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An Online Vignette Study to Examine the Outcomes of a Preclinical Alzheimer Disease Diagnosis

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Dedicated to my mother. I know you would be proud.

ABSTRACT OF THE DISSERTATION

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by

Matthew J. Wynn

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Professor Brian D. Carpenter, Chairperson

As Alzheimer disease research forges ahead, and new potential treatments are developed, a conceptualization is emerging of a presymptomatic disease stage. This stage, known as preclinical Alzheimer disease, is characterized by the buildup of amyloid beta and tau proteins in the brain to abnormal levels in a cognitively normal person. There are unknown potential risks and benefits of communicating biological marker risk information for Alzheimer disease using the preclinical Alzheimer disease diagnostic label. The current study uses a vignette methodology to measure older adults' understanding of risk information when presented with information regarding their risk for developing Alzheimer dementia. Participants (n = 300) were randomized to receive biomarker results and risk information (with or without the preclinical disease label) pertaining either to heart disease or Alzheimer disease. Participants then reported on their individual perceptions, based on the Health Belief Model, and declared their behavioral intentions in response to this information. Results support the idea that the addition of a preclinical Alzheimer disease label does not influence perception of the disease or behavioral intentions. Results also highlight differences in individual perceptions of Alzheimer disease versus heart disease such that participants in the Alzheimer disease conditions perceived their

risk information as implying a more severe condition, perceived fewer benefits to knowing their risk, and reported lower self-efficacy about doing anything to address that risk. Despite these perceptions, older adults who received risk information for Alzheimer disease maintained interest in undertaking behavioral changes that may improve their quality-of-life. These findings have implications for the development of empirically supported disclosure processes for preclinical Alzheimer disease.

Chapter 1: Introduction

Alzheimer disease is a progressive neurological condition that affects approximately 6 million adults in the United States (Alzheimer's Association, 2019). This number is expected to escalate rapidly as a large portion of the American population reaches age 65 and older. By 2050, the prevalence of Alzheimer disease is expected to triple without the development of an effective disease-modifying treatment. Over the past five years, some researchers have begun to expand the conceptualization of Alzheimer disease to include a preclinical stage (known as preclinical Alzheimer disease), which is characterized by the buildup of amyloid beta and tau proteins in the brain to abnormal levels (Jack et al., 2018). The preclinical stage of Alzheimer disease is thought to be asymptomatic, with the biological indicators suggesting disease, even in the absence of the measurable cognitive or behavioral changes. These biological abnormalities are detectable via neuroimaging (e.g., positron emission tomography (PET)) or cerebrospinal fluid (CSF) up to a decade or more before clinical symptoms appear (Sperling et al., 2011). Efforts to refine these biological measurements, or biomarkers, are critical in a new wave of clinical trials focused on testing potential disease-modifying treatments at the earliest, preclinical, asymptomatic stages of the disease. These trials will require enrollment of many individuals who have evidence of the biological changes of Alzheimer disease but do not have symptoms – that is, a large number of individuals who have preclinical Alzheimer disease (Cummings, 2019). As interest regarding the opportunities represented by the expanded conceptualization of Alzheimer disease has built, so too have feelings of hesitation regarding what the preclinical Alzheimer disease label may represent, as well as concern regarding the possibility for misunderstanding that label by patients and by the general population (Chiong et al., 2021; Molinuevo et al., 2016; Schermer & Richard, 2019).

Alzheimer disease is one of the most feared diseases (Caselli et al., 2014), and there is worry that diagnosis of disease, in the absence of symptoms, with an unclear timeline of progression, could lead to despair or distress (Grill, Johnson, & Burns, 2013; Sperling, Karlawish, & Johnson, 2013). However, pursuing an evaluation for Alzheimer risk factors, such as genetic markers or amyloid status, even before symptoms appear, may help people plan for the future, engage in adaptive behaviors, and adjust psychologically to the prospect of potential future symptoms (Smith & Beattie, 2001; Werner, Karnieli-Miller, & Eidelman, 2013). While preclinical Alzheimer disease is not yet a label given to patients outside of research settings, biomarker status is currently being communicated to patients in research and clinical trials, though there has been little research to date on disclosure of that label. Healthcare providers must prepare for how to communicate information about preclinical Alzheimer disease safely and effectively (Largent et al., 2020; Mozersky et al., 2018; Rabinovici et al., 2016). Thus, research is needed to examine perceptions of a preclinical Alzheimer disease diagnosis and how these perceptions interact with a person's knowledge, experience, and motivation to act on this risk information.

I begin with a brief review of terminology, as definitions for many of the terms I will use have shifted over time. Following that, I will define preclinical Alzheimer disease, describe how the designation came to be used in research, and explore the potential consequences of a preclinical Alzheimer disease diagnosis. Finally, I will review an existing theory of health behavior to develop hypotheses regarding potential reactions to a diagnosis of preclinical Alzheimer disease.

1.1 The Shifting Classification of Alzheimer Disease

Alzheimer disease has been characterized as a "dual clinical-pathologic" disease (Elahi & Miller, 2017). Clinically, Alzheimer disease is diagnosed through detailed interviews, histories, and neuropsychological assessment, focused on cognitive and behavioral changes. In contrast, pathologically, Alzheimer disease is definitively diagnosed at autopsy by examining amyloid and tau in brain structures (Jack et al., 2018; McKhann et al., 2011). Advances in both our knowledge and technological capabilities have led researchers and clinicians to rethink the traditional clinical-pathologic picture and to revise diagnostic and staging criteria to incorporate both clinical and pathologic features that enable a more precise characterization of Alzheimer disease (Dubois et al., 2016; Jack et al., 2018; McKhann et al., 2011).

A 2011 National Institute on Aging (NIA-AA) work group devised a set of diagnostic criteria for Alzheimer disease focused in part on incorporating a burgeoning knowledge about biomarkers (McKhann et al., 2011). In that framework, dementia due to Alzheimer disease was fundamentally a clinical diagnosis, and while biomarker results could increase the certainty that Alzheimer pathology was the basis for clinical symptoms, only the core clinical features were required for a diagnosis of Alzheimer disease (McKhann et al., 2011). Eight years later, the workgroup reconvened in light of empirical evidence that certain biomarkers are valid proxies for neuropathologic changes of Alzheimer disease previously only measured at autopsy (Jack et al., 2018). In a substantial reconfiguration of diagnostic criteria – at this point to be used in research only – the term "Alzheimer *disease*" (emphasis added) refers to an aggregation of neuropathologic changes indicated by biomarkers and by postmortem examination, not by clinical symptoms (Jack et al., 2018). The authors of the revised 2018 research criteria sought to

make clear a distinction between Alzheimer pathology and clinical Alzheimer symptoms (see Table 1).

In order to be consistent with the current conceptualization, I will use the term Alzheimer dementia to refer to clinical symptoms, such as memory loss, problem solving difficulties, and functional impairment caused by Alzheimer pathology. Alzheimer pathology refers to amyloid, tau, and neurodegeneration, as measured by biomarkers (Jack et al., 2018), and Alzheimer disease refers to the disease state implied by Alzheimer pathology that exceeds some threshold. Details on these distinctions in nomenclature appear below.

1.1.1 Alzheimer Dementia

This term describes a clinical state characterized by cognitive impairment, usually involving memory. The 2011 NIA-AA workgroup characterized impairment at two levels, mild cognitive impairment (MCI) and dementia (Albert et al., 2011; McKhann et al., 2011). The workgroup also addressed people who are asymptomatic, described as "cognitively unimpaired" and having "subjective cognitive impairment," and these subtle differences may reflect different stages of progression between total cognitive health and MCI (Sperling et al., 2011). The current study focuses on people who are asymptomatic and do not meet criteria for MCI or Alzheimer dementia yet possess evidence of underlying Alzheimer pathology.

1.1.2 Alzheimer Pathology

Alzheimer pathology is classified using the A/T/N descriptive classification scheme, which recognizes three general classes of biomarkers (A = amyloid; T = tau; N = neurodegeneration; see Table 1) and refer to separate pathologic processes (Jack et al., 2016). In studies from the Mayo clinic with cognitively normal participants, A/T/N results appear to confer additional predictive utility of future memory performance beyond clinical markers alone (Jack

et al., 2019). The current study focuses on people who receive results concerning their Alzheimer pathology but do not exhibit the clinical symptoms of Alzheimer dementia.

