p. 106). The gene regulating the production of the protein is expressed in three natural occurring alleles, namely e2, e3, and e4. Depending upon which allele is present, a different isoform of APOE is produced by the macrophages throughout the body or astrocytes in the central nervous system, leading to impactful changes to the structure of the protein and its subsequent function. Specifically, the differences in amino acids 112 and 158 of the 299 amino acids that make up the protein impact how the protein binds with AB and what role it plays in AB accumulation and clearance in the brain (Liu et al., 2013).

While e3, the most frequently occurring allele, has no impact and e2 seems to have a protective effect against the development of Alzheimer disease by some unknown mechanism, the APOE-4 gene produces an isoform of APOE that enhances AB accumulation and reduces AB clearance from the brain. The aggregation of excess AB in the brain is a major contributor to the formation of senile plaques that damage neurons and are associated with Alzheimer disease (Alzheimer’s Association, 2016). Furthermore, genome-wide association studies and next-generation sequencing have found approximately 20 risk loci for Alzheimer disease in which the
occurrence of Alzheimer disease with variants (APOE-4) on this genetic loci is quite high, further exhibiting the causative impact of APOE-4 (Sperling et al., 2014).

While carriers of APOE-4 are clearly at increased risk of deteriorating cognitive function, recent research has indicated that there may be steps they can take to diminish this risk and slow the onset of symptoms. Indeed, Roberts, McLaughlin, and Connell (2014) noted that though “there are no proven strategies to prevent the disease, much has been learned in recent years about possible risk and protective factors for AD” (p. 381). In recent years, cerebral spinal fluid (CSF) biomarkers have helped researchers determine that the onset of Alzheimer disease begins at least ten years before symptoms of cognitive decline lead to a diagnosis (McGeer, Rogers, and McGeer, 2016). In this ten-year window, there is opportunity to slow the progress of the disease. McGeer et al. (2016) describe a promising treatment involving non-steroidal, anti-inflammatory agents (NSAIDs) that have a sparing effect on Alzheimer development. Additionally, Sperling et al. (2014) describe a new wave of research, known as “secondary prevention trials,” which include at-risk individuals and seek to slow the onset of Alzheimer symptoms through anti-amyloid therapy.

Other studies have noted the potential impact of exercise on cognitive decline. Liu et al. (2013) suggest that “active leisure activities and exercise, and maintenance of vascular health could be beneficial in reducing the risk of Alzheimer disease and cognitive decline, particularly in APOE-4 carriers” (p. 113), while a study by Head et al. (2012) indicates that those carriers who live a sedentary lifestyle are at greater risk of increased AB deposition. In a longitudinal study of a sample of adults ages 65-89, Smith et al. (2014) demonstrated that physical activity could help reduce shrinking of the hippocampus in individuals deemed at risk for Alzheimer disease based on genetic testing. Furthermore, de Saá Guerra et al. (2016) have noted that exercise can produce increased cerebral cytoarchitecture and improve electrophysiological
properties of the brain, slowing the progression of Alzheimer disease and reducing levels of
cognitive deterioration. Researchers have demonstrated that individuals with diabetes,
depression, those engaged in smoking or have not achieved a high level of education may be
more at risk for developing Alzheimer disease (Manrique de Lara et al., 2018).

Public Perceptions of Alzheimer Disease Diagnosis

Despite the promising research regarding the early treatment of Alzheimer disease, it is
important to note that no known treatment prevents the disease entirely. Therefore, it is perhaps
unsurprising that studies suggest people vary in their desire to learn about links to Alzheimer
disease in their lives. Roberts et al. (2014) found in a study of public perceptions of Alzheimer
disease that among participants over age 50, the older participants were less likely to desire
information about their odds of an Alzheimer disease diagnoses than were those closer to age 50.
Additionally, participants in the study who personally knew someone with Alzheimer disease
were more likely to want to know about their own chances of developing the disease than were
participants who did not know someone with Alzheimer disease (Roberts et al., 2014). In the
same study, the authors noted discrepancies in awareness about preventive measures among
people of different ethnic backgrounds: African Americans were more likely than Caucasian
Americans to believe that people could make healthy lifestyle changes as a protective measure
against developing the disease, whereas Hispanic Americans were less likely to believe this.

The potential variability in people’s views toward the awareness of genetic
predispositions for Alzheimer disease makes Alzheimer disease a compelling case for testing the
TRA. As discussed previously, research suggests individuals having risk for Alzheimer may have
treatment options to slow onset or reduce its severity—but there is no cure or clear-cut method
for the complete prevention of symptoms. Consequently, incidental findings may provide
individuals with information that they might use to reduce the severity of a future Alzheimer diagnosis—but at this time, information from incidental findings will not eliminate Alzheimer risk entirely.

Given these circumstances, the question at hand is whether those individuals would want to know about such findings and why. Taken one step further, could the TRA predict these health behaviors, specifically the decision to receive incidental findings linking one’s genes to Alzheimer disease?

The Role of Nursing in Genetic Research and the Treatment of Alzheimer Disease

With the plethora of advances in genomic studies and in particular Alzheimer disease, nurses have come to play an integral role in both caring for a patient afflicted with the illness in addition to contributing to genomic science. The declining cost of DNA sequencing has made it imperative that nurses understand the resulting information and formulate action plans that could provide patients with better outcomes. The introduction of new therapeutic modalities and the evolution of new public policies indicate that nursing curricula must be updated, and in-service educational programs need be provided to those nurses already engaged in nursing practice (Taylor, Wright, Hickey & Houseman, 2017). Understanding the correlation between “the sequencing result and the individual therapy based on that sequencing result will be essential for the most effective nurse-provided care and support for patients” (Taylor et al., 2017, p. 203). After sequencing data is classified in the laboratory and given to health care professionals, the information can be reviewed and dispensed to individuals and families for use in the clinical setting. Nurses at the bedside can assume a valuable role in the healthcare setting by communicating both clearly and in an ethical manner just what impact and/or relevance results of sequencing technology can have overall on the improvement of individuals’ health (Taylor et al.,
2017). Programs have been developed that educate nurses to understand and analyze complex genomic data. The National Institute of Nursing Research offers a Big Data Bootcamp and the National Heart, Lung, and Blood Institute offers a program known as “(PRIDE), Programs to Increase Diversity Among Individuals Engaged in Health-Related Research” (Taylor et al., 2017, p. 204). The importance to nurses of these resources will be further addressed in Chapter Five.

**Research Questions**

The purpose of this study is to explore the role that the TRA plays in explaining participants’ likelihood of requesting details of a hypothetical, incidental finding from a study that might indicate a genetic link to Alzheimer disease.

The research question is: *Does the TRA predict the likelihood to request results of incidental findings related to Alzheimer disease risk?*

**Conceptual and Operational Definitions**

The expansion of genomic research in recent years has increased the incidence of incidental findings (Wolf et al., 2008) and the potential to benefit from the information they provide through preventive measures. In this study:

- The likelihood to request hypothetical incidental finding results (LRIF) served as the dependent variable and was operationalized by way of a 7-point Likert-type scale administered to participants, ranging from *not at all likely* (1) to *very likely* (7) to permit the disclosure of the findings.
- In keeping with the core tenets of the TRA, the independent variables in this study included participants’ attitudes toward genetic screening for Alzheimer disease, as well as their subjective norms around Alzheimer disease testing that reveals a link.
• These variables were operationalized by three subscales from the PRISM-PC survey, which served as the instrument in this study (see Appendix B).
• Specifically, the “acceptance of dementia screening” and the “benefits” subscales formed the attitudes subscale (AS), and the “stigma” subscale formed the subjective norms subscale (SNAS).
• Additional independent variables that may contribute to findings include participants’ age, gender, ethnicity, level of education, and familiarity of an individual with Alzheimer disease (defined as having an immediate family member or close friend currently or formerly living with Alzheimer disease).

Research Hypotheses
• Hypothesis 1: Attitudes toward dementia screening among participants will predict their LRIF related to Alzheimer disease.
• Hypothesis 2: Subjective norms surrounding Alzheimer disease testing and treatment among participants will predict their LRIF related to Alzheimer disease.

Summary
Researchers have increasingly employed genetic testing as a means for understanding and treating diseases like Alzheimer disease. With the increased use of genetic research comes a greater likelihood of “incidental findings,” or findings that are not central to the aim of a study but are informative about a participant’s health. Too few studies have examined the attitudes of participants toward the disclosure of incidental findings, and it is critical that nurses and other healthcare professionals understand these attitudes so that they may appropriately discuss findings with participants and encourage health measures to slow the onset of the disease where
applicable. This study sought to understand the predictive nature of the TRA in explaining hypothetical genetic research participants’ LRIF related to Alzheimer disease.
CHAPTER TWO: REVIEW OF THE LITERATURE

Introduction

In this chapter, the researcher provides an overview of the existing research and literature regarding incidental findings, the TRA, and Alzheimer disease. The chapter begins with an overview of genetic research laboratories and the ethics surrounding incidental findings. It continues with an overview of the genetics of Alzheimer disease and concludes with a discussion of the TRA and its applications.

Research Laboratories and Incidental Findings

Under the federal Clinical Laboratory Improvement Amendments and Regulations (CLIA), laboratories that “analyze human tissue for the purpose of clinical diagnosis, prevention, or treatment of disease, or impairment or assessment of health” are required to obtain federal certification and accreditation before disclosing research results for patient care (Yassin, Weil & Lockhart, 2012, p. 256). Unlike clinical laboratories working to support patients, research laboratories (where research studies are generally conducted) are not regulated by CLIA. Research studies that take place in non-CLIA laboratories often result in incidental findings (Yassin et al., 2012).

The disclosure of these findings could potentially provide life-saving information to participants. Indeed, incidental findings are commonly recognized as a consequence of genomic sequencing by researchers and clinicians alike. Pathogenic variants of 56 genes have been designated to be returned to patients undergoing clinical genomic testing in the policy set forth by the ACMG in 2015, unless the patient declines to be so informed (Wynn et al., 2017). Numerous debates have ensued among the genomic community about the disclosure of those incidental findings.
When can, or should, researchers and research institutions from non-CLIA labs disclose such findings to participants? This issue poses an ethical, moral, and legal dilemma that has been the subject of an increasing amount of scholarly commentary and controversy. For example, in an article on the front page of the *New York Times* on August 26, 2012, entitled “Genes Now Tell Doctors Secrets They Can’t Utter,” the author describes a number of studies where the researcher faced the issue of whether to disclose incidental findings that had potentially life-saving consequences. In one instance discussed in the article, results of a federal study of gene sequences for colon cancers found genetic changes in 5% of the participants that were the same as the changes found in breast cancer patients whose prognoses were dramatically improved by treatment with Herceptin (Kolata, 2012). Another 15% of the participants had a gene mutation that is common in melanoma patients, whose disease had shown improvement when treated by a certain drug. Under the rules of the study, however, the researchers could not disclose these findings to any of the affected participants, even though the findings could have provided critical information to at least some of them (Kolata, 2012).

From the perspective of the researcher and the research institution, whether or not patients (or their family members) can benefit from the disclosure of incidental findings is only one aspect of the disclosure calculus. The institution must also consider the non-clinical purpose of the research and, perhaps most importantly, the potential risks of misleading the participants or their families if the results are disclosed but have not been properly tested and turn out to be invalid (Yassin et al., 2012). Non-CLIA labs must take great care in determining which study results are both significant enough to a participant or family members’ health, and the subject of rigorous enough testing that the researchers have good reason to believe that disclosure would
not only benefit the recipient but is necessary to prevent or help treat a serious ailment (Yassin et al., 2012).

**Are Researchers Obligated to Disclose Incidental Findings?**

Among others, the literature raises two critical questions with respect to the disclosure of incidental findings: (i) what information is important and reliable enough to be disclosed? and (ii) who should decide if and what to disclose?

Regarding the first question, in a 2001 study, a Center for Disease Control-sponsored group focusing on population based genetic research concluded that “when the risks identified in the study are both valid and associated with a proven intervention for risk reduction, disclosure may be appropriate” (Wolf et al., 2008, p. 31). In a 2004 study by a National Heart Lung Blood Institute Working Group, the conclusion was that where genetic research results showed a significant risk of disease with important health or reproductive implications, and the availability of therapeutic or preventive interventions, the results should be disclosed (Wolf et al., 2008). Yet, it must be remembered that incidental findings are not variables under study; it is not clear whether researchers would have the necessary credentials to interpret or analyze incidental findings correctly so as to disclose accurate conclusions to the participants (Wolf et al., 2008).

These studies suggest that there are two aspects to the issue of what information should be disclosed. First, is the incidental finding of such health or reproductive importance that it would be morally wrong to withhold it from the participant? As Miller, Mello, and Joffe (2008) point out, most incidental findings are “probably not sufficiently serious, urgent, and easily treatable” to require disclosure (Miller et al., 2008, p. 273). The second is whether the finding has been sufficiently vetted such that the information disclosed is accurate. A Stanford Working Group on Reporting Results of Genetic Research created three categories of incidental findings
that help distinguish those findings with important health or reproductive implications and analytical validity from those that do not carry such significance (Wolf et al., 2008):

- The first category is information that if not disclosed could be life threatening or pose serious health or reproductive consequences, and which is deemed analytically valid and of high clinical validity and utility.
- The second category is information deemed important but not as significant as that in category one.
- The third category is information that fails to meet the baseline of analytical and clinical validity standards.

Thus, for example, genetic or genomic data that indicates that the participant carries a potentially fatal genetic disease would, if deemed analytically and clinically valid, fall into category 1 and would be disclosed to the participant (Wolf et al., 2008). In contrast, data regarding misattributed paternity may be important for certain purposes but does not reach the level of category 1 data, and might be disclosed, but only where the participant’s consent form indicated that it was the type of finding of which he or she would want to be informed. In the final category, even if the information would be of health or reproductive importance had it been sufficiently tested, it could not be disclosed because the testing that was done did not sufficiently validate the results (Wolf et al., 2008). As Ravitsky and Wilfond (2006) argued with respect to genetic information, a result is analytically valid when it “accurately and reliably identifies a particular genetic characteristic such as a nucleotide sequence or a gene expression profile. Results should not be offered when they are not analytically valid because such information is not reliable … [and] incorrect information may lead to harmful outcomes such as unnecessary interventions, emotional distress, or a false sense of security” (p. 10).
How can the researcher be certain that the findings are sufficiently valid to be disclosed? One suggestion is that the data be rechecked at least once to make sure that there have been no errors (Wolf et al., 2008). This may even require running a second sample. A second suggestion is that the results be shared with a colleague with expertise in the field to ensure that there is agreement on the validity of the findings. A third is a final evaluation to confirm the presence of the incidental finding and of the significance of the likely health impact (Wolf et al., 2008).