1.1.3 Alzheimer Disease

Alzheimer disease is a label in limbo, as research findings begin to be translated to the clinic. In research, Alzheimer disease is present when individuals have elevated amyloid and tau levels (Jack et al., 2018), whereas in clinic, Alzheimer disease is a diagnosis defined by cognitive impairment (McKhann et al., 2011). Advancements in testing and staging guidelines have introduced nuances and shifts in the way researchers think about Alzheimer disease from a syndrome to a strictly biological construct. This shift complicates our ability to describe an already complicated disease process consistently and concisely to an individual and their family. Although this shift is not yet part of routine clinical care, disclosure of Alzheimer pathology information is occurring currently in observational and interventional research. It is unclear what effect, if any, this dual representation may have on how a person understands a diagnostic label that does not imply the presence of clinical symptoms yet signifies an "at-risk" disease state. The current study focuses on the effect of receiving information suggesting that a person has Alzheimer pathology without Alzheimer dementia, that is, that they have preclinical Alzheimer disease.

1.1.4 Preclinical Alzheimer Disease

Preclinical Alzheimer disease is the newest term to join the nomenclature. Preclinical Alzheimer disease is a research diagnosis used to refer to a person who shows an elevated biomarker profile but is cognitively unimpaired according to objective assessment. Preclinical Alzheimer disease is an "at-risk" state, meaning that it signifies the presence of an amyloid and tau burden, risk factors that are associated with an increased chance of developing Alzheimer

dementia (i.e., developing clinical symptoms). However, as an at-risk state, some individuals who have Alzheimer pathology will develop dementia symptoms and some will not. For instance, among older adults from the Alzheimer's Disease Neuroimaging Initiative (ADNI) cohort, persons with elevations in baseline biomarker levels were twice as likely to develop symptoms consistent with mild cognitive impairment over 4 years compared to those without elevated biomarkers (Donohue et al., 2017). Another analysis of ADNI data from cognitively unimpaired individuals found that amyloid beta positive participants, on average, declined in general cognition (-1 to -1.5 standard deviations), delayed list recall (-1 standard deviations), and executive function consistent (-0.5 standard deviations) and their scores on a cognitive composite measure were consistent with MCI by six years after baseline (Insel et al., 2019). Finally, a recent meta-analysis of 36 studies estimated the overall prevalence of preclinical Alzheimer disease among cognitively unimpaired participants at 22% [95% CI = 18%, 26%]. They estimated a 20% [95% CI = 10%, 34%] risk of progression for those with preclinical Alzheimer disease without any evidence or complaint of cognitive impairment, 38% [95% CI = 21%, 59%] risk for those with subjective complaints only, and 73% [95% CI = 40%, 92%] risk for people with subtle cognitive decline that does not meet criteria for mild cognitive impairment (Parnetti et al., 2019).

What this research suggests is that having Alzheimer pathology is a risk factor for Alzheimer dementia. However, a diagnosis of preclinical Alzheimer disease comes with uncertainty about whether an individual will ever develop cognitive impairment (i.e., progress to Alzheimer dementia). At this time, the diagnosis of preclinical Alzheimer disease is only used in research, but we need to know how the risk information implied by this ambiguous diagnostic label is understood by patients and their care partners. Previous evidence from both research and

clinical settings where people are told their Alzheimer pathology test results may provide a window into this question.

1.2 Disclosure of Alzheimer Risk Information

Alzheimer risk information is currently disclosed to people in both clinical and research settings, and results from studies of disclosure provide information on how people understand, appraise, and apply that information. Aspects of this prior research are relevant to the use and impact of the new preclinical Alzheimer disease label. In the section that follows I review results from studies in which information regarding apolipoprotein E (*APOE)* gene status was provided to individuals without dementia. Then I turn to results from the Anti-Amyloid Treatment in Asymptomatic Alzheimer's Disease (A4) study, which explored disclosure of Alzheimer pathology, via amyloid PET scan results, to cognitively unimpaired individuals.

1.2.1 Risk Evaluation and Education for Alzheimer's Disease

A major source of information regarding how people understand risk information for Alzheimer disease comes from the Risk Evaluation and Education for Alzheimer's Disease (REVEAL) trial, a series of studies examining the impact of disclosing *APOE* status to first-degree relatives of individuals diagnosed with Alzheimer disease (Roberts, Cupples, Relkin, Whitehouse, & Green, 2005). While REVEAL centered on genetic risk factors, not amyloid and tau, the trial's focus on participants receiving Alzheimer disease risk information in the absence of clinical symptoms makes it a useful parallel for the disclosure process for preclinical Alzheimer disease. An early REVEAL study investigated the effect of different methods of presenting risk information on knowledge and recall of risk estimates (Eckert et al., 2006). First, genetic counselors provided education on the general prevalence of Alzheimer disease, an overview of genetic principles, the principle of lifetime risk estimates, and information about the

APOE gene and risk for developing Alzheimer disease. Following this in-person session, each participant received three pieces of risk information: their lifetime risk estimate, their *APOE* genotype, and whether they carry the e4 allele that conveys additional risk for developing Alzheimer disease. Recall after six weeks was worse for the lifetime risk estimate (59% of participants recalled the estimate within a 5% range) compared to recollection of *APOE* genotype (69% recalled correctly, from multiple choice). However, even among participants who recalled information accurately, some still misinterpreted their risk estimate. For example, one year following education and disclosure, 76% of participants correctly recalled how many copies of the e4 allele they had, but only 62% of participants correctly identified which form of the *APOE* susceptibility gene conveys increased risk for developing Alzheimer disease, meaning that a subsample of participants correctly recalled their risk information but could not accurately interpret the meaning of that information.

A more recent systematic review included 13 studies from the REVEAL research program examining psychological and behavioral effects of genetic risk information disclosure (Bemelmans et al., 2016). Across studies, participants who received information indicating their increased risk of Alzheimer disease were no more likely than participants in the control group to report increased symptoms of depression or anxiety. Participants who were informed about a positive *APOE* e4 status reported significantly higher test-related distress, but also reported adaptive health-related behavior change. At one-year follow up, participants who were told they were *APOE* e4 positive were more likely to report adaptive behavior changes (e.g., purchasing long-term care insurance, adopting healthy lifestyle habits) than participants who were told they were *APOE* e4 negative (52% versus 24%, adjusted odds ratios 2.73) and participants in the control group (52% versus 30%, adjusted odds ratios 1.5) (Chao et al., 2008).

1.2.2 Anti-Amyloid Treatment in Asymptomatic Alzheimer's Disease

The Anti-Amyloid Treatment in Asymptomatic Alzheimer's Disease study (A4; Sperling et al., 2014) was a randomized clinical trial conducted with cognitively unimpaired older adults who had PET scan evidence of increased amyloid. The trial, designed to explore whether anti-amyloid treatments could slow amyloid accumulation and/or cognitive decline, also explored how individuals reacted to receiving the news of their positive scan through an affiliated study, The Study of Knowledge and Reactions to Amyloid Testing (SOKRATES). Researchers interviewed participants over the telephone in order to understand their experience following a standardized disclosure of an amyloid PET scan result (Harkins et al., 2015). In interviews with 50 cognitively normal participants following disclosure, a majority (64%) of participants used the word "amyloid" to describe their results, and a similar majority (62%) understood that this correlated with an increased but uncertain risk of developing Alzheimer disease (Mozersky et al., 2018). However, 32% misunderstood their risk, including both over- and underestimation of their risk for developing Alzheimer disease. Importantly, 40% expressed dissatisfaction with the lack of specificity of their results and requested more information to understand them.