Assuming all of these steps are taken, should it be left to the researcher to decide whether to make the disclosure to the participant? This question is far more hotly contested in the literature.

A group of clinical laboratorians proposed a patient-centric approach to making an informed decision as to what genomic results and secondary results to return to participants (Roche & Berg, 2015). Individuals need a wide breadth of understanding and a very thorough grasp of the consent process. According to Roche and Berg (2015), what elements should be included on a standard consent form has yet to be concluded. Items such as protections to ensure confidentiality, expected benefits and risks and use of data in the future may have subtle meanings. Consent forms may differ when designed for diagnostic purposes as opposed to learning secondary results or incidental findings. Discovering the results of secondary findings where an individual would pursue medical treatment would differ from assessing the risks and or benefits of diagnostic results serving as an explanation for a health condition that the individual is suffering from. Alternatively, those individuals might feel empowered when receiving a medical result that he or she can act upon, whereas individuals with a degenerative and/or progressive condition may become overwhelmed and perhaps distressed.
The Case for Disclosure

The principle of beneficence posits that “all actions should be taken in consideration of the overall condition of the individual, safeguarding that individual’s autonomy” (Rainer, 2011, p. 83). Individuals are said to be autonomous to the extent that they are not subject to any outside control and use reason and free will to make choices. Autonomy is defined by the Institute of Medicine’s Committee on Assessing Genetic Risks as “self-determination, self-rule or self-governance” (Manrique de Lara et al., 2018, p. 8). Whether or not an individual consents to or withholds consent in regard to receipt of incidental findings exemplifies their right to autonomous decision making. Respecting and safeguarding an individual’s right to autonomy involves the provision of information and guidance to enable the individual to decide whether or not he or she wants to be tested and what should become of the results from the tests.

In medical terms, beneficence “concerns the duty one has to maximize benefits and minimize harm to the patient” (Grace, 2009, p. 22). Some theorists have cited the principle of beneficence as a justification for the disclosure of incidental findings to research participants. According to Ravitsky and Wilfond (2006), beneficence requires that investigators offer results to participants where the information is expected to be valuable to the participants’ physical or psychological well-being, their reproductive decision making, or their life planning. Miller, Mello, and Joffe (2008) similarly cite the general duty of beneficence that arises out of the professional relationship between the researcher and subject, and they argue that this duty requires the disclosure of incidental findings unless the subject does not want to be told of them.

Beyond beneficence, other ethical theories also support disclosure as well. One is the principle of non-malfeasance. The fundamental tenet of this principle is to minimize harm (Grace, 2009). If a researcher has an opportunity to provide information that can help a
participant prevent or minimize future harm, by engaging in genetic testing, taking preventive measures or finding early treatment, the failure to do so would violate non-malfeasance. A second is the theory of consequentialism. This theory posits that an action is moral if “good consequences are the focus of action” (Grace, 2009, p. 14). In other words, when examining a particular action in light of ethical principles, one must primarily consider the outcome that the actor had in mind when performing the action. One of the most prominent theories falling under the consequentialist umbrella is utilitarianism, which stresses human happiness and utility as the ultimate ends of any action (Grace, 2009, p. 15). Championed by philosophers such as Jeremy Bentham and John Stuart Mill, utilitarianism specifies that an action will be deemed “moral” only where consequences expected to result from the action would maximize the happiness of those affected and reduce overall pain and suffering (Grace, 2009). Proponents of utilitarianism would argue that although the findings in the gene sequencing study discussed by Kolata (2012) in The New York Times were incidental to the study, because they could be clinically useful and potentially reduce the overall pain and suffering of participants, the investigators in the study were morally obligated to create rules that would have allowed them to disclose their findings. Simply stated, disclosing incidental findings under the umbrella of utilitarianism can be beneficial for a person’s health.

When taking into consideration an individual’s desires, the fulfillment of individuals’ preferences become the primary focus and individuals are no longer focused on maximizing their health or minimizing their pain and suffering. Known as preferentialism or desire-satisfaction theory, this theory posits that an action’s value is determined independent of whether it leads to better health (Viberg, Sergerdahl, Langenskiold & Hansson, 2016). This theory
supports the idea that participants in research studies should be allowed to voice their preferences and not leave the decision in the hands of the researcher.

Other ethicists take the argument one step further. For example, bioethicists Beskow and Burke (2010) contend that there is a “special relationship” between an investigator and a participant that gives rise to a “duty to rescue” (p. 3). Under this model, researchers have an ethical, and perhaps even a legal obligation to disclose results to participants where the failure to do so could prevent the participants from pursuing potentially life-saving testing or treatment. Thus, when a researcher discovers “genetic information that clearly indicates a high probability of a serious condition for which an effective intervention is readily available,” they argue (Beskow & Burke, 2010, p. 2) there is a duty to disclose the information to the participant. For example, where an investigator discovers a mutation that creates a high risk of early onset colorectal cancer, information that would likely be otherwise unavailable to the participant, Beskow and Burke (2010) argue that the investigator has such a duty to disclose. Similarly, Michael Ulrich (2013) espouses the view that the duty to rescue model “provides an inherent mechanism to appropriately balance the obligations to individual subjects with the overall research study” (pp. 50-51). Indeed, “the duty to rescue arises when there is a risk of significant harm that the rescuer’s action has a high probability of mitigating, there is little risk of harm to the rescuer, and the benefit gained outweighs the potential risks” (Beauchamp & Childress, 2001, p. 171).

From a more pragmatic perspective, Viberg, Segerdahl, Langenskiold and Hansson (2016) note that disclosure of incidental findings could increase participation in research studies, as participants may recognize these possible personal health disclosures as an incentive. Indeed, Ravitsky and Wilfond (2006) assert that respect for participants justifies the disclosure of results
to them where the results may be of interest to them and were acquired based on their participation in the research study. This is consistent with the position taken by Fernandez et al. (2003), in which the authors argue that the disclosure of research results avoids treating persons solely as a means to an end and places the welfare of the individual in focus.

The Case Against Disclosure

Ethicists like Meltzer (2006) contend that researchers have no fiduciary obligations to their patients but rather to society as a whole—and as such, they have no obligation to disclose findings specific to individual participants. As Meltzer (2006) writes, “the primary goal is not, and indeed cannot be, to benefit any one participant. The very distinction between research and clinical care rests on the fact that research aims to produce generalizable knowledge for society at large, whereas clinical care aims to meet individuals’ specific needs, interests, and preferences” (p. 29). Indeed, while Meltzer (2006) agrees with those in favor of disclosure that beneficence is an important component of ethical research, in his view, it requires investigators to maximize potential benefits to participants and society as a whole and to minimize possible harms. As such, the issue of beneficence is reflected not in the disclosure of individual findings, but in the Institutional Review Board’s decision whether or not to approve the research study in the first place. At that point, there would be no way for the board to anticipate whether any participants could gain individually useful results from the study (Meltzer, 2006). Additionally, if individual results are generated by a study, these results may apply only to “participants with certain genomic characteristics … and even in this case it is not possible to determine whether a given participant will perceive the information as a benefit or harm once confronted with it” (Meltzer, 2006, p. 28).
Meltzer (2006) also challenges the argument that respect for persons mandates disclosure. Respecting participants, Meltzer contends, means “treating human beings capable of self-determination as autonomous agents,” and requires investigators to provide participants with adequate information about a study, honor their decision whether to enroll, and accept their decisions to withdraw should they choose (Meltzer, 2006, p. 28). It does not mean that researchers must provide them with individual results or findings once the study is undertaken (Meltzer, 2006).

Meltzer points to two other reasons why researchers have no ethical obligation to disclose individual results. First, he argues, offering individualized information to research participants invites them into what he calls “therapeutic misconception,” whereby the participants expect to receive clinically relevant information as they would in a physician-patient relationship (Meltzer, 2006, p. 29). Second, he asserts, if investigators became obligated to disclose individual results to participants, courts could impose the same duties and standards of conduct on them as they do on physicians, subjecting investigators to the same risks of legal malpractice claims as physicians. This, he contends, would affect the willingness of investigators to engage in research studies (Meltzer, 2006).

Others have analyzed the issue of individual versus societal benefits from a more practical than theoretical perspective. Ossorio (2012) argues that the resources necessary to return research results or incidental findings to individual participants will likely come from research budgets, which are already limited, rather than from additional funds. In that event, she asserts that “money spent on returning incidental findings and/or research results will not be spent on generating socially beneficial knowledge,” but will be spent instead on generating individual benefits (p. 461). If the conflict is between helping some current research
contributors and helping a greater number of future beneficiaries of medical science, “it will be morally preferable for scientists to act so as to bring about the greater good of producing socially beneficial knowledge” (Ossorio, 2012, p. 463). Selgelid (2008) makes the same argument from a more general perspective, asserting that in deciding how to allocate medical resources, the government should “aim to achieve the greatest possible payoff in terms of overall positive impact on human lives” (Selgelid, p. 118).

Some nursing research scientists question the reliability and accuracy of the genetic variants revealed by genomic sequencing and how they exactly manifest themselves in individuals (Taylor et al., 2017). In the last five years, two entities, the ACMG and the Association of Genetic Nurses and Counsellors in the United Kingdom and Ireland (AGNC), issued policy guidelines around the disclosure of incidental findings in light of the question of findings’ validity. The ACMG recommendation was to inform patients in regard to actionable variants that were identified as a result of genome sequencing and to provide patients with the opportunity to “opt out” receipt of said findings (Kalia et al., 2017). In particular, the ACMG in 2013 suggested a category of results that participants could opt out of; the intent was to inform individuals that this was indeed a reasonable option, and the guidance was updated in 2017 (Kalia et al., 2017). The two organizations fundamentally differ on the ethical implications surrounding the screening of patients. Warning that screening is “opportunistic,” the Association of Genetic Nurses and Counsellors purport that the screening of individuals should be undertaken only when it can be determined that screening will be beneficial to the patient, not harmful (Taylor et al., 2017).

In light of the risks of disclosing unreliable or invalid information to research participants the disclosure of individual results or incidental findings may be in violation of a second family
of ethical principles known as the “deontological theoretical framework.” Unlike consequentialist theories, deontological theories focus not on the consequences and outcomes of particular actions, but instead consider the “rightness or wrongness of the actions themselves” (Rainer, 2011, p. 84). Specifically, deontological theories emphasize duty and ask whether a person engaging in an action is following his or her societal, professional or other obligations (Grace, 2009). Falling within the umbrella of the deontological framework are theories concerning the role of duty in the morality of a given behavior.

Among the best-known deontological philosophies is that of Immanuel Kant, who argued that humans are supremely rational beings with a duty to use reasoning in deciding upon whether or not to carry out an action (Grace, 2009). For Kant, an individual selecting a course of action must consider whether it would be acceptable if others acted the same way (Rainer, 2011). According to Kant, humans should “act so that you treat humanity, whether in your own person or in that of another, always as an end and never as a means only” (Wood, 2002, p. 46). Kant’s categorical imperative implies that “people should not treat each other in ways to make gains for the self, but to help each other gain maximum potential” (Ranier, 2011, p. 91). In the case of researchers, the danger of requiring disclosure is that it will change their motivation from designing and carrying out the best study possible so as to obtain information that will be useful to society, to protecting their own interests, undermining the purpose of research studies and the societal benefit they can provide.

The Role of the Genetic Research Participant

In light of the heated debate described above regarding the ethics of whether a researcher should disclose incidental findings to participants, it follows that the views of the participants should weigh on this decision. A qualitative study by Ryan, de Vries, Uhlmann, Roberts and
Gornick (2017) examined in-depth the views of participants in genetic testing and determined that where incidental findings were concerned, individuals strongly desired the choice over whether researchers would disclose findings relevant to the participants’ health. Additionally, Halverson, Clift and McCormick (2016) reported that with respect to genomic sequencing results, the majority of research participants and patients “desire that information even when there is no clinical utility” (p. 146). On that basis, the theory of preferentialism would support the idea that the decision should lie with the participants; the theory argues that what matters most is whether an act fulfills a person’s preferences—regardless of the actual health outcome (Viberg et al., 2016). But according to Viberg et al. (2016), asking participants about their preferences for incidental findings disclosure may not be a simple matter. They argue that “triggered feelings, the cognitive bias and the framing of the question might invite participants to make a decision that does not represent what they truly prefer” (Viberg et al., 2016, p. 207). It is also possible that returning incidental findings to participants—or even soliciting their consent to do so—can cause distress among participants, such as if it brings up memories of serious illness in one’s family (Fernandez et al., 2003).

A recent study by Wynn et al. (2017) found that research participants with a preference for the return of incidental findings are dependent on their feelings and how much control they could exert over their current state of their health. Participants queried about the kind of results they would like to obtain cited that their decision would be influenced by whether the results could potentially impact not only their sense of self but also their relationship with their families. Individual research participants worried about suffering from some form of discrimination once they were told about the incidental finding(s). The cost of receiving the incidental finding(s) also exerted an influence upon their decision making (Wynn et al., 2017).
A further complication to interpreting participants’ views on incidental findings is that the demographics of the participants may play a critical role in their decision making on this matter. Factors such as age, gender, race, ethnicity, socioeconomic status, and cultural differences are highly relevant to who a person is and thus, it is hypothesized here, are also highly relevant to disclosure decisions. Earlier studies that examined the disclosure decision to be made by the participant, as opposed to the researcher, generally did not consider whether demographic distinctions affect such decision making. For example, Murphy et al. (2008) queried 16 focus groups in six locations across the United States, including urban and rural, consisting of individuals from a range of socioeconomic statuses, whites and African Americans, young and elderly, regarding their preferences concerning the disclosure of individual research results involving various gene variants. Despite the differences in demographics among the focus groups, the researchers did not consider the differences in examining their results. A similar focus group study, involving 10 focus groups from a broad demographic range, including race, gender, age, ethnicity, and socioeconomic status, was conducted by Bollinger, Scott, Dvoskin and Kaufman (2012). The participants were questioned regarding their preferences concerning the disclosure of individual research results. Yet again the researchers did not examine whether participants with demographic differences answered the questions differently.

Similarly, Facio et al. (2013) studied the preferences regarding the disclosure of individual research results by surveying 311 participants in the National Institutes of Health ClinSeq study of individuals who volunteered to be subjects of whole genome sequencing. In this study, the participants were homogeneous demographically: they were described as “primarily white, well-educated and earning a high income” (Facio et al., 2013, p. 263). Also, in a study of the ethical aspects of the disclosure of individual results to participants in genomic
studies, Kohane and Taylor (2010) constructed a model for the disclosure of multidimensional results. The model involved three key variables: participant preference, significance of information, and communicability. Demographic differences were not discussed.

Some more recent studies have identified compelling differences in individuals’ willingness to receive incidental findings based on demographics. Wynn et al. (2017) found that among those who practiced Christianity, 78% opted to receive the results while those of the Jewish faith only did so 58% of the time. Individuals of the Jewish faith expressed the desire to have the results kept secret, especially some genetic disorders in their offspring that could diminish their chances of marrying if made public. The study results indicated that those individuals with a bachelor’s degree tended to have a stronger preference toward receipt of the results than those with higher degrees, although the study was limited by the modest sample size (N=298). Individuals with insurance other than Medicaid would be more likely to request secondary results, although again, a larger sample would be needed to assess just how the type of insurance an individual subscribed to would impact their desire toward the return of secondary findings. Wynn et al. (2017) demonstrated for the first time a relationship between desire to know and families with children who were already afflicted with a severely debilitating medical condition. Parents of multiple children with the genetic disease were less likely to desire the information about the secondary finding than participants who did not have children or had only one child with a serious genetic disease (Wynn et al., 2017). This study was limited by the fact that the participants studied were from a homogenous group and as such were not representative of the US population as a whole (Wynn et al., 2017); thus, when it comes to incidental findings in genetic research, there is clearly a need for additional exploration.
Alzheimer Disease: A Case for Incidental Findings

What is Alzheimer Disease?

Alzheimer disease currently affects more than 5 million Americans and that number is expected to triple in the decades to come (Roberts, McLaughlin & Connell, 2014; Warshaw & Bragg, 2014). It is a leading cause of death in the United States and the “most common neurodegenerative disorder worldwide” (Blanken et al., 2017, p. 56). According to de Saá Guerra et al. (2016), Alzheimer disease is a “neurodegenerative disease characterized by an accumulation of proteins such as Tau or B-amyloid, which causes progressive dementia in adulthood, leading to a state of total disability and death” (p. 121). The disease involves “severe neuronal loss” and “is clinically characterized by progressive deterioration of memory and cognitive functions, leading to loss of autonomy” (Van Cauwenberghe, Van Broeckhoven & Sleegers, 2016, p. 421). Typically, patients show clinical symptoms once older than 65 years (“late onset”), although up to 10% of individuals exhibit symptoms at a younger age (Van Cauwenberghe et al., 2016). Individuals may suffer from Alzheimer for a duration of seven to ten years, with more adults experiencing severe dementia in the last stage of the disease (Warshaw & Bragg, 2014). Symptoms include “memory loss, poor judgment, expressive or receptive aphasia, severe difficulty with completion of activities of daily living, and neuropsychiatric symptoms” (e.g., anxiety, agitation, depression; Staedtler & Nunez, 2015, p. 108).

Patients suffering from Alzheimer disease experience three “stages” of the disease, each presenting unique challenges for patients and their caregivers (Warshaw & Bragg, 2014). In its earliest stage, Alzheimer symptoms mimic conditions such as depression or may exhibit symptoms equivalent to side effects of medications that elderly individuals may be prescribed.
One of the first symptoms to show is the loss of episodic memory, making it difficult for individuals to learn and recall new information (Karantzoulis & Galvin, 2011). Additionally, patients may demonstrate difficulty with language (e.g., forgetting the right word for a given moment), as well as spatial/visual challenges such as the inability to find items in the house or drive a car (Karantzoulis & Galvin, 2011). Family members more often than not recognize and seek help for the individual suffering, though this might not be done as quickly as with other chronic illnesses because of the stigma surrounding a diagnosis of Alzheimer and the inability of many, including healthcare workers themselves, to distinguish between memory loss and Alzheimer (Warshaw & Bragg, 2014). In the second stage, patients exhibit increased symptoms, including personality and mood changes. Many patients require constant supervision at home by family members. In the final stage, extensive brain damage leads to a major physical decline and the patient generally requires institutional care (Warshaw & Bragg, 2014).

At the most basic level, brain inflammation is a driving force behind Alzheimer disease (McGeer, Rogers & McGeer, 2016). Blanken et al. (2017) notes that “the main pathologic indicators of Alzheimer disease are amyloid plaques and neurofibrillary tangles,” and structural changes and shrinking of the hippocampus are warning signs for development of Alzheimer disease (p. 57). According to McGeer et al. (2016), two key discoveries pointed researchers to inflammation: activated microglia associated with legions in the brains of Alzheimer patients, and the finding that individuals with rheumatoid arthritis (who regularly were prescribed anti-inflammatory agents) had lower rates of Alzheimer disease.

Researchers have studied “biomarkers”—biological signals occurring in Alzheimer patients—to help track progression of Alzheimer disease, and there is a consensus that Alzheimer disease develops a decade before an affected individual’s symptoms first show
Biomarkers report “a single absolute value reflecting degree of abnormality” that can then be used to determine how far along a given individual’s brain is in the Alzheimer development process (Jack et al., 2016, p. 541). According to Frisoni and Hansson (2016), “molecular biomarkers that reflect either the deposition of aggregated B-amyloid or hyper phosphorylated tau ... can be detected in the CSF and visualized by PET imaging” (p. 650). Though three biomarkers (AB, T-tau, P-tau) have proven most important for understanding the progression of Alzheimer, extensive research in the last twenty years has helped geneticists uncover additional cerebrospinal fluid (CSF) and blood biomarkers that demonstrate differences between Alzheimer and non-Alzheimer patients (Olsson et al., 2016). These include neurofilament light chain (NFL), Neuron-specific enolase (NSE), Visinin-like protein 1 (VLP1), Heart fatty acid binding protein (H-FABP), and YKL-40 (Olsson et al., 2016). Recent research conducted at Washington University in St. Louis has indicated that “measures of tau protein in the brain more closely track cognitive decline due to Alzheimer disease compared with long-studied measures of amyloid beta” (Strait, 2016, p. 1).

Along with the rapid progression in the field of genetics came the usage of polygenic risk scores (PRS), which serve as an estimation of how susceptible an individual is to developing a disease on the basis of his or her genetic profile. Accounting for the additive effect of multiple variants, PRS are a powerful tool in not only identifying at-risk individuals but in predicting their overall risk of developing Alzheimer disease. According to Manrique de Lara et al (2018), “each score is based on known risk and protective alleles in genome-wide data, and it is calculated from Genome-Wide Association Study summary statistics for the trait of interest” (p. 6). The scores have been demonstrated to remain constant throughout an individual’s lifetime and thus can be utilized at any age. Since pathological changes and abnormalities in biomarkers may
appear as early as 20 years prior to the onset of Alzheimer disease, this tool may prove useful in identifying individuals at risk earlier than once thought possible. By using this tool, researchers were able to identify mild cognitive impairment, which is an intermediary stage in an individual’s decline to dementia in 50-year-old subjects (Manrique de Lara et al., 2018).

However, the scores have not yet reached peak accuracy. Researchers using PRS genotype data have predicted one’s risk of developing Alzheimer disease 74% of the time as compared to the theoretical maximum for this method of 82% accuracy (Manrique de Lara et al., 2018).

Though the biomarkers help researchers understand the progression of Alzheimer disease, the biomarkers themselves are not the causes of the disease. In recent years, genetic studies have vastly improved researchers’ understanding of the genetic causes of the disease as well. One area of focus has been the Apolipoprotein E (APOE) region of chromosome 19. APOE is responsible for lipid transport, regulating cholesterol levels, and exists in three forms/alleles; epsilon 2 (e2), epsilon 3 (e3), and epsilon 4 (e4; Liu et al., 2013). While nearly 80% of humans around the world have APOE-e3, researchers have known since the 1990s that the presence of APOE-e4 is associated with increased cholesterol levels and is a strong genetic risk factor for late-onset Alzheimer development (Jarvik et al., 1995; Liu et al., 2013). APOE is a major cholesterol carrier, and Liu et al. (2013) note that APOE genotypes “strongly affect deposition of AB to form senile plaques and cause cerebral amyloid angiopathy,” key components to the pathology of brains affected by Alzheimer disease (p. 107). The genotype APOE-e4 together with type 2 diabetes, vascular disease, or atherosclerosis puts individuals at particularly high risk of developing Alzheimer disease (Liu et al., 2013). More recently, researchers have taken their understanding of the genetic underpinnings of Alzheimer a step further: research has identified 31 SNPs in addition to APOE that are associated with Alzheimer disease (Tan et al., 2017). Tan
et al. (2017) have used genome-wide association studies to develop the polygenic hazard score (PHS) that integrates these 31 SNPs in addition to APOE-e4; their research suggests that the PHS is a better predictor of Alzheimer risk than APOE-e4 alone.

**Treatment of Alzheimer Disease**

No cure exists today for Alzheimer disease, so treatment efforts typically focus on management of the disease and slowing its onset (Staedtler & Nunez, 2015). In general, the literature describes three approaches to treatment, the latter two of which are non-invasive: pharmacology, cognitive training, and physical exercise.

In treating Alzheimer patients with medication, researchers have employed drugs to strengthen patients’ cognition (Tricco et al., 2017). One area of research has considered the impact of “amyloid-modifying therapies” (Sperling et al., 2014, p. 1). Clinical trials have demonstrated that many patients receiving such therapies receive them too late; the most effective approach to slow (or perhaps even prevent) the onset of the disease would require the administration of therapy before symptoms begin to show (Sperling et al., 2014). Nonetheless, there may be opportunities for drug therapies to slow cognitive decline once a patient has been diagnosed with Alzheimer disease. One approach involves cholinesterase inhibitors, which are “believed to improve cognitive impairment in mild to moderate AD by inhibiting neuronal acetylcholine breakdown” (Tricco et al., 2017, p. 2). Another approach involves the use of memantine, which is a cognitive enhancer that “is believed to block flow-through channels of N-methyl-d-aspartate receptors--glutamate receptors involved in cognition” (Tricco et al., 2017, p. 2). Researchers continue to test these and other approaches.

As clinical trials continue regarding numerous drug-related therapies for Alzheimer disease, many families prefer non-pharmacological treatments for loved ones suffering from the
Researchers have found that non-invasive cognitive therapies may lead to improvements in key cognitive functions (Kallio, Kautiainen & Pitkala, 2017; Giovagnoli et al., 2017). Three primary cognitive therapies exist: cognitive rehabilitation, cognitive training, and cognitive stimulation. Rehabilitation “refers to a tailored approach that helps patients and their families to identify personal goals and strategies to overcome cognitive, psychological and behavioral failures focusing on everyday activities” (Giovagnoli et al., 2017, p. 1486). Cognitive training, on the other hand, is based on the concept of brain plasticity and attempts to use problem-solving or other guided mental exercises to “improve, maintain, or restore the impaired functions” (Giovagnoli et al., 2017, p. 1486; Kallio et al., 2017). Finally, cognitive stimulation is “usually administered in a group setting, is often recreational in nature, and involves non-specific cognitive activities, such as group discussions” (Kallio et al., 2017, p. 1349).

In addition to drug and cognitive therapies for the treatment of Alzheimer disease, a third non-invasive and promising area of treatment involves physical exercise and activity. According to de Saá Guerra et al. (2016), “exercise can increase levels of brain-derived neurotrophic factor (BDNF) and other growth factors, stimulate neurogenesis, increase resistance to brain injury, improve learning and mental performance, arouse the growth of blood vessels, and reduce amyloid load” (p. 121). Additionally, researchers at the University of Maryland (2014) have demonstrated that moderate physical activity can protect and prevent shrinkage of the hippocampus, which is the region of the brain that controls memory and is one of the first regions affected by Alzheimer disease. Relatedly, evidence suggests that physical inactivity is associated with an individual having a greater risk of developing Alzheimer disease (Chmielewski, Kaur & Holmes, 2016).
Perceptions of Genetic Screening for Alzheimer Disease

In addition to genetic research surrounding the causes, risk factors, and potential treatments for Alzheimer disease, researchers have studied the social side of the disease: the perceptions of Alzheimer disease among patients, family members, and other individuals. This is particularly important to understand, as direct-to-consumer genetic testing companies make it easier and easier for people to learn about their genetic risk profiles (Van Cauwenberghe et al., 2016). According to Van Cauwenberghe et al. (2016), clinical and survey research have demonstrated that most people at risk for Alzheimer disease want to learn more about their genetic profile. In the REVEAL study, individuals who learned they were at risk of developing Alzheimer disease as a result of the presence of APOE-e4 did not generally demonstrate major psychological impact after genetic testing and commonly began taking nutritional supplements to potentially aid in slowing disease onset (Van Cauwenberghe et al., 2016). With respect to screening for dementia in primary care, Fowler et al. (2012) found that individuals who held stronger beliefs about the benefits of screening (e.g., ability to treat the disease early) were more likely to seek screening than those who did not believe screening would yield actionable, positive outcomes.

Given the increasingly promising research around slowing and treating the progression of Alzheimer disease, it is important for researchers to understand individuals’ desire (or lack of desire) to learn about their own personal risk factors for the disease. As Fowler et al. (2012) noted, the more that individuals believe genetic screening for dementia will produce beneficial outcomes for their long-term health, the more likely they were to desire such screening. Could the same hold for incidental findings, which may have implications for individuals’ health but
are not findings the participants initially seek out? In the present study, the researcher considered the role that the TRA may play in explaining individuals’ intentions in this area.