Another SOKRATES study utilized semi-structured interviews to examine emotional and behavioral changes as a result of disclosure within the same cohort (Largent et al., 2020). Approximately one third reported that receiving their result was "validating" to their worries regarding their subjective memory complaints (though they had no objective memory impairments). However, for another third, receiving an elevated amyloid result "amplified" their worry regarding their memory and caused them to question whether potentially age-normative decline was instead due to disease-related amyloid. Furthermore, participants had heterogeneous thoughts and feelings about the future. Some described their future as bleak (24%), slightly more

felt it was bright (28%), and the majority (54%) acknowledged it was unknown. The majority of participants also reported that receiving an amyloid PET scan result was unlike receiving results from other medical tests. Participants spoke of the stigma associated with Alzheimer disease and the fear of a "brain disease" as opposed to losing their hearing, vision, or having a more routine chronic medical condition. Finally, compared to participants who were told their amyloid levels were not elevated, people who were told their levels were elevated were more likely to report intended changes in health behaviors (e.g., exercise, cognitive enrichment) (67% versus 76%) and in future plans (e.g., increasing leisure time, financial planning, medico-legal planning) (43% versus 72%) (Largent et al., 2020), though no longitudinal data were collected on actual follow through on those intentions.

In an exploration of psychological outcomes in a larger A4 sample, 1167 participants with elevated amyloid results were surveyed using validated measures of depression (Geriatric Depression Scale), anxiety (State-Trait Anxiety Inventory), suicidality (Columbia Suicide Severity Rating Scale), and concern regarding Alzheimer disease (Concerns About AD Scale). Disclosure of elevated amyloid status was not associated with short-term adverse psychological reactions on any of these measures compared to participants who were told amyloid was not elevated (Grill et al., 2020).

Taken together, the REVEAL and SOKRATES studies illustrate four points. First and foremost, they demonstrate that cognitively unimpaired individuals are being told their amyloid status in research settings and that researchers agree on the importance of studying outcomes of Alzheimer risk disclosure. Second, it appears that recall and comprehension of Alzheimer risk information is variable, and some people misunderstand their risk status, even when it is shared with them in controlled research settings. Third, emotional reactions to risk information appear

to be relatively mild, at least on average. And fourth, information about risk can influence behavioral intentions, both for specific health-related behaviors and for future planning. At this moment, however, it is unclear how individuals may react if a label of preclinical Alzheimer disease is attached to their Alzheimer dementia risk information and by what mechanism researchers and clinicians may be able to promote positive outcomes of disclosure.

1.2.3 Outcomes of Disclosure of Alzheimer Risk Information

One may argue that the most important factor in determining whether to disclose health information is whether it is deemed "actionable" (Wolf et al., 2013). Therefore, critics of preclinical Alzheimer disease disclosure cite low clinical utility, since medical or pharmacologic interventions based on Alzheimer disease biomarkers have not been available historically, with one very recent and controversial exception, aducanumab. However, other actions after receiving personal risk information are possible, such as accessing support groups, planning for the future, or engaging in lifestyle changes intended to reduce risk (Largent et al., 2020). These behavioral changes represent one way for someone in an at-risk state to take action despite their uncertain prognosis. What remains unclear is what factors may motivate someone toward behavior change in response to their risk information. One potential framework for understanding the impact of a diagnostic label of preclinical Alzheimer disease is the Health Belief Model (HBM; Janz & Becker, 1984).

1.3 The Health Belief Model

The Health Belief Model (Janz & Becker, 1984; see Figure 1) describes why people engage in health behaviors (e.g., preventative measures, screenings, and interventions) by framing these behaviors in terms of perceptions and knowledge regarding illness and health. At the center of the model are individual perceptions about an illness, such as perceptions of risk,

severity, and the ability to handle illness-related consequences. Those perceptions are themselves influenced by modifying factors, including personal and contextual characteristics such as demographic characteristics and knowledge regarding disease, and cues to action, such as diagnostic information. Altogether, these forces influence actual or intended actions that a person might take either to reduce their risk or adapt to consequences of the disease. Applied to preclinical Alzheimer disease, the HBM is a useful way of conceptualizing the individual differences that potentially drive the psychological and behavioral reactions to learning the results of assessments (or even wanting an assessment or those results). The current study seeks to investigate the influence of a specific cue to action, receiving the diagnostic label of preclinical Alzheimer disease, on individual perceptions and behavioral intentions, while taking into account relevant modifying factors. Next, I review the components of the HBM in more detail and describe potential applications to preclinical Alzheimer disease disclosure.

1.3.1 Individual Perceptions

Beginning with the central constructs of the HBM in the middle of Figure 1, individual perceptions refer to a wide-ranging set of beliefs that people hold in regard to their illness and health. Even when given the same health information, people may have different beliefs about their individual risk, disease severity, and self-efficacy in relation to the disease, and these beliefs combine to form an overall perceived threat of the disease, which interacts with perceived benefits and barriers to influence action. Benefits and barriers refer to an individual's perception regarding the positive health and non-health related consequences of pursuing actions to reduce disease threat, as well as potential obstacles or negative aspects of a particular health action (Champion & Skinner, 2008). Put simply, if individuals regard themselves as susceptible to a condition, believe the condition would have serious consequences, believe that a course of

available action would be beneficial, and believe that those benefits outweigh the barriers, then they are likely to take that action.

1.3.2 Modifying Factors

A number of sociodemographic characteristics are thought to influence perceptions of risk and disease and, indirectly, health-related behaviors. Included in this category are age, sex, gender identity, race/ethnicity, socioeconomic status, education, health literacy, personal experience with the health condition, and knowledge regarding the health condition (Champion & Skinner, 2008). Modifying factors, as their name suggests, are thought to influence a person's perceptions. For example, a person may underestimate the severity of a disease due to their personal experience with a relative who had a mild form of the disease. Similarly, a person may misperceive the benefits and barriers of a course of action due to a lack of education or low health literacy.

1.3.3 Cues to Action

Cues to action are behavior-triggering events in the body (a cough, a lapse in memory) or environment (reading a brochure, having a conversation with a physician) that may potentiate action. Cues to action are wide ranging in potential content and conscious impact and are thought to instigate action by prompting self-evaluation of one's individual perceptions of risk, severity, self-efficacy, barriers, and benefits (Champion & Skinner, 2008). For example, a diagnostic label can serve as a cue to action by bringing to mind one's beliefs regarding how likely they are to develop the symptoms of the disease and what the consequences would be.

1.3.4 The Health Belief Model and Preclinical Alzheimer Disease

Most previous studies of Alzheimer risk information that have investigated concepts in the HBM have focused on a single pathway or a few constructs as opposed to testing a full model

(Champion & Skinner, 2008). For example, REVEAL studies have shown that predisclosure knowledge and experience with Alzheimer disease are related to perceived risk of developing Alzheimer disease (Rostamzadeh et al., 2020). In addition, REVEAL studies have illustrated that cues to action in the form of *APOE* information changed perceived risk, and increased perceived risk is associated with increased depressive and anxiety symptoms (Ashida et al., 2010). Another study in the dementia realm found that a social cue to action (encouragement from a spouse) prompted older adults' intention to seek cognitive testing in response to vignettes describing themselves with memory loss and a family history of dementia (Werner & Heinik, 2003). Finally, results from the A4 study indicate that individuals who received an elevated amyloid result reported a change in their concern regarding developing dementia on the Concerns About AD scale (Grill et al., 2020). Given this suggestive literature, the present study conceptualizes a preclinical Alzheimer disease diagnosis and related dementia risk information as cues to action and seeks to investigate the influence of these cues on perceptions of risk, as well as their subsequent influence on behavioral intentions.

1.4 Current Study

The current study uses an HBM framework to investigate the effect of a preclinical Alzheimer disease label on cognitive, psychosocial, and behavioral outcomes. Participants read vignettes that communicated hypothetical information regarding their status in a preclinical state of Alzheimer disease based on fictional biomarker test results that suggest they are at risk of developing Alzheimer dementia in the future. In a "preclinical Alzheimer disease" condition, participants were told they meet criteria for preclinical Alzheimer disease and given a numeric risk estimate for disease progression. In a "numeric risk" condition, participants were given a numeric risk estimate for Alzheimer disease progression, but not the

preclinical disease label. In order to investigate changes in perceived risk due to stigma of the cue rather than type or number of cues participants receive, one group of participants received information regarding a different preclinical disease, preclinical heart disease. Participants in this group served as a reference condition, similarly split into receiving either a "preclinical disease label" or "numeric risk only." Heart disease was chosen as a reference condition due to previous research that found that heart disease and Alzheimer disease were the two most feared diseases for older adults but differed in their perceptions of severity and control such that heart disease was generally perceived as less severe and having more available treatment options than Alzheimer disease (Boeldt et al., 2015). Participants were then asked a series of questions exploring their understanding of the results, their individual perceptions of disease, and their intentions to pursue several behaviors. The first aim focuses on exploring how these variables (understanding, perceptions, intentions) change as a function of the type of disease information participants see. The second aim focuses on the relationships between cues to action, individual perceptions, and behavioral intentions, while the third aim analyzes the role of modifying factors, such as disease type, in influencing these relationships.