**The Theory of Reasoned Action**

Martin Fishbein and Icek Ajzen developed the TRA in 1967 to explore the intent of individuals to engage in a behavior based upon their beliefs and social influences (Fishbein, 1967; Ajzen & Fishbein, 1980). The theory is predicated upon the assumption that all individuals are rational, and as such take all information into account when making a decision. To do so, individuals bracket information into two separate determinants: their own thoughts and beliefs about a behavior and the subjective norm, which is the outside pressure they feel to engage in a behavior. The TRA “consists essentially of a series of hypotheses linking beliefs to behavior, with each hypothesis requiring empirical verification” (Ajzen & Fishbein, 1980, p. 80).

The first of these hypotheses states that a person’s thoughts and beliefs about a behavior form his or her “attitude” (Fishbein & Ajzen, 1975). The attitude is a function of a person’s evaluation of the behavior’s consequences and the strength of his or her belief that performing the behavior will lead to the given consequence (Ajzen & Fishbein, 1980, p. 67). The immediate determinant of the attitude is known as a “salient belief,” which is a self-generated, inferred belief that results from direct observation or accepting information from outside sources (Ajzen & Fishbein, 1980, p. 63). The sum total of all salient beliefs about a behavior establishes one’s attitude towards said behavior.

The attitude towards a behavior, in combination with the individual’s subjective norm, produces a person’s “intention” about whether or not to engage in the behavior. Under the terms of this theory, the subjective norm is defined to be the “perception that important others desire
the performance or nonperformance of a specific behavior” (Ajzen & Fishbein, 1980, p. 57).

The system is described in the diagram below.

*Figure 1. Theory of Reasoned Action*

According to the theory, three conditions can impact the link between intention and behavior: the specificity of the respective measures of intention and behavior, the stability of intentions between the time of measurement and the time that the behavior is carried out, and the degree to which the behavior is truly under the control of the individual (Madden, Ellen & Ajzen, 1992, p. 4). Fishbein and Ajzen claim that “the predictive power of an intention should vary inversely with the time between the measurement of that intention and the observation of the behavior” (Hausenblas, Carron & Mack, 1997, p. 39). Whether or not the behavior is performed depends on resources and opportunities available. Time, money, skills, and cooperation of others come into play here. It is conceivable that as time goes by, new information may be presented and the individual’s intention might change. External variables such as demographic variables and personality traits can provide some insight into factors determining an individual’s beliefs, but according to the TRA, these variables do not predict an individual’s attitudes or social norms.
Researchers have applied the TRA in many contexts, including numerous studies regarding healthcare decision making. For example, Barling and Moore (1996) surveyed adult women and employed a regression analysis to determine that the key tenets of the TRA—attitude and social norms—helped explain the women’s decisions to engage in a Pap screening test; those who viewed the tests more favorably and felt stronger social norms around the testing were more likely to engage. In a study of teenage sexual behavior, Doswell, Braxter, Cha and Kim (2011) found that “the TRA significantly predicted early sexual behavior among young teen African American girls in the study” and a model with “attitudes, norms, and intention was able to correctly classify slightly more than 75% of the girls who had engaged in sexual behavior” (p. 50). Furthermore, Davis (2005) found that attitudes and subjective norms predicted substance abuse counselors’ intentions to employ confrontational approaches in their treatment programs, though attitudes proved to be stronger predictors than subjective norms. Additionally, researchers have utilized the TRA to help predict voting choices in a presidential election, seat belt use, drug use, alcohol use in adolescents, smoking behaviors, mother infant-feeding behavior, and consumers’ attitudes.

This study aims to continue the approach of the aforementioned studies and to apply the TRA to a different area of healthcare decision making: intention to seek incidental findings. It seeks to determine whether participants’ attitudes and subjective norms regarding incidental findings linking them to Alzheimer disease predict their decision to receive or reject reports of the incidental findings.

The Theory of Planned Behavior is an extension of the TRA and was added by Ajzen (1985) to encompass the idea that individuals can have control over their behavior. The concept of perceived behavior control is defined by the individual’s perception of the ease or difficulty
involved with the performance of a behavior, which involves taking into account past experiences and perceived obstacles or impediments. According to Ajzen, perceived behavioral control has “an indirect or direct effect through behavioral intentions” (Hausenblas et al., 1997, p. 38). Ajzen developed this extension of the TRA to help explain why intention may not always predict behavior: if the individual does not have full control, he or she cannot carry out a behavior, no matter the intention (Ajzen, 1985). It stands to reason that the more favorable the attitude and subjective norm in conjunction with greater behavioral control, the stronger the intent to perform the behavior in question.

In this study, the researcher focused on the TRA, not the Theory of Planned Behavior. As Ajzen (2015) notes on his website, “In the development of the TRA it was assumed that people have volitional control over the behavior of interest (and that they realize that they are capable of performing the behavior if they so desire). Under these conditions, perceived behavioral control becomes irrelevant and the theory of planned behavior reduces to the theory of reasoned action.” In a true genetic test scenario, it is possible that there would exist a gap between participants’ desires for disclosure of incidental findings (“intention”) and their perception of their ability to successfully make that request of the researchers (“behavior”). But in this study, participants answered survey questions regarding a hypothetical genetic test. As such, intention to receive incidental findings is the end behavior of interest—there is no “extra step” after intention required and therefore no gap between intention and behavior to explain with the Theory of Planned Behavior (Ajzen, 2015).

Summary

Unlike clinical laboratories that exist to serve patients, research laboratories are not required under federal Clinical Laboratory Improvement Amendments and Regulations to obtain
certification before disclosing research results to participants. Consequently, there has been much debate among researchers and theorists regarding whether research laboratories should disclose to genetic-testing participants incidental findings with potentially life-altering implications. Some theorists have cited the principles of beneficence, non-malfeasance, consequentialism, and utilitarianism in arguments in favor of disclosure (Beauchamp & Childress, 2001; Beskow & Burke, 2013; Ravitsky & Wilfond, 2006; Viberg et al., 2016), while others have cited deontological theories and pragmatic concerns in arguments against disclosure (Meltzer, 2006; Ranier, 2011; Selgelid, 2008).

Too few studies have considered this question from the point of view of the genetic research participants. In this study, the researcher sought to apply the TRA to understanding participants’ views toward incidental findings with respect to Alzheimer disease. Alzheimer disease—a widely researched yet still incurable disease that generally affects people later in life—is an ideal case example for this application of the theory.
CHAPTER THREE: RESEARCH DESIGN AND METHODS

Introduction

In this chapter, the researcher describes the procedures employed in the study. The chapter begins with an overview of the online survey-based methodology employed to assess participants’ likelihood to request incidental findings, as well as a discussion of the participant recruitment process for the study. The chapter continues with a description of and a justification for the PRISM-PC as the study survey instrument. The chapter concludes with an explanation of statistical methodology for the analysis of survey results.

Method

The study employed a survey-based design to explore the role that the TRA plays in explaining participants’ intention to receive an incidental finding, which may indicate a potential genetic link to Alzheimer disease. According to Creswell (2009), “survey design provides a quantitative or numeric description of trends, attitudes or opinions of a population, by studying a sample of that population. From sample results, the researcher generalizes or makes claims about the population” (p. 145). In particular, this study included an online sample of participants. Researchers have previously noted a number of advantages to online sample methodology, including the ability to reach a diverse (or, if desired, concentrated) group of individuals around the country or world, and automated data-collection processes (Wright, 2005). Additionally, Viberg et al. (2016) note that contact with individuals through “individual IT interfaces makes it possible for new recruitment and provision of information and results” (p. 203).
Participants and Sample Size

The population for the study consisted of individuals who have signed up to participate in online studies via SurveyMonkey®. SurveyMonkey’s ® Survey Panel includes a diverse sample of individuals from around the United States who volunteer to participate in surveys in exchange for SurveyMonkey® donations to the participants’ favorite charities. Conducting a survey with participants from SurveyMonkey® was appropriate for this study as the online panel represented a national population who could be reached with the instrument efficiently at scale (Bentley, Daskalova & White, 2017). Participants responded to questions about hypothetical genetic testing and were not subject to actual genetic research as part of this study.

To be included in the study, a potential participant must have been at least 18 years old and English literate. There were no restrictions on gender or household income. Though Roberts et al. (2014) found that participants in a sample of patients over 50 were less likely to desire information about their odds of an Alzheimer diagnosis the older they were, it was uncertain whether this age-based impact would continue to hold for incidental findings. Unlike seeking genetic testing for Alzheimer, a proactive behavior, receiving incidental findings of Alzheimer represents a passive action. This difference made it of value for the study to include participants of all ages to verify if this age effect holds true for incidental findings. As such, age was included as a covariate in the model to determine whether it was a predictor of LRIF. Potential subjects were asked whether they have or previously had an immediate family member or close friend diagnosed with Alzheimer disease. The answer to this question served as a covariate for the study.

In order to assess the results of the study, the researcher conducted a multiple regression analysis. To determine an adequate sample size for conducting such data analysis, the researcher
conducted a power analysis, a recommended method for estimating required sample size, with the G*Power Data Analysis software recommended by Faul, Erdfelder, Buchner and Lang (2009). Using the power analysis procedure for a generalized linear model (which includes multiple regression), the researcher calculated the minimum recommended sample size with values of 8 potential predictors (results of the three subscales employed in the survey, age, gender, ethnicity, level of education, and presence of a close family member or friend diagnosed with Alzheimer disease), a standard power level= 0.8, a significance level= 0.05, and a “medium effect size” of 0.15 (Cohen, 1988, p. 413). A minimum of approximately 109 participants was suggested. For additional power, and given the efficiencies of online survey tools, this study sought to recruit at least double that number. Recruitment proved straightforward and the study concluded with $N=298$.

**Setting**

The researcher conducted this study using a population of online survey participants organized by SurveyMonkey® as part of its SurveyMonkey® Contribute program. Participants completed the survey online via SurveyMonkey.com.

**Human Subjects Protection**

Prior to conducting the study, the researcher obtained the approval of the Molloy College Institutional Review Board (see Appendix D). The researcher provided an explanation about the purpose of the study and time involved in completing study documents. Completion of the survey implied consent to participate. The researcher enabled SurveyMonkey’s® “anonymous responses” feature to ensure participants remain anonymous and no personally identifiable information is transmitted in the results. Participants who desired to obtain the results of the study upon its completion were instructed to email the researcher, who would reply upon
completion of the study. In order to preserve anonymity of responses, the researcher would only provide participants with aggregated results upon their request; no information about individual responses would be disclosed.

**Participant Recruitment**

For this study, the researcher purchased an online sample of survey respondents from SurveyMonkey’s® *SurveyMonkey Contribute* panel. Bentley et al. (2017) compared a SurveyMonkey® sample of 150 participants against a large-scale market research study of 1,000 participants regarding consumer product preferences and found a high degree of accuracy for SurveyMonkey®, with an average error of less than 5% versus the larger scale study. Panel members are recruited via SurveyMonkey’s® website from around the United States. As an incentive for individuals to join the panel, SurveyMonkey® offers both the opportunity to win prizes such as an Amazon gift card, as well as a $0.50 donation to the participants’ preferred charities per completed survey. When joining the SurveyMonkey® panel, individuals are required to answer a number of demographic questions, which SurveyMonkey® uses to offer targeting options to researchers seeking survey responses.

The researcher paid a $26 monthly service fee to SurveyMonkey® for the use of its platform to collect data. The recruitment process via *SurveyMonkey® Contribute* included an additional charge determined on the basis of the specified criteria. At the outset of the recruitment process, the researcher specified in SurveyMonkey® that the sample should include SurveyMonkey’s® default Census-based gender balancing (which seeks a male/female participant split consistent with the latest Census data), United States-based individuals above the age of 18, and expected participant qualification (incidence) rate range of 75%-100%. These criteria resulted in a price per participant of $3.75 for up to 250 completed responses, totaling
$937.50. Because the actual incidence rate was on the higher end of the expected range (91%), the final \( n \) of 298 included 48 participants above the SurveyMonkey® target who were included free of charge. Additional details on the recruitment process are documented by SurveyMonkey® at https://help.surveymonkey.com/articles/en_US/kb/SurveyMonkey-Contribute.

Data Collection Procedures

The researcher administered the study survey in order to explore the role that the TRA plays in explaining participants’ LRIF. In order to complete the survey, participants first needed to log in to their SurveyMonkey® Contribute Panel accounts. On the account home screen, SurveyMonkey® presented panelists with surveys to complete, in exchange for the incentives described above. Participants completed the survey online via the SurveyMonkey® website. The average completion time was under 5 minutes.

Survey Instrument

The Perceptions Regarding Investigational Screening for Memory in Primary Care (PRISM-PC) is a questionnaire developed by Boustani et al. (2008) to systematically measure the attitudes of primary care patients regarding dementia screening. The instrument consists of a series of statements aimed at what patients perceive as harms and benefits that might be derived from such a screening (Boustani et al., 2008). These scales consist of a number of sub-scales, including: “acceptance of dementia screening,” “benefits of dementia screening,” “stigma of dementia screening,” “negative impact of dementia screening on independence,” “suffering related to dementia screening,” “screening for other conditions,” and “beliefs related to treatment for Alzheimer disease” (Fowler et al., 2012). The instrument underwent thorough testing and evaluation prior to finalization. A panel of clinical experts examined the instrument for face
validity. Subsequently, three convenience samples of individuals were selected to complete the questionnaire (Boustani et al., 2008). In the study, 315 individuals aged 65 and older were chosen from seven outpatient clinics under the umbrella of the Indiana University’s Medical Group system. Eligibility requirements for the study consisted of participants who had no documented history of depression, schizophrenia, bipolar disorder or dementia. For construct validity, the researchers conducted a factor analysis. The researchers found:

- Two dimensions regarding the acceptance of dementia (“knowledge about dementia risk” and “knowledge about dementia testing”).
- Four dimensions regarding benefits and harms of dementia screening (“perceived benefits of screening,” “stigma of screening,” “suffering from screening,” and “impact of screening on patients’ independence”).