Aim 1: Document the impact of disclosing risk information pertaining to preclinical Alzheimer disease versus preclinical heart disease on recall of health information, components of perceived threat, and behavioral intentions.

Hypothesis 1.A. The HBM acknowledges a potential moderating effect of factors such as type of disease. Thus, half of participants will receive information regarding preclinical heart disease, and the other half will receive information about Alzheimer disease. Heart disease was chosen as a comparison condition based on previous findings that it is feared by older adults and is associated with variable perceptions regarding risk, severity, barriers, benefits, and self-

efficacy (Boeldt et al., 2015). I hypothesize that participants in the heart disease condition will report lower levels of perceived risk, lower levels of perceived severity, and higher levels of self-efficacy compared to participants in the Alzheimer disease conditions.

Hypothesis 1.B. Both diseases will be presented in the same way, with the same information regarding diagnosis and risk estimate. Therefore, I predict no differences in recall between the disease conditions.

Hypothesis 1.C. Given the increased access to pharmacological and lifestyle interventions for heart disease, I predict higher behavioral intentions in response to heart disease information than Alzheimer disease information.

Aim 2: Investigate the effect of diagnostic label on perceived threat of dementia and on intentions to pursue adaptive behaviors.

Hypothesis 2.A. The HBM predicts that cues to action influence perceptions of subjective threat by triggering self-evaluation of what the disease represents. The specific words "Alzheimer disease" likely carry stigma and fear, leading to greater perceived threat when they are presented to participants. Therefore, I hypothesize a main effect of risk information condition, such that participants who receive a diagnostic label of preclinical Alzheimer disease will report greater perceived threat (higher perceived risk and perceived severity, and lower self-efficacy) than participants who receive a numeric risk alone. Given that the risk information conditions do not convey information regarding potential actions the person may undertake in response to this information, I hypothesize there will be no difference across conditions in terms of perceived barriers and benefits.

Hypothesis 2.B. The HBM predicts that people who perceive greater threat for developing a disease are more likely to engage in behavior modification. Therefore, I hypothesize that

participants who report higher perceived threat (that is, higher perceived risk, higher perceived severity, and lower self-efficacy) for developing dementia will report more intentions to pursue adaptive behavior changes. Following from Hypothesis 2.A, compared to participants in the numeric risk condition, participants in the preclinical Alzheimer disease condition will experience the highest perceived threat for dementia and will, in turn, report an intention to make the most behavioral changes.

Aim 3: Explore the effects of modifying factors on the influence of cues to action on individual perceptions, and of individual perceptions on behavioral intentions.

Hypothesis 3.A. The HBM acknowledges a potential moderating effect of factors such as demographic characteristics, knowledge of disease, experience with disease, and type of disease. Exploratory post-hoc cross-sectional analyses will be used on demographic and contextual variables of interest, based on initial results, within an HBM context in order to inform future studies and provide context for how Alzheimer disease may or may not fit into this framework compared to other medical diseases, such as heart disease.

Chapter 2: Method

2.1 Participants

Data collection for this study occurred online. Participant recruitment targeted adults aged 50 or older via two sources. One sample (n = 150) was recruited using Amazon Mechanical Turk (MTurk), an online tool for data collection that has been shown to yield reliable data, while the second sample (n = 150) consisted of community dwelling older adults, recruited from the St. Louis area using a psychology department subject pool. The participant age range was chosen in order to include individuals most likely to have risks about dementia communicated to them and most likely to be the targets of future interventions for preclinical Alzheimer disease

(Alzheimer's Association, 2019; Cummings, 2019). In order to maximize comprehension of study materials, other inclusion criteria included individuals who self-reported English fluency, completion of at least eight years of education, and no self-reported memory or thinking problems. Of the 635 individuals who agreed to participate in the study, 335 were ineligible and excluded from the final sample. Of those excluded, 41 (12.2%) self-reported memory problems, 49 (14.6%) self-reported age below 50 years, and 29 (8.7%) self-reported that they were not fluent in English. Furthermore, 117 (34.9%) were excluded due to incomplete (i.e., less than 20% complete) or inappropriate survey responses (e.g., copy and pasted or nonsensical free-response answers), and 99 (30%) were excluded due to attempts to access the survey more than once.

Regarding the MTurk subsample, evidence from survey and interactive experiments focused on psychological and behavioral research questions suggest that MTurk respondents produce results that are as valid and reliable as that of people in laboratory experiments (Amir & Rand, 2012; Casler et al., 2013; Horton, Rand & Zeckhauser, 2011; Mullinix, Leeper, Druckman, & Freese, 2015; Rand, 2012; Shapiro, Chandler, & Mueller, 2013; Thomas & Clifford, 2017). In addition, a review of studies that utilized MTurk workers concluded that MTurk is a reliable and valid tool for studying a variety of health and medical issues, although results may not be generalizable to the US population, a concern that is mirrored elsewhere in the literature (Mortensen & Hughes, 2017; Walters, Christakis, & Wright, 2018). Cross-sectional studies comparing national samples and MTurk workers generally find that MTurk workers tend to be healthier (e.g., lower rates of depression and smoking, better general health) (Walters, Christakis, & Wright, 2018; Yank et al., 2017).

2.2 Materials

This study presented participants with hypothetical vignettes and asked them to imagine themselves receiving disease risk information. This approach mirrored contemporary web-based health communication approaches that have been shown to be effective at increasing knowledge and supporting positive change in health behaviors (e.g., Rogers et al., 2017). Vignette studies are widely used in medical and dementia research in order to gauge participant, caregiver, and provider reactions to situations that are either logistically difficult or unethical to capture in the laboratory or clinic (Randhawa, Jiwa, & Oremus, 2015). The authors of one recent scoping review of clinical vignettes in Alzheimer disease research (Randhawa, Jiwa, & Oremus, 2015) offered several recommendations for development and use of Alzheimer disease vignettes that were incorporated into the current study. These include writing the vignette from the second person and utilizing expert consultation in the development of vignettes.

The present study was developed using expert consultation from the Washington University Alzheimer Disease Research Center. Researchers at that center currently studying disclosure of test results with healthy older adults shared their materials and worked with the author to adapt those materials into the current study vignette materials. Following vignette design best practices, participants were asked to imagine they are in the position of the person described, and second-person pronouns were used. After an introduction, participants were led through a four-step vignette designed to simulate disclosure of risk information regarding either Alzheimer dementia or heart disease (see Appendix A).

In Step 1, participants were asked to imagine that they had enrolled in a research study regarding either dementia or heart disease. Embedded audio guided them through the rest of Step 1 as a hypothetical research assistant asked them questions regarding their demographics, current

behaviors, and memory and thinking. They were administered an auditory list-learning task and engaged in a hypothetical "brain scan" where they saw an image of the inside of an MRI machine and heard embedded audio of a scanner. In Step 2, participants were shown graphics and heard embedded audio that described their baseline risk of disease. Based on consultation with experts from the Knight Alzheimer Disease Research Center, baseline risk was communicated as 5% baseline risk of disease and 25% risk after a positive amyloid test result in order to both mirror real-world possibilities and simulate post-disclosure conditions. In Step 3, participants saw a summary of their abnormal biomarker findings. In vignettes describing heart disease, participants received identical risk estimates based on biomarkers related to heart disease in place of amyloid and tau test results. In Step 4, participants were again shown graphics and heard embedded audio that described an estimate of their new risk for developing either Alzheimer dementia or heart disease, informed by their recent elevated biomarker results. This disclosure graphic was manipulated by condition. In the preclinical Alzheimer disease/preclinical heart disease condition, participants were told they met criteria for a preclinical state of disease and given a numeric risk estimate for disease progression (Altomare et al., 2019). In the numeric risk condition, participants were given the numeric risk estimate for disease progression based on biomarker test results, but the specific preclinical label was not provided.