For the present study, the researcher included only three of the above dimensions necessary to compose the two components of the TRA (Attitudes and Subjective Norms). The “AS” (Attitudes Subscale) for the present study consisted of the “acceptance” (Cronbach’s alpha 0.88) and “perceived benefits of screening” (Cronbach’s alpha 0.79) dimensions from the PRISM-PC referenced above. Participants indicated their agreement or disagreement on a Likert scale with respect to these specific prompts:

- I would like to know if I am at higher risk than others for developing Alzheimer disease.
- I would like to know if I have Alzheimer disease.
- I would like to be tested for the presence of Alzheimer disease on a regular basis with a short questionnaire.
- I would like to be tested for the presence of Alzheimer disease on a regular basis with a blood sample.
• I would like to be tested for the presence of Alzheimer disease on a regular basis with pictures of my head or brain (CT-scan or MRI).

• I would like a doctor to examine me every year to know if I have developed Alzheimer disease.

• I believe that early detection of Alzheimer disease increases the chance to treat the disease better.

• If I knew that I had Alzheimer disease earlier, my family would have a better chance to take care of me.

• If I found out early that I had Alzheimer disease, I would have more time to plan my future.

• If I found out early that I had Alzheimer disease, I would have more time to talk with my family about my health care.

• If I found out early that I had Alzheimer disease, I would have more time to talk with my family about my finances.

• If I found out early that I had Alzheimer disease, I would sign my advance directive or my living-will.

• If I knew that I had Alzheimer disease earlier, I would be motivated to have a healthier lifestyle.

• If I knew that I had Alzheimer disease earlier, I would be more willing to participate in research about this disease.

The “SNAS” (Subjective Norms about Alzheimer Subscale) for the present study consisted of the “stigma of screening” subscale from the PRISM-PC referenced above (Cronbach’s alpha 0.74; (Boustani et al., 2008). Participants indicated their agreement or disagreement on a Likert scale with respect to these specific prompts:

• If I had Alzheimer disease, I would not want my family to know.
• If I had Alzheimer disease, I would feel humiliated by my family members and/or others who would treat me poorly or laugh at me.

• If I had Alzheimer disease, I would no longer be taken seriously.

• If I had Alzheimer disease, I would be considered stupid and unable to do things.

• If I knew that I had Alzheimer disease, I would be ashamed or embarrassed.

• If I knew that I had Alzheimer disease, I would give up on life.

• If I had Alzheimer disease, my doctor would not provide the best care for my other medical problems.

• If I had Alzheimer disease, my doctor and other health professionals would not listen to me.

• If I had Alzheimer disease, I would be concerned that my health insurance company would find out.

• If I had Alzheimer disease, I would be concerned that my employer would find out.

Table 1. List of Variables and Operational Definitions

<table>
<thead>
<tr>
<th>Variable</th>
<th>Conceptual Definition</th>
<th>Operational Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Likelihood to request incidental findings</td>
<td>The likelihood that an individual would request the disclosure of incidental findings from a hypothetical genetic test indicating a future Alzheimer disease diagnosis.</td>
<td>Survey question on a 7-point Likert-type scale asking participants how likely they would be to request incidental findings from a hypothetical genetic test. See Appendix B, Question 26.</td>
</tr>
<tr>
<td>Attitudes toward genetic screening for Alzheimer disease</td>
<td>A person’s belief about a given behavior—in this case, participating in genetic screening for Alzheimer disease. A function of a person’s assessment of the behavior’s consequences and his or her belief that performing the behavior will actually produce the given consequence (Ajzen &amp; Fishbein, 1980).</td>
<td>Attitudes Subscale (AS) consists of the following subscales from the PRISM-PC created by Boustani et al. (2008): “acceptance of dementia screening” and “benefits.” 5-point Likert scale; items 2-9, 16-19, 21 and 23.</td>
</tr>
</tbody>
</table>
Table 1. (Continued)

<table>
<thead>
<tr>
<th>Subjective norms regarding Alzheimer disease</th>
<th>How one believes the important figures in his or her life view the behavior in question. The “perception that important others desire the performance or nonperformance of a specific behavior” (Ajzen &amp; Fishbein, 1980, p. 57).</th>
</tr>
</thead>
</table>

*Subjective Norms about Alzheimer Subscale (SNAS)* consists of the “stigma of screening” subscale from the PRISM-PC created by Boustani et al. (2008). 5-point Likert scale; items 10-15, 20, 22, 24-25.

The PRISM-PC questionnaire was developed with the Health Belief Model (HBM) as its theoretical underpinning (Boustani et al., 2008). The Health Belief Model was first developed in the 1950s by Drs. Godfrey Hochbaum, Stephen Kegeles, Howard Leventhal, and Irwin Rosenstock (Rosenstock, 1974). It posits that four key constructs explain an individual’s healthcare decision making: *perceived susceptibility* (likelihood of getting a disease), *perceived severity* (how serious the disease is believed to be), *perceived benefits* (of various treatment options), and *perceived barriers* (that might prevent the person from engaging in a treatment-related behavior; Champion & Skinner, 2008).

Ajzen (1998) notes that the TRA is a “general” theory, which may be applied in many contexts, whereas the Health Belief Model is “content-specific” (p. 737). In addition, it is worth noting that the TRA contains a more explicit construct for “perceived social norms,” which makes it particularly useful as the main theory for this study because many research participants may base their understanding of Alzheimer on what they perceive to be the beliefs of others regarding the disease.

Despite the different theoretical backing, however, the PRISM-PC questionnaire was an appropriate instrument for use in this study. Fundamentally, both the Health Belief Model and the TRA rest on the premise that behavioral decisions can be explained by people’s attitudes and
beliefs. Taylor et al. (2006) suggest that both models are therefore “value-expectancy theory based,” and that the TRA “in some respects may be seen as refining and taking forward approaches embodied in the Health Belief Model” (p. 6).

Regarding the specific measures, Taylor et al. (2006) note that while the TRA does not always involve a “threat” in the way the Health Belief Model does, the TRA’s constructs reflect the “susceptibility/severity” and “benefits/barriers” incorporated into the Health Belief Model (p. 7). And indeed, the PRISM-PC incorporates the measurement of the TRA’s attitudes and subjective norms into three of its subscales: “acceptance” of dementia screening, “benefits,” and “stigma.” These scales were contained in two sections of the PRISM-PC, and the researcher administered a survey including these two sections in the present study. Please see Appendix B for the instrument used in this study. The instrument began with a description of recent advances in genetic testing and a definition of “incidental findings,” along with an overview of the questions the participants answered.

SurveyMonkey® automatically includes gender, age range, region, and annual household income information for respondents via its panel. The researcher followed U.S. National Institutes of Health Collaboratory (2014) guidelines to add demographic questions regarding ethnicity and race, as well as participants’ level of education and whether the participants had immediate family members or close friends diagnosed with Alzheimer disease. In order to measure participants’ LRIF in a hypothetical genetic study, the researcher included a prompt that states, “Imagine you were undergoing genetic testing for something other than Alzheimer disease. You could be participating in a genetic research project, or perhaps, you ordered a popular home genetic testing kit. How likely would you be to request the results of any incidental findings related to your risk for Alzheimer disease that resulted from your test?” After
reading this prompt, participants responded on a 7-point, Likert-type scale to indicate their intentions, ranging from “Very Unlikely” to “Very Likely.” These questions are included in the survey instrument in Appendix B.

**Data Analysis**

In order to assess the extent to which the TRA explains participants’ decisions regarding incidental findings related to Alzheimer disease, the researcher conducted several regression analyses. To evaluate the impact of demographic variables (age, gender, ethnicity, socioeconomic status, level of education, and presence of an immediate family member or close friend diagnosed with Alzheimer disease) on participants’ attitudes and subjective norms, multiple regression analysis was conducted. A linear model was adequate to describe the relationship as the subscales taken from the PRISM-PC constitute continuous variables and the underlying distribution of the data and the random error inherent in the measurements are approximately Gaussian. Pearson product moment correlation coefficients between the independent variables were calculated to determine if there existed any multicollinearity in the data and to help determine which covariates not to include in the regression. Exhaustive automatic variable selection was then used to determine the best-fitting combinations of covariates to include in the models. The extra sum of squares values for each of the included covariates were also calculated through an ANOVA to give insight into which variables showed the greatest impact on the model fit and were most related to the participant’s attitudes and beliefs. To assess the impact of all subscales and demographic explanatory variables on the likelihood to receive or reject incidental findings, ordinal logistic regression was conducted. This methodology was favored, as the response variable is a single, 7-point Likert type item, which is
an ordinal variable and thus cannot be modeled by traditional least squares regression. Statistical analyses were conducted using The R Project for Statistical Computing (R).

**Summary**

The researcher recruited a sample of participants and administered the questionnaire online via SurveyMonkey®. The survey instrument employed in the study included items used with permission from the PRISM-PC questionnaire. The instrument consisted primarily of two subscales: Attitudes toward genetic screening for Alzheimer Subscale (AS) and Subjective Norms about Alzheimer Subscale (SNAS). ANOVA was used to assess the impact of the subscales and demographic variables on the dependent variable (LRIF).
CHAPTER FOUR: FINDINGS

Introduction

In this chapter, the researcher reports the results of the study, identified through the statistical analyses and data collection methodologies discussed in Chapter Three. The chapter begins with summary statistics regarding the participant sample and the questionnaire. It continues with descriptive results regarding the independent and dependent variables, including a discussion of correlations between explanatory variables and an analysis of variance in the subscales. The chapter concludes by addressing the research question directly through results of an ordinal logistic regression linking the subscales representing the TRA to participants’ intention to request incidental findings.

Summary Statistics

For the purposes of this study, a sample of 298 adults participated using the SurveyMonkey® online survey platform. This group represented a mix of different age, gender, race, ethnicity, household income, and education levels, allowing the researcher to examine the interaction effects of demographic information with the independent variable.

Table 2. Sample Characteristics: Age

<table>
<thead>
<tr>
<th>Age</th>
<th>N</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>18-29</td>
<td>48</td>
<td>16.1%</td>
</tr>
<tr>
<td>30-44</td>
<td>89</td>
<td>29.9%</td>
</tr>
<tr>
<td>45-60</td>
<td>62</td>
<td>20.8%</td>
</tr>
</tbody>
</table>
Participant ages ranged from 19 to 93, with the largest age group being above the age of 60 (33.2%). The mean age of the sample was approximately 49 years old, the median age was 50, and the standard deviation was 17.3, indicating a wide distribution. The sample saw an approximately even gender split, with women making 53% of the sample and men 47%. Such an even division was important given the inclusion of gender as a covariate, though as reported below, gender did not significantly predict the intention to request incidental findings.

Table 3. Sample Characteristics: Household Income

<table>
<thead>
<tr>
<th>Income Level</th>
<th>N</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>$0-$9,999</td>
<td>24</td>
<td>8.1%</td>
</tr>
<tr>
<td>$10,000-$24,999</td>
<td>35</td>
<td>11.7%</td>
</tr>
<tr>
<td>$25,000-$49,999</td>
<td>50</td>
<td>16.8%</td>
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<tr>
<td>$50,000-$74,999</td>
<td>49</td>
<td>16.4%</td>
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Table 3. (continued)

<table>
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<tr>
<th>Income Range</th>
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</tr>
</thead>
<tbody>
<tr>
<td>$75,000-$99,999</td>
<td>25</td>
<td>8.4%</td>
</tr>
<tr>
<td>$100,000-$124,999</td>
<td>15</td>
<td>5.0%</td>
</tr>
<tr>
<td>$125,000-$149,999</td>
<td>17</td>
<td>5.7%</td>
</tr>
<tr>
<td>$150,000-$174,999</td>
<td>13</td>
<td>4.4%</td>
</tr>
<tr>
<td>$175,000-$199,999</td>
<td>8</td>
<td>2.7%</td>
</tr>
<tr>
<td>$200,000+</td>
<td>23</td>
<td>7.7%</td>
</tr>
<tr>
<td>Prefer not to answer</td>
<td>39</td>
<td>13.1%</td>
</tr>
</tbody>
</table>

Much like with age, the sample represented a broad spectrum of income levels. Participants ranged from earning less than $10,000 per year to earning more than $200,000 per year. The largest income brackets were between $25,000 and $50,000 and between $50,000 and $75,000 and nearly two thirds of the sample earned less than $100,000 per year.

Table 4. Sample Characteristics: Race

<table>
<thead>
<tr>
<th>Race</th>
<th>N</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>White</td>
<td>259</td>
<td>86.9%</td>
</tr>
<tr>
<td>Black or African American</td>
<td>16</td>
<td>5.4%</td>
</tr>
<tr>
<td>Asian</td>
<td>12</td>
<td>4.0%</td>
</tr>
</tbody>
</table>
In terms of race, the sample consisted primarily of Caucasian participants (includes those of Hispanic ethnicity), who comprised approximately 87% of the sample. Most of the other 13% of participants were either African American or Asian. This indicates that the panel offered very limited racial diversity; the racial makeup of the sample is likely a by-product of the SurveyMonkey® user base.

Table 5. Sample Characteristics: Education

<table>
<thead>
<tr>
<th>Education Level</th>
<th>N</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Some high school but no diploma</td>
<td>5</td>
<td>1.7%</td>
</tr>
<tr>
<td>High school degree/GED</td>
<td>33</td>
<td>11.2%</td>
</tr>
<tr>
<td>Some college but no diploma</td>
<td>43</td>
<td>14.6%</td>
</tr>
<tr>
<td>Bachelor's degree</td>
<td>81</td>
<td>27.5%</td>
</tr>
<tr>
<td>Associate's degree</td>
<td>35</td>
<td>11.9%</td>
</tr>
<tr>
<td>Master's degree</td>
<td>68</td>
<td>23.1%</td>
</tr>
<tr>
<td>Professional degree (e.g., JD)</td>
<td>15</td>
<td>5.1%</td>
</tr>
<tr>
<td>Doctorate degree</td>
<td>15</td>
<td>5.1%</td>
</tr>
</tbody>
</table>
Education demographic information indicates that the vast majority of the sample has completed a college education, with approximately 75% in possession of a bachelor’s degree or higher. The distribution is approximately bimodal with the two largest groups being those with a Bachelor’s degree and those with a Master’s degree. This distribution indicates that the majority of the sample is well educated and could hypothetically have a more informed view of Alzheimer disease and the benefits and drawbacks of screening.