2.3 Measures (see Appendix B)

2.3.1 Demographics

Information regarding participant age, sex, gender identity, education, race, and ethnicity were collected as part of the preliminary screening questions. This information was used to compare the demographics of the MTurk sample versus the departmental subject pool sample.

2.3.2 Memory

Participants engaged in a 16-item list-learning task adopted from the Dominantly Inherited Alzheimer Network (DIAN) study materials (Moulder et al., 2013). The 16-item list was presented visually in the middle of the screen as well as auditorily. The items in the list were matched to have relatively similar frequencies, concreteness, and length. Previous work (Storandt et al., 2014) within the DIAN cohort found that cognitively normal, older adult participants (e.g., those with CDR scores of 0) were able to recall approximately six words from the list immediately following presentation and approximately three words from the list after a short delay. Total scores on this measure were calculated as the total number of correct words recalled immediately following list presentation and after a short delay. This delay time varied slightly by participant, due to individual differences in answering intermediate questions but was approximately 10 minutes (M = 10.1 minutes, SD = 2.5 minutes, range = 8.2 – 14.4 minutes). Given the main aim of the study was to examine receiving a dementia diagnosis in the *absence* of memory issues, it was important that the sample be cognitively normal. This variable was included as an objective measure, supplementing the subjective screening question, to ensure study participants were cognitively normal.

2.3.3 Personality

Participants also completed the MINI-IPIP in order to assess their personality according to Big Five personality traits (Donnellan, Oswald, Baird, & Lucas, 2006). Participants rated how well each statement describes them on a scale from 1 (*strongly disagree)* to 5 *(strongly agree*). All five personality traits were assessed using four-item scales. Total scores for each trait were calculated by summing scores on the four individual items. Previous research has shown that neuroticism, in particular, may play a role in whether people are vigilant and focused on their

health (Weston & Jackson, 2018) and therefore neuroticism is included in analyses as a covariate. In previous studies the internal consistency reliability for this subscale was reported as .68 (Donnellan, Oswald, Baird, & Lucas, 2006), and in the current sample it was .65.

2.3.4 Prior Disease Experience

Participants in the Alzheimer condition provided a brief history of their experience with dementia by answering questions developed in a previous study (Kinzer & Suhr, 2016). These questions were adapted to capture experience with heart disease for participants in the heart disease condition. Participants indicated whether they know or have known someone with dementia and, if so, the nature of their relationship with that person (i.e., how frequently they see/saw them, how emotionally close they feel/felt to them, how related to them they are/were genetically). Participants also reported whether they had served as caregivers for family or friends with dementia. Based on a previous study, experience was coded as genetic (having a first or second-degree relative with the disease), nongenetic (any other personal exposure to the disease, including caregiving for a nonbiological relative), or no personal exposure to the disease. Previous research indicated that prior personal experience with Alzheimer disease is related to increased perceived threat of Alzheimer disease (Suhr & Kinkela, 2007) and therefore is included in analysis as a covariate.

2.3.5 Knowledge of Disease

Knowledge of disease was measured using one of two questionnaires, depending on disease condition. The Alzheimer's Disease Knowledge Scale (ADKS; Carpenter et al., 2009) is a 30-item, true/false questionnaire designed to measure a person's basic knowledge regarding Alzheimer disease symptoms, course, progression, and treatment. The original validation study reported adequate psychometric properties (e.g., coefficient alpha = 0.71), and the scale has been

used with many additional samples of older adults without cognitive impairment (e.g., community dwelling older adults). The Heart Disease Knowledge Questionnaire (Bergman et al., 2011) is a 30-item, true/false questionnaire designed to measure a person's basic knowledge regarding heart disease symptoms, epidemiology, risk factors, and treatment. The original validation study established adequate psychometric properties (coefficient alpha = 0.73) and was shown to be reliable in a sample including older adults (mean age = 57 years, range = 40 – 79). Both scales include questions regarding knowledge of risk factors, severity, and treatments and are directly associated with the study outcome variables of interest. Therefore, knowledge of disease is included in analysis as a covariate. Participants were given the knowledge scale corresponding to the disease in their study condition, and analyses using knowledge as a covariate treat scores from the Alzheimer Disease Knowledge Scale and the Heart Disease Knowledge Questionnaire as a unitary construct, disease knowledge.

2.3.6 Recall and Understanding of Risk Information

To check whether the experimental manipulations were successful in conveying disease and risk information, participants were asked what their test results indicated about dementia or heart disease, depending on the experimental condition. Participants were first asked to identify the disease label and numeric risk they had received via a multiple-choice question. Following this, participants explained what they understood or took away from the information by answering free-response questions. Answers to multiple-choice questions were utilized to identify whether participants correctly recalled their disease label and numeric risk. Participants were categorized as either correctly recalling both the disease label and numeric risk, correctly recalling one of the two pieces of information, or failing to recall correctly either disease label or numeric risk information. Free-response answers were used to exclude participants who engaged

in inappropriate data-response practices such as copy and pasting paragraphs from common Alzheimer or heart disease websites (e.g., Alzheimer's Association website, American Heart Association website) that suggested insufficient engagement with the experimental tasks.

2.3.7 Individual Perceptions

The individual perceptions described by the HBM were measured using selected portions of the Motivation to Change Lifestyle and Health Behaviors for Dementia Risk Reduction Scale (MCLHB-DRR; Kim, Sargent-Cox, Cherbuin, & Anstey, 2014), a 27-item scale that includes questions designed to measure all aspects of the HBM model. Questions regarding perceived risk (4 questions), perceived severity (5 questions), perceived benefits (4 questions), perceived barriers (4 questions), and self-efficacy (2 questions) were responded to using a 5-point Likert scale (1 = *strongly disagree* to 5 = *strongly agree*). Overall scores for each subscale were calculated by adding the scores to the individual questions. The original validation study demonstrated acceptable reliability for the scale overall and subscales (coefficient alphas ranged from .65 to .86) and similar reliability when tested in community samples of cognitively unimpaired older adults (aged 50 to 96). Participants also answered a one-item question regarding their current level of anxiety ("I feel anxious, upset, or worried").

2.3.8 Current Behaviors and Behavioral Intentions

Participants indicated current behavioral engagement prior to exposure to the risk information and biomarker test results. Following exposure to the vignette, participants indicated which behaviors they intend to change. The list of behaviors included health behaviors, leisure pursuits, financial planning, medico-legal planning, living arrangement changes, and employment changes, and was based on previous studies that examined behavioral intentions following disclosure of amyloid PET results (Largent et al., 2020) and dementia risk (Merz,

Wynn, & Carpenter 2017). Scores on this measure were the total number of behaviors currently engaged in, as well as the total number of behaviors intended following disclosure.

2.4 Study Design & Procedure

This study used a 2 x 2 between-subjects design that presented participants with different disease risk information within an online Qualtrics (Qualtrics, Provo, UT) survey. The study was posted to Amazon Mechanical Turk (MTurk) where interested participants accessed the study materials via a link to a Qualtrics survey. Department subject pool participants were called on the telephone to gauge interest before being sent a link to the Qualtrics survey via e-mail. Participants first answered the screening and demographic questions which served to assess eligibility and then gather basic information about the participant. Eligible participants were then randomized into either the Alzheimer disease or heart disease condition and completed pre-disclosure measures. After completion of the pre-disclosure measures, participants were assigned to one of two disclosure conditions using block randomization as they progressed through the four-step process described above, with materials presented in Appendix A. Immediately following the disclosure process, participants responded to the recall and understanding questions before completing the post-disclosure measures. At this point, their study participation was complete and participants were paid $5.00 for their participation.

2.5 Data Analysis

Two quality control questions designed to detect highly unmotivated or programmed ("bot") MTurk workers (and department subject pool participants) were included as part of the screening measures. One question required participants to type their answer to a previous question, while the other required participants to give the name for a common vegetable in response to a picture (see Screening Items #11 and #12 in Appendix B). In addition, final survey

responses were checked for completion and problematic response patterns, such as guessing or random responses. Participants were dropped from analysis when their survey completion was faster or slower than the mean completion time by three standard deviations or more. Patterns of missing data were reviewed for random responses, and free-response data were used to detect copy and paste responses. Chi-square tests were used to compare MTurk and department subject pool participants for any demographic or contextual differences as well as to compare recall scores between risk information disclosure conditions. Descriptive statistics were calculated in order to characterize the sample and test assumptions for planned analyses. Specifically, univariate and multivariate outliers, normal distribution of residuals, homogeneity of variance, and homoscedasticity were checked as appropriate prior to performing all statistical analyses and all relevant assumptions were met for each analysis reported below. The HBM describes perceived risk, perceived severity, and self-efficacy as belonging to a single, underlying construct of perceived threat, and a correlation matrix was reviewed in order to determine whether analyses involving individual perceptions should treat those variables as one unitary construct or as three separable constructs.

Following these initial analyses, analyses of covariances (ANCOVAs) were used to examine the effect of disease condition on 1) post-vignette behavioral intentions and 2) components of the HBM, with age, pre-vignette behaviors, disease knowledge, disease experience, and neuroticism as covariates (Aim 1). Following this, a conditional process analysis model (i.e., a moderated mediation model) was used to evaluate Aims 2 and 3. These analyses were undertaken using the PROCESS macro in SPSS (Hayes, 2018) to analyze the direct effect of label condition on individual perceptions (Aim 2), the direct and mediated effects of label condition on behavioral intention, mediated by individual perceptions (Aim 2), and the

moderating effects of disease condition on the effects outlined in the previous aims (Aim 3). Additional post-hoc models will be used following initial analyses to explore other demographic and contextual variables of interest as potential modifying factors that can guide future research.

Research in related areas has shown small to medium effect sizes for education and disclosure group differences in knowledge and mental health outcomes (Johnson et al., 2015; Roberts et al., 2012). Conservatively hypothesizing a small (i.e., 0.2) effect size for both paths in the mediation model, taking into account the need to power the model for interaction and moderated mediation effects, and referencing available literature regarding sample sizes for conditional process analysis (Fritz & MacKinnon, 2007; Hayes, 2017), the estimated sample size necessary to achieve a power of 0.8 was approximately 200 participants.

Chapter 3: Results

In the following sections I first review characteristics of participants and note differences between the MTurk participants and subject pool participants. Next, I describe outcome variables, beginning with the manipulation check before reviewing results from ANOVA analyses describing differences in individual perceptions and behavioral intentions based on disease condition. Finally, I review the PROCESS models for each component of perceived threat and their associations with behavioral intentions.

3.1 Participant Characteristics

The final sample was composed of 300 individuals (47.2% of the total who initiated the survey) who were eligible and completed all study measures. The pool of 300 individuals was randomized so half (n = 150) the individuals received information regarding Alzheimer disease and the other half (n = 150) received information regarding heart disease. Participants were further randomized into disclosure conditions such that one quarter (n = 75) participants were in

each cell of the 2x2 design described above. Demographic and contextual information for the total sample and both subsamples are summarized in Table 2.

Summarizing characteristics and comparisons across subsamples, the majority of participants were cis-gender female (63%), wide ranging in their age (M = 64.1, SD = 7.41, range = 50-89), mostly white (89%), non-Hispanic or Latino (96.3%), and highly educated (37.7% completed college). In addition, the majority of participants were in good health (77.4% good or very good) and denied current memory or thinking concerns (84.3% denied, 15.7% unsure). The MTurk workers were significantly younger than the subject pool participants, $t(298) = 3.385$, $p < .001$, mean difference = 3.02 years. There were no differences between the two samples in sex assigned at birth ($\chi^2(1, N = 300) = .007$, $p = .933$), race ($\chi^2(8, N = 300) = 8.04$, $p = .429$), ethnicity ($\chi^2(1, N = 300) = .755$, $p = .385$), or education level ($\chi^2(4, N = 300) = 7.38$, $p = .123$). There were also no differences between samples in self-reported memory issues ($\chi^2(1, N = 300) = 1.526$, $p = .217$) or health ($\chi^2(4, N = 300) = 4.857$, $p = .302$). MTurk participants reported less neuroticism than subject pool participants ($t(298) = 2.485$, $p = .013$, mean difference = .665), however the difference was small (i.e., less than the value of endorsing one additional item on the scale) and unlikely to be clinically meaningful.

Participants, on average, were able to recall about half of the words immediately after presentation in the list learning task (M = 8.35, SD = 3.16, range = 1-16) and recalled most of what they learned after approximately a 10-minute delay (M = 7.11, SD = 3.29, range = 0-16). This is consistent with the performance of cognitively normal participants on the same task as part of the DIAN study (Storandt et al., 2014). There were no differences between MTurk workers and subject pool participants in terms of their immediate ($t(298) = -.749$, $p = .454$, mean

difference = -.290 words recalled) or delayed recall performance ($t(298) = .161$, $p = .872$, mean difference = 0.065 words recalled).

Participants in both conditions were moderately knowledgeable about Alzheimer and heart disease, averaging scores of approximately 22 out of 30 ($M_{AD} = 22.40$, $SD_{AD} = 4.88$; $M_{HD} = 22.27$, $SD_{HD} = 4.43$). There was not a difference between MTurk workers and subject pool participants in terms of their heart disease knowledge ($t(148) = .400$, $p = .690$, mean difference = .280) or their Alzheimer disease knowledge ($t(148) = .279$, $p = .780$, mean difference = .200). Participants also had similar experience with disease ($\chi^2(2, N = 300) = 3.287$, $p = .193$), as 43.3% (37.3% in Alzheimer disease, 49.3% in heart disease) had known a genetic relative with the disease, 24% (27.3% in Alzheimer disease, 20.6% in heart disease) had a non-genetic connection to the disease (e.g., non-genetic relative or friend), and 32.6% (35.3% in Alzheimer disease, 30% in heart disease) had no personal experience with the disease.

Prior to exposure to the vignette, participants indicated their current behaviors. On average, participants listed approximately 10 behaviors in which they were currently engaged ($M = 10.32$, $SD = 3.73$, range = 1-26). The most commonly endorsed behaviors were Health Behaviors ($M = 3.35$, $SD = 1.49$, range = 0-8) and Leisure Time Activities ($M = 2.78$, $SD = 1.32$, range = 0-6), while Financial Planning ($M = 1.60$, $SD = .929$, range = 0-5) and Employment ($M = 1.12$, $SD = .959$, range = 0-6) activities were less commonly endorsed, and Living Arrangements ($M = 0.87$, $SD = .641$, range = 0-3) and Medical and Legal Planning ($M = 0.61$, $SD = .876$, range = 0-4) were uncommonly endorsed. Subject pool participants endorsed significantly more Leisure Time Activities than MTurk workers ($t(298) = 1.791$, $p < .001$, mean difference = .540), however no other significant differences were noted between the two groups in terms of their current behaviors.

In summary, participants recruited from MTurk were slightly younger, slightly less neurotic, and engaged in slightly fewer leisure activities but appeared adequately matched on all other characteristics. While there is reason for caution regarding generalizability of an MTurk sample (Mortensen & Hughes, 2017; Walters, Christakis, & Wright, 2018), comparisons between the MTurk sample and the subject pool sample revealed minimal differences and generally support combining them into a single sample for the remainder of analyses.

Demographic and contextual variables were also analyzed across the four study conditions in order to ensure that randomization procedures were successful in minimizing the effects of pre-existing differences in demographic and contextual variables among participants. Descriptive statistics for these variables across the four study conditions appear in Table 3. Chi-square analysis indicated no differences across conditions in terms of sex assigned at birth ($\chi^2(3, N = 300) = 7.02$, $p = .07$), race ($\chi^2(24, N = 300) = 25.09$, $p = .401$), ethnicity ($\chi^2(3, N = 300) = 3.30$, $p = .347$), or education level ($\chi^2(12, N = 300) = 6.03$, $p = .915$). There were also no differences between conditions in self-reported memory issues ($\chi^2(3, N = 300) = 3.911$, $p = .271$), health ($\chi^2(12, N = 300) = 14.40$, $p = .28$), or experience with disease ($\chi^2(6, N = 300) = 6.30$, $p = .390$).