Table 6. Sample Characteristics: Relationship with Alzheimer disease

<table>
<thead>
<tr>
<th>Have a relative or close friend with Alzheimer disease</th>
<th>N</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>94</td>
<td>31.5%</td>
</tr>
<tr>
<td>No</td>
<td>204</td>
<td>68.5%</td>
</tr>
</tbody>
</table>

An important demographic consideration for this study was the proportion of the population who had a relative or close friend with Alzheimer disease. As described earlier, the TRA is predicated on using an individual’s attitudes and interpretation of subjective norms to explain a decision. Those with first-hand knowledge of the impacts of Alzheimer disease are likely predisposed towards a specific attitude and view of subjective norms surrounding screening of the disease. However, because there is no universal attitude or social norm that this experience could engender, there is reason to explore its interaction with desires to receive Alzheimer-related incidental findings. As such, approximately one third of the sample meets this criterion while two thirds have no relationship with someone with Alzheimer disease.
Descriptive Results

This section elucidates the descriptive results of the key variables measured in this study as described in Table 7: the attitude subscale, the subjective norms subscale, and the response variable. For the subscales, the descriptive statistics were calculated after summing the responses to each question and dividing by the number of items on the scale.

Table 7. Descriptive Statistics of Scales

<table>
<thead>
<tr>
<th>Scale</th>
<th>N</th>
<th>Min</th>
<th>Q1</th>
<th>Median</th>
<th>Mean</th>
<th>Q3</th>
<th>Max</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>AS</td>
<td>298</td>
<td>1.29</td>
<td>3.36</td>
<td>3.86</td>
<td>3.83</td>
<td>4.36</td>
<td>5</td>
<td>0.72</td>
</tr>
<tr>
<td>SNAS</td>
<td>298</td>
<td>1</td>
<td>2.1</td>
<td>2.6</td>
<td>2.613</td>
<td>3.1</td>
<td>5</td>
<td>0.76</td>
</tr>
<tr>
<td>Response Variable</td>
<td>298</td>
<td>1</td>
<td>4</td>
<td>6</td>
<td>5.091</td>
<td>7</td>
<td>7</td>
<td>2.13</td>
</tr>
</tbody>
</table>

The Attitude Subscale (AS) serves to assess a participant’s attitude towards genetic screening for Alzheimer disease. The scale consisted of 14 questions on a 5-point Likert-type scale from strongly disagree to strongly agree. The mean score across the scale was 3.83 and the median score was 3.857, indicating that most of responses were in the affirmative towards the statements regarding screening. Furthermore, the first quartile of the data set was 3.357 and the standard deviation 0.72, further indicators that most of the responses were favorable towards screening and that very few respondents had strongly negative attitudes towards screening. The items included in this subscale were items 2-9, 16-19, 21 and 23 (see Appendix B). Cronbach’s alpha for the AS was 0.91.

The Subjective Norms about Alzheimer Subscale (SNAS) serves to assess how a respondent believes important figures in his or her life feel about Alzheimer disease and screening. It consists of 10 questions on the same 5-point Likert-type scale as the AS. The mean
and median score for this scale were approximately 2.6 and the third quartile was 3.1, indicating that most respondents disagreed or were neutral with the statements regarding negative perceptions about Alzheimer disease. The items included in this subscale were items 10-15, 20, 22, 24-25 (see Appendix B). Cronbach’s alpha for the SNAS was 0.85.

The dependent variable for this study is the likelihood that an individual would request the disclosure of incidental findings from a hypothetical genetic test indicating a future Alzheimer disease diagnosis. To assess this, participants were asked this question at the end of the survey on a 7-point Likert-type scale measured from very unlikely to very likely. Of the 298 respondents, more than half responded that they would be more likely than not (5-7 on the scale) to request their incidental finding results. The mean response on the item was approximately 5 and the third quartile was 7, indicating that there was a significant portion of the sample (39.3%) that had strong feelings towards requesting the incidental findings. The standard deviation of 2.13 indicated a range of responses for the dependent variable, rather than homogeneity.

**Correlations Between Explanatory Variables**

Prior to evaluating the impact of the demographic variables on the subscales and all independent variables on the response variable, correlations between the independent variables were calculated as measured by Pearson’s correlation coefficient. Figure 2 presents a visual representation of the correlation matrix. Larger, light-shaded boxes represent stronger positive correlations; larger, dark-shaded boxes represent stronger negative correlations. Most of the independent variables show weak pairwise correlations with the other independent variables. Outside of race and ethnicity (.32), all correlation coefficients remain between -.2 and .2, indicating very little relationship; none of the correlations was statistically significant. This provides confidence for the validity of the results of the regression analysis (to be subsequently
discussed) as high-correlation coefficients can be indicators of multicollinearity in the data, a phenomenon in which multiple independent variables are related and explain the same variance in the data, providing a skewed interpretation of the significance and fit of a regression model. 

*Figure 2. Correlation Matrix*

![Correlation Matrix](image)

**Analyses of Variance in Subscales**

This section enumerates the results of the ANOVA estimations built to describe the influence of demographic factors on the two subscales. Prior to assessing the primary research question, the researcher felt it appropriate to analyze the key demographic drivers behind participants’ attitudes towards Alzheimer disease screening and their beliefs around subjective norms regarding Alzheimer disease screening.

To describe the relationship between the demographic variables and each of the two subscales (AS and SNAS), one-way ANOVA models were developed. The researcher employed the “leaps” package in R to automatically test each permutation of explanatory variables in order to arrive at the best fitting model. This procedure uses the Bayesian Information Criterion (BIC) value to identify the best fit. The BIC identifies the combination of variables that create the best fit.
model for the data. For each of the two analyses in the following tables, the model and therefore the variables included were those dictated by this procedure to be the best fit.

Table 8 displays the results of the ANOVA on the AS subscale for a regression model including household income, age, education level, presence of a relative or close friend with Alzheimer disease, and race as covariates. The data indicate that the two most impactful variables in predicting a participant’s score on the attitude subscale were household income and education level, both of which pointed in the negative direction. These variables had the highest sum of squares values and \( p \)-values below .05, indicating that both were statistically significant predictors. While it is possible that these two variables are both proxies for how well informed a participant is on the benefits of screening of Alzheimer’s and thus are significant predictors, more investigation would be needed to substantiate this hypothesis. The low Variance Inflation Factor (VIF) values across the model provide confidence in the validity of the results and allay any concerns of multicollinearity.

Table 8. ANOVA Table: AS

<table>
<thead>
<tr>
<th>Explanatory Variable</th>
<th>( SS^2 )</th>
<th>( F ) Value</th>
<th>( p )</th>
<th>VIF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Household income</td>
<td>378.4</td>
<td>3.9248</td>
<td>0.04854*</td>
<td>1.016941</td>
</tr>
<tr>
<td>Age</td>
<td>202.1</td>
<td>2.0959</td>
<td>0.14879</td>
<td>1.104243</td>
</tr>
<tr>
<td>Education level</td>
<td>430.3</td>
<td>4.4637</td>
<td>0.03549*</td>
<td>1.10726</td>
</tr>
<tr>
<td>Relative/Close friend with Alzheimer</td>
<td>232.8</td>
<td>2.4144</td>
<td>0.12133</td>
<td>1.048648</td>
</tr>
<tr>
<td>Race</td>
<td>343.0</td>
<td>3.5578</td>
<td>0.06028</td>
<td>1.050739</td>
</tr>
</tbody>
</table>

\* \( p < .05 \), two-tailed. \( SS^2 \) refers to the sum of squares value, where a higher value corresponds to more variance explained by the variable.
Table 9 displays the results of the ANOVA on the SNAS subscale for a regression model including the AS subscale, age, education level, presence of a relative or close friend with Alzheimer disease, and ethnicity as covariates. These variables were included as a result of the output of the automatic selection criteria used by the researcher as described above. Of these covariates, the most influential on the model fit was age, which had a sum of squares value of 108.9 and pointed in the negative direction (indicating that younger participants viewed screening more favorably). Unlike with the AS, there were no significant predictors of the SNAS subscale. VIF values remain low and multicollinearity was not observed in the model.

Table 9. ANOVA Table: SNAS

<table>
<thead>
<tr>
<th>Explanatory Variable</th>
<th>SS²</th>
<th>F Value</th>
<th>p</th>
<th>VIF</th>
</tr>
</thead>
<tbody>
<tr>
<td>AS</td>
<td>76.3</td>
<td>1.3366</td>
<td>0.2486</td>
<td>1.036273</td>
</tr>
<tr>
<td>Age</td>
<td>108.9</td>
<td>1.9063</td>
<td>0.1684</td>
<td>1.086417</td>
</tr>
<tr>
<td>Education level</td>
<td>31.9</td>
<td>.5579</td>
<td>0.4557</td>
<td>1.053086</td>
</tr>
<tr>
<td>Relative/Close friend with Alzheimer</td>
<td>58.7</td>
<td>1.0276</td>
<td>0.3116</td>
<td>1.119987</td>
</tr>
<tr>
<td>Ethnicity</td>
<td>33.8</td>
<td>0.5912</td>
<td>0.4426</td>
<td>1.026680</td>
</tr>
</tbody>
</table>

Research Question Results Through Ordinal Logistic Regression

This section describes the ordinal logistic regression model used to assess the predictors of participants’ LRIF related to Alzheimer disease risk. While linear regression was adequate to assess significant predictors of the subscales, it is insufficient for the dependent variable. In this study, the dependent variable is measured through a single, 7-point Likert-type scale item in
which unit increments are not inherently equal (i.e., the distance from 1 to 2 does not necessarily equal the distance from 4 to 5). As a result, the output of a traditional linear regression model, a continuous variable, would have little meaning. To account for this, ordinal logistic regression was run, a method that calculates coefficients of covariates as log odds. Unlike linear regression, the output of this model would be the probability of each of the 7 response options occurring, a better representation of the response variable.

Table 10 is a tabular representation of the results of the ordinal logistic regression model. The results provided the researcher with the information needed to address the primary research question of this study: *does the TRA predict LRIF related to Alzheimer disease risk?*

**Table 10. Ordinal Logistic Regression Results**

<table>
<thead>
<tr>
<th>Explanatory Variable</th>
<th>Coefficient</th>
<th>S.E.</th>
<th>t value</th>
<th>p</th>
<th>VIF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.0698</td>
<td>0.104</td>
<td>0.672</td>
<td>0.502</td>
<td>1.123</td>
</tr>
<tr>
<td>Gender</td>
<td>-0.0841</td>
<td>0.225</td>
<td>-0.374</td>
<td>0.708</td>
<td>1.013</td>
</tr>
<tr>
<td>AS</td>
<td>0.1423</td>
<td>0.014</td>
<td>10.241</td>
<td>0.000*</td>
<td>1.070</td>
</tr>
<tr>
<td>SNAS</td>
<td>-0.0418</td>
<td>0.016</td>
<td>-2.661</td>
<td>0.008*</td>
<td>1.018</td>
</tr>
<tr>
<td>Household Income</td>
<td>-0.0132</td>
<td>0.034</td>
<td>0.387</td>
<td>0.699</td>
<td>1.032</td>
</tr>
<tr>
<td>Relative/close friend with Alzheimer</td>
<td>0.0154</td>
<td>0.237</td>
<td>0.065</td>
<td>0.948</td>
<td>1.063</td>
</tr>
</tbody>
</table>

* p < .05, two-tailed; Note: SE= Standard Error

The model indicates that of the covariates included, the only significant predictors of a participant’s response to the item used to measure the dependent variable are the AS and the
SNAS. This is shown by each subscale’s \( p \) value, both of which fall below .01. The coefficients in the model represent increases in the expected value of the dependent variable on a log odds scale. Significant predictor AS has a coefficient of 0.1423, indicating that a 1-unit increase in AS would produce a 0.1423 increase in the expected value of the participants’ LRIF on a log odds scale. In other words, all else equal, for every 1 unit increase in AS, there is a 15% increase (\( e^{0.1423} = 1.15 \)) in the probability that a participant reported a higher LRIF than he or she would in the absence of this increase. In the case of the SNAS, every 1-unit increase yields a 4% decrease (\( e^{-0.0418} = 0.96 \)) in the probability that a participant reported a higher LRIF than he or she would in the absence of this increase. Given that these two subscales were the representations of the two elements of the TRA, namely the attitudes towards the subject and beliefs around subjective norms regarding the subject, the results support the hypothesis. Positive attitudes toward screening predicted increased LRIF, and negative subjective norms reduced the LRIF. Furthermore, the results provide no indication that any demographic trait of a participant nor his or her relationship with someone with Alzheimer disease is predictive of his or her LRIF. Discussion of these outcomes will be described in the following section.

**Summary**

The sample for this study included primarily white men and women of varying ages and income levels. The results of statistical analysis of the participants’ responses to the questionnaire can be summarized as below:

- The researcher identified weak pairwise correlations between independent variables.
- The researcher found two independent variables (household income and level of education) that were statistically significant predictors of participants’ attitudes toward Alzheimer disease and screening, as measured by one of the subscales.
• The researcher confirmed the hypothesis of the study: there was a predictive relationship between the tenets of the TRA (attitudes and subjective norms toward Alzheimer disease) and individuals’ LRIF.

These results provide researchers and clinicians with important information regarding individuals’ decision-making process with respect to Alzheimer disease and incidental findings. Further discussion of the findings and their implications for the field of nursing is in Chapter Five.
CHAPTER FIVE: DISCUSSION

Introduction

This study aimed to determine whether the TRA informs individuals’ willingness to seek the disclosure of incidental findings from genetic research that might link them to Alzheimer disease. It hypothesized that participants’ attitudes toward Alzheimer disease screening and perceptions about the social stigma of the disease would predict their intention to request incidental findings. The results of the study support this hypothesis: there was a statistically significant relationship among attitudes, subjective norms, and LRIF. The data also indicate that individuals’ household income and education levels inform their attitudes about Alzheimer disease screening. In this chapter, the researcher discusses the study’s results in the context of the literature, addresses study limitations, and identifies the study’s implications for nursing practice.

Sample Demographics

A sample of 298 participants responded to the questionnaire. Just over half (53%) of the participants reported their sex as female, and 47% reported their sex as male; they ranged in age, with 16% reporting that they were between 18 and 29 years old, 30% reporting that they were between 30 and 44 years old, 21% reporting that they were between 45 and 60 years old, with the remaining 33% reporting an age greater than 60.