ANOVA results indicated no interaction effect between label and condition for age ($F(1,296) = .01$, $p = .932$), and there was not a significant main effect of label ($p = .74$) or disease ($p = .90$) on age. There was no interaction effect between label and disease for pre-disclosure behaviors ($F(1,296) = 3.11$, $p = .07$), and there was not a significant main effect of label ($p = .15$) or disease ($p = .59$) on pre-disclosure behaviors. Objective memory, measured by immediate and delayed recall scores, also did not significantly differ across the four conditions. There was no observed interaction effect between label and condition for immediate recall ($F(1,$

296) = .776, p = .38) or for delayed recall (F(1,296) = .543, p = .46) and there were no significant main effects of label (p = .06) or disease (p = .71) on immediate recall nor of label (p = .12) or disease (p = .70) on delayed recall. Knowledge of disease was not associated with a significant main effect of label (p = .10) or disease (p = .80) and there was no evidence for an interaction between disease and label for knowledge of disease (F(1, 296) = 1.741, p = .19). Finally, no interaction effect between label and disease was observed for neuroticism (F(1,296) = .01, p = .92) and no main effects of label (p = .88) or disease (p = 1.00) on neuroticism were found.

Given these results it appears that block randomization was effective in reducing demographic and contextual differences between participants across the four study conditions.

3.2 Study Outcomes Following Vignette Exposure

Descriptive statistics and comparisons between Alzheimer and heart disease conditions were performed to characterize the outcome variables of interest (Aim 1). Means and standard deviations for the outcome variables in the four disclosure conditions are summarized in Table 4.

3.2.1 Diagnostic Label and Risk Condition Recall

Following the vignette, participants across conditions were asked multiple choice questions regarding the risk and disease information they were presented. Sixty-eight percent of participants (205 out of 300) correctly recalled both the disease label (e.g., preclinical Alzheimer disease or heart disease) and numeric risk (i.e., 25%) information they had been shown during the vignette. Looking at recall of just one of the two pieces of information, participants recalled numeric risk information at a greater rate than disease label (88% correct versus 73% correct, respectively). Seven percent of participants (20 out of 300) did not recall either disease label or numeric risk information. There were no significant differences in recall between disease

conditions ($\chi^2(3, N = 300) = 4.164$ $p = .244$), however there were significant differences in recall between label conditions ($\chi^2(3, N = 300) = 60.51$ $p < .001$) such that participants in numeric label only conditions were less likely to recall the diagnostic label they received (or, in this case, the fact that they did not see a diagnostic label). Recall of numeric risk information was the same across all four conditions.

Given the aims of the study to investigate the influence of diagnostic label and numeric risk exposure, all subsequent analyses were conducted both with the full sample and with a smaller sample of participants ($n = 205$) who correctly identified both their disclosed disease label and numerical risk. Results obtained using the more constricted of the two datasets were the same in terms of significance and magnitude, and therefore only results obtained using the full sample of 300 participants are reported below.

3.2.2 Individual Perceptions Following Disclosure

Overall, participants reported mild levels of anxiety ($M = 2.17$, $SD = 0.92$, range = 1-4 on this 4-point scale). A two-way ANOVA revealed no statistically significant interaction between the disease and label conditions ($F(1,296) = 1.60$, $p = .207$). Additionally, there were no significant main effects, although there was a non-significant trend for disease ($p = .08$) such that participants in the Alzheimer condition reported slightly more anxiety (mean difference = ~0.2 points on the 4-point scale) than participants in the heart disease condition. There was no significant main effect of label ($p = .38$) on anxiety.

Participants were also asked questions corresponding to the main constructs of the Health Belief Model: perceived risk, perceived severity, perceived benefits, perceived barriers, and self-efficacy. Overall, following disclosure, participants endorsed moderate levels of risk ($M = 11.75$, $SD = 3.53$, range = 4-20, out of a possible 20 points), and there was no difference in perceived

risk between Alzheimer and heart disease conditions ($t(298) = .212$, $p = .186$, mean difference = .832). Overall, participants endorsed moderate-to-severe levels of severity ($M = 16.28$, $SD = 3.43$, range = 5-25, out of 25 possible points), and participants in the Alzheimer disease condition perceived a greater severity in their disease than participants in the heart disease condition ($t(298) = 2.806$, $p = .005$, mean difference = 1.10). Overall, participants endorsed high perceptions of benefits ($M = 15.53$, $SD = 2.48$, range = 5-20 out of 20 possible points), and participants in the heart disease conditions endorsed higher perceptions of benefits than participants in the Alzheimer disease condition ($t(298) = 5.73$, $p < .001$, mean difference = 1.560). In terms of barriers, participants endorsed low perceptions of barriers ($M = 8.61$, $SD = 3.35$, range = 4-18 out of 20 possible points), and there was no difference between perceptions of barriers between Alzheimer and heart disease conditions ($t(298) = .585$, $p = .559$, mean difference = .227). Participants indicated high self-efficacy ($M = 7.71$, $SD = 1.41$, range = 3-10 out of 10 possible points), and participants in the heart disease condition indicated higher self-efficacy than participants in the Alzheimer disease condition ($t(298) = 3.02$, $p = .003$, mean difference = .487).

3.2.3 Post-Vignette Behavior Intentions

Following exposure to the vignette, participants indicated which behaviors they would intend to engage in or change in response to the test results they received. Means, standard deviations, and ranges for pre-vignette and post-vignette behavioral reports appear in Table 5. A two-way ANOVA was conducted to compare reported changes in behavioral intentions across the four study conditions, and these models indicated main effects of disease group on intended Health Behaviors ($F(1,296) = 18.59$, $p < .001$, mean difference = .913 behaviors) and Living Arrangements ($F(1,296) = 3.96$, $p = .048$, mean difference = .207 behaviors) such that

participants in Alzheimer disease conditions reported greater, though modest, behavioral intention change in these two domains than participants in heart disease conditions.

The current study did not make specific hypotheses regarding which domains of behavior change would be most influenced by risk information or diagnostic label disclosure and, considering the need for interpretable and appropriately powered models, subsequent analyses focused on post-disclosure behavior changes as a whole, rather than individual domains. Similarly, previous work concerning the HBM have combined perceived risk, severity, and self-efficacy into one measure, called perceived threat. However, bivariate correlations among components of the HBM were not strong enough to rationalize creation of a composite measure (see Table 6). As such, the three individual components of the HBM were tested using separate models in order to predict overall post-disclosure behavior change.

3.3 PROCESS Model Analysis

In a series of moderated mediation analyses (see Figure 2), the effect of diagnostic label (X; diagnostic label versus numeric risk) on post-vignette behavioral intentions (Y) was examined both directly (c') and indirectly (a*b), mediated through the HBM variable (M) and potentially moderated by disease condition (W; Alzheimer disease versus heart disease). Age, pre-vignette behaviors, experience with disease, knowledge of disease, and neuroticism were included as covariates in all models. Results are organized by HBM component.

3.3.1 Perceived Risk

A moderated mediation analysis was used to examine the relationship between label condition and behavioral intentions, mediated by perceived risk and moderated by disease condition (Figure 3). For means and standard deviations across all four study conditions, see Table 4. Full regression output is presented in Table 7. Participants told they had a preclinical

diagnosis of Alzheimer disease (a_{AD} = -.01 [-1.10, 1.09], p = .99) or heart disease (a_{HD} = .07 [-1.25, 1.34], p = .85) did not report greater perceived risk than participants who were told only a numeric risk. There was evidence of a moderated effect of perceived risk on behavioral intentions such that there was a significant difference ($F(1,289) = 3.91$, p = .04) in the association between perceived risk and behavioral intentions for participants in the Alzheimer disease condition (b_{AD} = -.001 [-.26, .26], p = .99) compared to participants in the heart disease condition (b_{HD} = .37 [.09,.64], p = .009). In the heart disease condition only, increased perceived risk was positively associated with increased behavioral intentions. A bootstrap confidence interval based on 5,000 bootstrap samples for the indirect effect in both disease conditions contained zero (CI_{AD} = [-.23, .15], CI_{HD} = [-.41, .50]), meaning that label condition did not indirectly influence behavior through an effect on perceived risk. There was no evidence that diagnostic label independently influenced behavioral intentions in either disease condition (c'_{AD} = -.31 [-2.15, 1.53], p = .74; c'_{HD} = -.75 [-2.60, 1.09], p = .42).