In addition to age and gender, the researcher included education level, household income, race and ethnicity, and presence of an immediate family member or close friend diagnosed with Alzheimer disease as covariates. The sample primarily consisted of white participants (87%) with middle levels of income (more than 33% reported earning between $25,000 and $75,000 per year). A plurality of individuals reported a college degree as their highest level of education (27.5%), with a balance of participants reporting more advanced degrees than college degrees.
(approximately 33%) and less advanced degrees than college degrees (approximately 39%).

Perhaps a testament to the wide reach of Alzheimer disease, nearly one third (32%) of the sample reported having a relative or close friend diagnosed with Alzheimer disease.

The demographic diversity of the sample is particularly important in the context of this study because demographic variables were included as covariates, with an expectation from the researcher that participants of different backgrounds would form different attitudes or subjective norms toward Alzheimer disease. Though the sample of 298 participants included in this study demonstrated diversity in gender, household income, and education levels, the sample failed to yield racial diversity reflective of the overall United States population. According to the United States Census Bureau (2017), 76.6% of Americans reported their race as white and 13.4% reported their race as black or African American; in this sample, nearly 87% of participants reported their race as white and fewer than 6% reported as black or African American. This lack of racial diversity will be discussed further in the study limitations section below.

Demographics and the Attitudes and Subjective Norms Subscales

The results of the study indicate that two of the demographic variables were statistically significant predictors of participants’ beliefs about Alzheimer disease screening, as measured by the AS subscale: household income and education level. On the other hand, age, race, gender, and presence of a family member or friend with Alzheimer disease failed to predict beliefs about Alzheimer screening as measured by the AS. No demographic variables were statistically significant predictors of the subjective norms measured by the SNAS subscale.

\[1\]In both the Census and the present study, the percentages of individuals reporting their race as white are distinct from whether individuals reported their ethnicity as Hispanic.
Education Level

Numerous studies have demonstrated the importance of education toward reducing stigma and improving understanding of diseases and treatment. However, many of these studies have focused on education specific to the disease at hand rather than overall levels of schooling. For instance, Prince, Livingston, and Katona (2007) wrote, “…in the absence of understanding regarding its origins, dementia is stigmatized: for example, sufferers are specifically excluded from residential care, and often denied admission to hospital facilities” (p. 8). Though it speaks to the importance of education for reducing stigma, this statement does not directly address the finding from the present study that higher levels of overall education among participants weakly predicted lower scores on the AS (regarding attitudes toward Alzheimer screening).

It is somewhat counterintuitive that education level and attitudes toward Alzheimer screening were negatively correlated, though the correlation was weak. In a study of participants from Brazil, Blay and Peluso (2010) found that “those with fewer years of education were 2.32 times as likely to stigmatize persons carrying AD” (p. 163). This would seem to indicate a negative relationship between education and stigma, or a positive relationship between education and attitudes toward the disease. Additionally, recent research has demonstrated that individuals achieving higher levels of education may be less likely to test positive for Alzheimer than those with lower levels of education (Fowler, Perkins, Gao, Sachs, Uebelhor & Boustani, 2018). These results indicate that there is a link between education levels and Alzheimer disease—both in terms of testing results and societal stigma. Additionally, one would generally expect that individuals with greater levels of education might be more understanding of the value of scientific advancements in the treatment of Alzheimer disease. This was not directly borne out in the present study.
Household Income

Few studies have presented a direct link between household income and individuals’ attitudes toward dementia screening. However, there is evidence from areas of research outside of the dementia and Alzheimer realm suggesting that household income may affect individuals’ willingness to undergo medical screening. For instance, Garcia (2012) noted that “a low socioeconomic status has been associated with lower screening participation” with respect to colorectal cancer (p. 2). Additionally, with respect to Alzheimer disease, Sun, Hilgeman, Durkin, Allen and Burgio (2009) reported a link between household income and individuals’ perceptions of the financial strain that would accompany caring for a loved one with the disease. Specifically, the authors reported that household income was negatively correlated with “anxiety” around the financial burdens of caregiving (p. 6). On the basis of these two studies, one might expect that individuals with higher levels of income would have more favorable views toward Alzheimer screening. In the present study, however, the direction of the relationship was negative: individuals with higher income levels scored lower on the AS (though, as with education levels, the predictive strength was quite weak). It is possible that individuals with higher levels of income might be less concerned about what an Alzheimer disease screening could reveal and that higher income individuals may feel more prepared to handle the costs of the disease should screening reveal a likely future Alzheimer diagnosis. This perhaps may explain the finding in the present study that individuals with higher incomes scored lower on the AS – they found the prospect of regular testing and preparation for a possible diagnosis less important than those of lesser means who might need more time to prepare for the costs of treatment and care.
Age

The existing research regarding age and attitudes toward dementia screening have produced somewhat conflicting results. As noted in Chapter Three, Roberts et al. (2014) found that older individuals were less likely to desire information about their odds of acquiring Alzheimer disease, but that study focused on attitudes toward proactive screening rather than incidental findings. Conversely, Tang et al. (2017) found in online survey research that Americans older than 60 were significantly more likely to report an intention to be screened for Alzheimer disease than younger individuals.

With respect to subjective norms about Alzheimer and the stigma surrounding the disease, past studies have identified differences in opinion among individuals of different ages. According to Stites, Johnson, Harkins, Sankar, Xie, and Karlawish (2018), who studied Alzheimer stigma, “with each successive decade of age, adult respondents were less likely to believe others would feel supportive of a person with Alzheimer’s disease” and “Older respondents were also more likely to be concerned that a person with Alzheimer’s disease would be ignored or have his social interactions restricted by others” (p. 268). Ostergren, Heeringa, Mendes de Leon, Connell, and Roberts (2017) built a model to predict individuals “perceived threat” of Alzheimer disease and found that “Age was the only demographic characteristic that was significantly associated with perceived AD threat in the multivariate linear model” (p. 297). Specifically, cohorts of individuals aged 50-64 and 65-74 perceived the disease to be a greater threat to them than individuals over the age of 75; the authors speculate that individuals above 75, though at greater risk of developing the disease, may feel relieved that they lived so long without it (Ostergren et al., 2017).
On the basis of these studies, it is surprising that age did not significantly impact participants’ scores on the AS or SNAS in this study. One potential shortcoming of the data analysis method employed in this study was that it grouped all individuals age 60 and over as a single cohort, because the sample size of individuals older than 75 was extremely small ($n=11$). Earlier studies such as Roberts et al. (2014) have reported differences in individuals’ attitudes toward Alzheimer disease (and specifically their interest in learning about their own possible future diagnosis) depending on whether the individual was older or younger than 75. The present study may have benefitted from a larger sample specifically of older individuals in order to isolate any differences in the dependent variable present in this cohort.

**Race**

The literature also suggests there may be racial differences in individuals’ attitudes toward Alzheimer disease and dementia screening. One of the earliest studies on this topic, conducted by Roberts et al. (2003) reported, “We found race to be a more powerful variable than even family or caregiving history in explaining differences in illness perceptions” (p. 23). Gray, Jimenez, Cucciare, Tong and Gallagher-Thompson (2009) found that among caregivers for people with Alzheimer disease, Hispanic and Chinese American caregivers were more likely than white caregivers to believe that “AD is a normal part of aging” (p. 925). Akinleye et al. (2011) studied the differences among African American and White American attitudes toward and knowledge of Alzheimer screening and found a number of key differences, including less knowledge in the African American sample about AD. They reported that “African Americans are generally less concerned about the possibility of developing AD in comparison to their White counterparts” (p. 656), hypothesizing that African American communities may have familiarity instead with other diseases. Furthermore, Zhao, Elashoff, Kremen, Teng, Karlawish and Grill
(2017) reported that “African Americans were less likely to express a willingness to participate in AD prevention trials, than were whites, a finding that remained after adjusting for potential confounders such as knowledge about AD, perceived risk for AD, attitudes toward research, perceived cognitive decline, retirement status, and residential distance from the medical center” (p. 62).

In light of these findings, it is curious that the results of the present study failed to demonstrate any statistically significant differences among individuals of different racial or ethnic backgrounds with respect to both the AS and SNAS subscales. A likely explanation concerns the lack of diversity of the sample, nearly 87% of whom reported their race as white. It is possible that the study failed to observe any existing differences between African American and white respondents as a result of the relatively small number of African American respondents participating in the study.

Gender

Tang et al. (2017) reported that women were significantly more likely than men to be worried or very worried about a diagnosis of Alzheimer, and that women were also more likely to agree to undergo screening if they noticed a decline in their memory or cognitive function. With respect to subjective norms about Alzheimer, Stites et al. (2018) found that women were more likely to report the belief that others would express compassion and sympathy toward individuals with Alzheimer disease than men. No statistically significant differences were observed in this study between men’s and women’s attitudes or subjective norms toward Alzheimer, nor their LRIF. Further exploration would be necessary to more deeply understand the discrepancy between the results of this study and those of prior studies.
Family or Friend Connection to Alzheimer Disease

Participants’ connections to a friend or family member with Alzheimer disease did not significantly predict their attitudes toward the disease or screening. This is unexpected, given the results of numerous prior studies. For example, Boustani et al. (2011) found that individuals who served as caregivers to older adults with dementia reported less willingness to be screened for dementia and greater perceptions of suffering associated with screening. Similarly, as noted in Chapter Three, Roberts et al. (2014) reported that individuals who knew someone with Alzheimer were more likely to demonstrate an interest in receiving information about their own prospects for developing the disease. Ostergren et al. (2017) found that the effects of a personal connection to an individual with Alzheimer depend on the strength of the connection: people with first-degree family connections to Alzheimer perceived the disease to be more of a threat than did people with more distant connections. Given this result, one possible explanation for the lack of statistical significance found in the present study regarding the relationship between this variable and attitudes toward Alzheimer is that the questionnaire in the present study insufficiently identified participants with immediate family connections to the disease. By including “close friends” as a prompt, the questionnaire may have grouped together individuals with too diverse a connection to the disease, “watering down” any effects.

The Theory of Reasoned Action and Likelihood to Request Incidental Findings

The results of this study confirm the predictive nature of the TRA with respect to individuals’ intention to request hypothetical incidental findings linking them to Alzheimer disease. That is, participants’ attitudes toward Alzheimer screening and subjective norms regarding Alzheimer disease predicted their likelihood of requesting information that might indicate a future Alzheimer diagnosis. Let us consider each component of the theory in turn.
Numerous studies have demonstrated the link between attitudes toward dementia screening and individuals’ willingness to undergo screening. Martin et al. (2015) found that “the decision to screen is inextricably linked to the lack of ability to change dementia prognosis” – a fact that led participants to question the need for screening and express more negative attitudes toward the process (p. 12). Fowler, Perkins, Turchan, Frame, Monahan, Gao, and Boustani (2015) reported that “findings from this study corroborate previous results that have shown that people’s perceptions about the benefits of dementia screening are associated with their willingness to be screened” (p. 6). Specifically, participants who scored higher on the PRISM-PC subscale regarding the benefits of dementia screening were significantly less likely to refuse screening (Fowler et al., 2015b). In another study that employed the PRISM-PC instrument in order to gauge differences in attitudes toward dementia screening among people in the United States and United Kingdom, Justiss et al. (2009) concluded, “Low acceptance rates and high rates of perceived harms might be a significant barrier for the introduction of treatment or preventive methods for dementia in the future” (p. 632). In other words, negative attitudes toward the benefits of screening and a strong belief in the stigma surrounding dementia would serve as an impediment to a person undergoing screening. Though these studies have not generally focused on the specific concept of incidental findings, it is unsurprising that the results of the present study align directionally with the results of the prior research.

The finding that negative subjective norms about the disease were associated with less LRIF about Alzheimer disease is also consistent with results from prior, related research regarding dementia screening. Fowler et al. (2015a) also employed the PRISM-PC instrument and found that that “Patients' perceptions of the stigmas surrounding dementia and dementia screening were associated with the refusal of diagnostic assessment” (p. 239). In a similar vein,
Phillipson, Magee, Jones, Reis, and Skladzien (2015) applied elements of the PRISM-PC to survey Australian adult participants about their likelihood to seek help if they believed they were experiencing early stages of dementia. The authors reported that while most individuals indicated that they would seek assistance in such a scenario, 21% stated that they would delay seeking help. There were statistically significant relationships between participants’ views surrounding the stigma of dementia (e.g., the fear of being labeled by others) and their likelihood to report delaying treatment (Phillipson et al., 2015). It follows, then, that individuals in the present study who reported a greater sense of stigma regarding Alzheimer disease (as measured by the SNAS) would be less likely to request the disclosure of incidental findings that might link them to the disease.

**Study Limitations and Suggestions for Further Research**

Though the results of the study demonstrated a predictive link between the TRA and participants’ intention to request information about incidental findings connecting them to Alzheimer disease, the study’s design limits the generalizability of the results in three principal ways.

First, the participants included in the sample were not literally participating in a genetic study; they were asked to imagine a hypothetical scenario in which they were volunteers for such a study and that incidental findings regarding their own genetics might be available. It is possible that participants’ responses to the survey questions, particularly their willingness to request disclosure of incidental findings, would differ more in a real-life lab setting than a hypothetical one. It follows that an opportunity for future study would include a similar questionnaire regarding incidental findings and Alzheimer disease administered to a sample of individuals participating in true genetic research to assess whether their responses would differ from those of
individuals participating hypothetically. That said, such an in-lab setting could also introduce bias: individuals who agreed to participate in a genetic study might be predisposed to believe in the power of genetic testing and treatment of disease.

Second, the sample recruited via SurveyMonkey® included predominantly individuals identifying as white; the sample lacked racial and ethnic diversity. Differences in awareness about Alzheimer treatment among African Americans, Hispanic Americans, and white Americans identified by Roberts et al. (2014) may not have appeared in the results of this study on the basis of sample composition. Furthermore, Wright (2005) noted that “self-selection bias” is a limitation of online sampling: certain individuals “are more likely than others to complete an online survey…leading to a systematic bias” (p. 7). The results of this study must be considered with this in mind. Future studies should consider different avenues for participant recruitment to increase the diversity of the sample.

Third, the study focused exclusively on Alzheimer disease. It is possible that individuals’ attitudes and beliefs about social stigma regarding other diseases would produce different results. Consequently, one should not generalize the findings regarding the TRA and incidental findings beyond Alzheimer disease; future research could consider participants’ views toward other chronic diseases to determine where differences exist in intention to request the disclosure of incidental findings.

**Implications for Nursing**

The role of nurses in caring for individuals with Alzheimer and dementia will grow as the population ages (Digby, Williams & Lee, 2016). This includes not only the direct care for already-diagnosed individuals but also the responsibility to inform and guide people who may be identified through genetic testing as future Alzheimer patients. As Digby et al. (2016) note,
“dementia adds complexity to the nurse-patient relationship in hospital and requires specialized understanding in order to enable quality care to be delivered” (p. 57).

Research has demonstrated that nurse-led education programs for healthcare staff can increase professionals’ knowledge about dementia and approach to caring for affected patients (Wang, Xiao, Ullah, He & De Bellis, 2017). A patient-centered approach that carefully considers the perspective of patients and families is important to the success of such programs (Justiss et al., 2009). Indeed, as Justiss et al. (2009) wrote, “understanding the risks and benefits of early identification from the perspective of patients is one of the most important pieces of information needed to improve the process of early identification” (p. 636).

In addition to the genetic-testing training programs developed for nurses and discussed in Chapter Three, the results of the present study represent an important component of the knowledge base that nurses must develop to serve as effective caregivers to those actually or potentially diagnosed with Alzheimer. Understanding patients’ attitudes toward the disease, concerns about screening, and beliefs about the societal stigma of Alzheimer is crucial for communicating with patients about the disease. The findings of this study indicate that efforts to reduce the stigma surrounding Alzheimer disease and to emphasize the benefits of screening may be useful in encouraging individuals to seek—rather than avoid obtaining—information regarding their own likelihood of developing the disease. As Halverson et al. (2016) noted, participants undergoing genomic sequencing and testing have reported feeling “empowered over their own health” (p. 147). Nurses have and will play an important role in facilitating this empowerment.
Summary

This study sought to determine whether the TRA explained participants’ willingness to receive hypothetical incidental findings from a genetic study linking them to Alzheimer disease. The key components of the theory as applied in this study were participants’ attitudes toward Alzheimer disease and screening, and participants’ subjective norms about Alzheimer disease. Two demographic variables were found to be statistically significant predictors of participants’ attitudes toward Alzheimer disease: household income and level of education. Despite indications in previous research that other demographic factors, such as race, age, and gender might predict differences in participants’ attitudes toward Alzheimer, no such evidence was found in this study. Beyond the demographic factors, the central hypothesis of this study was confirmed: attitudes and subjective norms toward Alzheimer (the components of the TRA) were statistically significant predictors of participants’ intention to request disclosure of incidental findings. The results of this study, while limited, provide important insight for nurses working in both the research and clinical fields regarding how to approach discussions of incidental findings and Alzheimer disease with patients and research participants.
References


dementia and intention to be screened: An analysis of national survey data. *Archives of Gerontology and Geriatrics*, 71, 43-49.


Appendix A.

Permission to use PRISM instrument

Alix Forrest: alexfors@huntsman.med.utoronto.ca

To: mstoumang@hsn.edu

Dear Dr. Stoumang,

I am a nursing PhD student at Molloy College in New York currently preparing my dissertation proposal. I plan to study the role of the Theory of Reasoned Action in explaining the decisions of genetic research participants to receive or reject reports of ‘incidental findings’ discovered in a study. For example, genetic research studies may discover that a participant has genetic links to Alzheimer’s Disease, but in that finding is incidental to the aim of the study, an ethical dilemma results in which the researcher must decide whether to inform the participant. I intend to study the role of the TRA in explaining participants’ own choices to receive this information.

I recently read your 2006 study, "Measuring Primary Care Patients’ Attitudes About Dementia Screening," and was wondering whether it might be possible for me to adopt your Theory of Planned Behavior survey instrument for use in my dissertation study, with full attribution.

Sincerely yours,

Alix M. Forrest RN MPS PhD Candidate

Mstoumang, Walea J: mstoumang@hsn.edu

To: Alix Forrest <alexfors@huntsman.med.utoronto.ca>

Dear Alix,

More than happy for you to use our survey.

Walea

(Disregard text below)
Appendix B.

Survey Instrument

Thank you for participating in this study. As you may know, in recent years, genetic researchers have made great advances in their understanding of diseases like Alzheimer disease. Below you will find a series of questions and prompts designed to assess your opinions toward Alzheimer disease and genetic testing. Toward the end of the survey, you will have an opportunity to answer a few questions about your background, and whether you would be interested in receiving information about incidental findings if you were hypothetically participating in genetic testing. “Incidental findings” are findings from testing that were not the aim of the test but may provide information regarding your likelihood of developing certain diseases, such as Alzheimer disease. Please choose one answer to each of the following questions.

By clicking on the “accept” button below you are indicating that you consent to participate in this study.

Consent to participate in the survey:

1. I agree to participate in this study. I understand that Molloy College’s Institutional Review Board (IRB), whose members are responsible for the protection of human subjects’ rights for all Molloy-approved research protocols, have the right to review study records, but confidentiality will be maintained as allowed by law. □ Accept □ Decline

Please indicate whether you agree or disagree with the following statements:

2. I would like to know if I am at higher risk than others for developing Alzheimer disease.

□ Strongly agree □ Agree □ I don’t know □ Disagree □ Strongly disagree

3. I would like to know if I have Alzheimer disease.

□ Strongly agree □ Agree □ I don’t know □ Disagree □ Strongly disagree

4. I would like to be tested for the presence of Alzheimer disease on a regular basis with a short questionnaire.

□ Strongly agree □ Agree □ I don’t know □ Disagree □ Strongly disagree
5. I would like to be tested for the presence of Alzheimer disease on a regular basis with a blood sample.

□ Strongly agree □ Agree □ I don’t know □ Disagree □ Strongly disagree

6. I would like to be tested for the presence of Alzheimer disease on a regular basis with pictures of my head or brain (CT-scan or MRI).

□ Strongly agree □ Agree □ I don’t know □ Disagree □ Strongly disagree

7. I would like a doctor to examine me every year to know if I have developed Alzheimer disease.

□ Strongly agree □ Agree □ I don’t know □ Disagree □ Strongly disagree

8. I believe that early detection of Alzheimer disease increases the chance to treat the disease better.

□ Strongly agree □ Agree □ I don’t know □ Disagree □ Strongly disagree

9. If I knew that I had Alzheimer disease earlier, my family would have a better chance to take care of me.

□ Strongly agree □ Agree □ I don’t know □ Disagree □ Strongly disagree

10. If I had Alzheimer disease, I would not want my family to know.

□ Strongly agree □ Agree □ I don’t know □ Disagree □ Strongly disagree

11. If I had Alzheimer disease, I would feel humiliated by my family members and/or others who would treat me poorly or laugh at me.

□ Strongly agree □ Agree □ I don’t know □ Disagree □ Strongly disagree

12. If I had Alzheimer disease, I would no longer be taken seriously.

□ Strongly agree □ Agree □ I don’t know □ Disagree □ Strongly disagree

13. If I had Alzheimer disease, I would be considered stupid and unable to do things.

□ Strongly agree □ Agree □ I don’t know □ Disagree □ Strongly disagree

14. If I knew that I had Alzheimer disease, I would be ashamed or embarrassed.

□ Strongly agree □ Agree □ I don’t know □ Disagree □ Strongly disagree
15. If I knew that I had Alzheimer disease, I would give up on life.

☐ Strongly agree  ☐ Agree  ☐ I don’t know  ☐ Disagree  ☐ Strongly disagree

16. If I found out early that I had Alzheimer disease, I would have more time to plan my future.

☐ Strongly agree  ☐ Agree  ☐ I don’t know  ☐ Disagree  ☐ Strongly disagree

17. If I found out early that I had Alzheimer disease, I would have more time to talk with my family about my health care.

☐ Strongly agree  ☐ Agree  ☐ I don’t know  ☐ Disagree  ☐ Strongly disagree

18. If I found out early that I had Alzheimer disease, I would have more time to talk with my family about my finances.

☐ Strongly agree  ☐ Agree  ☐ I don’t know  ☐ Disagree  ☐ Strongly disagree

19. If I found out early that I had Alzheimer disease, I would sign my advance directive or my living-will.

☐ Strongly agree  ☐ Agree  ☐ I don’t know  ☐ Disagree  ☐ Strongly disagree

20. If I had Alzheimer disease, my doctor would not provide the best care for my other medical problems.

☐ Strongly agree  ☐ Agree  ☐ I don’t know  ☐ Disagree  ☐ Strongly disagree

21. If I knew that I had Alzheimer disease earlier, I would be motivated to have a healthier lifestyle.

☐ Strongly agree  ☐ Agree  ☐ I don’t know  ☐ Disagree  ☐ Strongly disagree

22. If I had Alzheimer disease, my doctor and other health professionals would not listen to me.

☐ Strongly agree  ☐ Agree  ☐ I don’t know  ☐ Disagree  ☐ Strongly disagree

23. If I knew that I had Alzheimer disease earlier, I would be more willing to participate in research about this disease.

☐ Strongly agree  ☐ Agree  ☐ I don’t know  ☐ Disagree  ☐ Strongly disagree

24. If I had Alzheimer disease, I would be concerned that my health insurance company would find out.

☐ Strongly agree  ☐ Agree  ☐ I don’t know  ☐ Disagree  ☐ Strongly disagree
25. If I had Alzheimer disease, I would be concerned that my employer would find out.

☐ Strongly agree ☐ Agree ☐ I don’t know ☐ Disagree ☐ Strongly disagree

26. Imagine you were undergoing genetic testing for something other than Alzheimer disease. You could be participating in a genetic research project, or perhaps, you ordered a popular home genetic testing kit. How likely would you be to request the results of any incidental findings related to your risk for Alzheimer disease that resulted from your test? (Please circle):

1  2  3  4  5  6  7

Very unlikely                                       Very likely

27. What is your gender?

☐ Male ☐ Female ☐ Other

28. How old are you? ___

29. What is the highest level of education you have completed?

☐ Some high school but no diploma ☐ High school degree / GED

☐ Some college but no diploma ☐ Associate’s degree

☐ Bachelor’s degree ☐ Master’s degree

☐ Professional degree (e.g., JD) ☐ Doctorate degree

30. Ethnicity (select one):

☐ Hispanic or Latino ☐ Not Hispanic or Latino

31. Race (select all that apply):

☐ American Indian or Alaska Native ☐ Asian ☐ Black or African American

☐ Native Hawaiian or other Pacific Islander ☐ White

32. Do you have a parent, child, sibling, spouse, or a close friend who was diagnosed with Alzheimer disease?

☐ Yes ☐ No
Appendix C.

CONSENT

Dear Prospective Research Participant:

My name is Alisa Forrest and I am a PhD student in Nursing at Molloy College. I am studying “incidental findings” from genetic research.

As defined by the National Institutes of Health, incidental findings are “apparent medical abnormalities that may have clinical implications and are observed in the course of research studies but are unrelated to the topic under study.” Examples might include:

- A study involving fractionation of normal human blood suggests a potential infection;
- A baseline study of mental status indicates a psychiatric condition;
- A screening protocol for an exercise intervention identifies a cardiac insufficiency;
- A brain imaging study of depressed individuals reveals a potential structural abnormality (see https://humansubjects.nih.gov/from-applicants for more information).

I am interested in surveying individuals about their opinions toward such incidental findings for a hypothetical genetic research study. I would like to invite you to participate in the survey for my research. The survey asks questions about hypothetical research findings regarding your risk for developing Alzheimer disease, and whether you would want to receive such information if available to you. No genetic testing is required in this study; it is hypothetical in nature. I estimate that participation will take up to 15 minutes of your time.
By clicking on the “accept” button below you are indicating that you consent to participate in this study. Please print out a copy of this consent form for your records. To ensure that this research activity is being conducted properly, Molloy College’s Institutional Review Board (IRB), whose members are responsible for the protection of human subjects’ rights for all Molloy-approved research protocols, have the right to review study records, but confidentiality will be maintained as allowed by law. However, because of the nature of web-based surveys, it is possible that respondents could be identified by the IP address or other electronic record associated with the response. Neither the researcher nor anyone involved with this survey will be capturing those data. Any reports or publications based on this research will use only group data and will not identify you or any individual as being affiliated with this project.

Should you have follow up questions regarding the study or like to receive results of the study after it is completed, please email me at the address below. Additionally, if you have any concerns or questions regarding this research study and the protection of human subject rights, you may contact the Molloy IRB at irb@molloy.edu or call 516-323-3000. Thank you in advance for your participation.

Alisa M. Forrest, MS RN

AForrest1@lions.molloy.edu
Appendix D.

Institutional Review Board Approval

Date: May 14, 2018
To: Alisa Forrest
From: Kathleen Maurer Smith, Ph.D.
       Co-Chair, Molloy College Institutional Review Board
       Patricia Eckardt, Ph.D., RN
       Co-Chair, Molloy College Institutional Review Board

SUBJECT: MOLLOY IRB REVIEW AND DETERMINATION OF EXEMPT STATUS
Study Title: Does the Theory of Reasoned Action Inform the Willingness of Individuals Undergoing Genetic Testing to Seek Disclosure of Incidental Findings Related to the Risk for Alzheimer Disease?

Approved: May 14, 2018
Approval No: 01061518-0514

Dear Alisa:

The institutional Review Board (IRB) of Molloy College has reviewed the above-mentioned research proposal and determined that this proposal is approved by the committee. It is considered an EXEMPT review per the requirements of Department of Health and Human Services (DHHS) regulations for the protection of human subjects as defined in 45CFR 46.101(b)(2) and has met the conditions for conducting the research. Please note that as Principal Investigator (PI), it is your responsibility to be CITI Certified and submit the evidence in order to conduct your research.

You may proceed with your research. Please submit a report to the committee at the conclusion of your project.

Changes to the Research: It is the responsibility of the Principal Investigator to inform the Molloy College IRB of any changes to this research. A change in the research may change the project from EXEMPT status that would require communication with the IRB.

Sincerely,

Kathleen Maurer Smith
Kathleen Maurer Smith, Ph.D.

Patricia Eckardt, Ph.D., RN