3.3.2 Perceived Severity

A second moderated mediation analysis was used to examine the relationship between label condition and behavioral intentions, mediated by perceived severity and moderated by disease condition (Figure 4). Full regression output is presented in Table 8. There was evidence for an interaction, such that there was a significant difference in the association ($F(1,291) = 6.77$, p = .009) between label condition and perceived severity for participants in the Alzheimer disease condition (a_{AD} = .79 [-.24, 1.81], p = .13) compared to participants in the heart disease condition (a_{HD} = -1.14 [-2.18, -.11], p = .03). Participants who received the diagnostic label of preclinical heart disease reported greater perceived severity than participants who received numeric risk regarding heart disease, and there was no difference in perceived severity between

label condition among participants who received Alzheimer disease information. Overall, perceived severity did not influence post-vignette behavioral intentions (b_{AD} = .25 [-.05, .53], p = .10; b_{HD} = .30 [-.20, .48], p = .35). A bootstrap confidence interval based on 5,000 bootstrap samples for the indirect effect in both disease conditions contained zero (CI_{AD} = [-.13, .65], CI_{HD} = [-.86, .02]), meaning that label condition did not indirectly influence behavior through an effect on perceived severity. There was no evidence that diagnostic label independently influenced behavioral intentions in either disease condition (c'_{AD} = -.52 [-2.38, 1.34], p = .58; c'_{HD} = -.35 [-2.22, 1.52], p = .71).

3.3.3 Self-Efficacy

A third moderated mediation analysis was used to examine the relationship between label condition and behavioral intentions, mediated by perceived self-efficacy and moderated by disease condition (Figure 5). Full regression output is presented in Table 9. Label condition did not influence self-efficacy (a_{AD} = .11 [-.34, .56], p = .63; a_{HD} = .13 [-.11, .60], p = .78), nor did self-efficacy influence post-vignette behavioral intentions (b_{AD} = .39 [-.23, 1.01], p = .22; b_{HD} = 1.12 [-.45, 2.67], p = .18) in either disease condition. A bootstrap confidence interval based on 5,000 bootstrap samples for the indirect effect in both disease conditions contained zero (CI_{AD} = [-.20, .36], CI_{HD} = [-.30, .73]), meaning that label condition did not indirectly influence behavior through an effect on self-efficacy. There was no evidence that diagnostic label independently influenced behavioral intentions in either disease condition (c'_{AD} = -.40 [-2.23, 1.43], p = .67; c'_{HD} = -.86 [-2.69, .98], p = .36).

3.3.4 Age and Disease Knowledge

Based on the moderation mediation analyses described above, age and disease knowledge had significant associations with HBM variables and were therefore candidates for further

exploration in post-hoc models. Additional moderated mediation models were used to explore the relationships between diagnostic label, individual perceptions, and behavioral intentions, while being moderated not by disease condition, but by age and disease knowledge, respectively.

In terms of age and perceived risk, age did not moderate the relationship between label condition and perceived risk ($F(1,289) = .06$, $p = .80$), but there was evidence that age moderated the relationship between perceived risk and behavioral intentions ($F(1,289) = 7.88$, $p = .005$). For participants who were older in age (84th percentile value = 71 years old), there was a significant, positive relationship between perceived risk and behavioral intentions ($b_{old} = .40$ [.15, .65], $p = .002$). However, for participants who were younger in age (16th percentile value = 58 years old), there was no significant association between perceived risk and behavioral intentions ($b_{young} = -.18$ [-1.88, 1.51], $p = .83$). There was no evidence that age moderated the indirect effect of label condition on behavioral intentions, mediated through perceived risk, nor evidence that age moderated the direct effect of label condition on behavioral intention. There was no evidence for any age-moderated relationships in models examining perceived severity or self-efficacy.

In terms of knowledge and perceived risk, disease knowledge did not moderate the relationship between label condition and perceived risk ($F(1,290) = .49$, $p = .48$), but there was evidence that knowledge moderated the relationship between perceived risk and behavioral intentions ($F(1,290) = 12.04$, $p = .001$). For participants who had greater disease knowledge (84th percentile value = 26/30) there was a significant, positive association between perceived risk and behavioral intentions ($b_{high\_knowledge} = .46$ [.21, .72], $p = .0003$). However, for participants who had relatively less disease knowledge (16th percentile value = 18/30) there was no significant association between perceived risk and behavioral intentions ($b_{low\_knowledge} = -.17$ [-.44, .11], $p = .23$). There was no evidence that knowledge moderated the indirect effect of label condition on

behavioral intentions, mediated through perceived risk, nor evidence that knowledge moderated the direct effect of label condition on behavioral intention.

A similar pattern was found in terms of knowledge and perceived severity, such that there was evidence for a knowledge-moderated association between perceived severity and behavioral intentions. Disease knowledge did not moderate the relationship between label condition and perceived severity ($F(1,290) = .02$, $p = .90$), but there was evidence that knowledge moderated the relationship between perceived severity and behavioral intentions ($F(1,290) = 5.05$, $p = .03$). For participants who had greater disease knowledge (84^{th} percentile value = 26/30) there was a significant, positive association between perceived severity and behavioral intentions ($b_{high\_knowledge} = .48$ [.23, .74], $p = .0003$). However, for participants who had relatively less disease knowledge (16^{th} percentile value = 18/30) there was no significant association between perceived severity and behavioral intentions ($b_{low\_knowledge} = .04$ [-.25, .34], $p = .77$). There was no evidence that knowledge moderated the indirect effect of label condition on behavioral intentions, mediated through perceived severity, nor evidence that knowledge moderated the direct effect of label condition on behavioral intention. There was no evidence for any knowledge-moderated relationships in models examining self-efficacy.

Chapter 4: Discussion

This online vignette study examined the influence of presenting diagnostic labels and numeric risk on participant's interpretation of disease information in the context of the Health Belief Model (HBM) and, subsequently, their post-diagnosis behavioral intentions. Older adults received hypothetical biomarker test results along with risk information regarding their likelihood to progress to a clinical stage of either Alzheimer or heart disease. First, I discuss results from descriptive and ANOVA analyses which compared HBM constructs across disease

conditions. Then, I discuss the results of the moderated mediation analyses and attempt to put the findings regarding the influence of a preclinical Alzheimer disease label in context. Finally, I highlight overall implications of this study for the HBM and its application to Alzheimer disease versus other diseases, before ending with limitations, clinical implications, and future directions for research. For a summary of the study hypothesis and results see Table 10.

4.1. Individual Perceptions and Behavioral Intentions Vary by Disease

Overall, participants differ in how they perceive risk information about heart disease and Alzheimer disease. Participants in the Alzheimer disease conditions perceived their risk information as implying a more severe condition, perceived fewer benefits to knowing their risk, and reported lower self-efficacy about doing anything to address that risk. No differences were found between diseases for perceived barriers or perceived risk. This result is consistent with previous research comparing heart disease and Alzheimer disease, where Alzheimer disease was perceived as more serious and less actionable to control or ameliorate its effects (Boeldt et al., 2015). This small but significant difference between perceptions of heart disease severity and Alzheimer disease severity (ranging from 1 to 1.5 points on the scales used to measure these constructs) potentially reflects the reality of the Alzheimer disease treatment landscape at present. Heart disease is treatable, but Alzheimer disease is not, despite a recently FDA-approved but tightly restricted anti-amyloid agent. Likewise, exercise, diet, and other lifestyle interventions may help reduce Alzheimer risk (and heart disease), but evidence supporting their effects in reducing risk of dementia or slowing progression of already developed Alzheimer disease is inconclusive (Bartochowski et al., 2020; Farina, Rusted, & Tabet, 2013; Kelly et al., 2014; Northey et al., 2018). Given the relatively high knowledge participants demonstrated about

both diseases, they appear to understand the relative differences in disease severity and potential treatment benefits between the diseases, resulting in an overall diminished sense of self-efficacy.

However, a reduced sense of self-efficacy and lower perception of benefits about knowing one's risk in the context of Alzheimer disease does not dampen willingness to pursue relevant behaviors across several domains. Across both disease groups, participants indicated a similar and proactive intention to undertake more behaviors related to health, living arrangements, medico-legal planning, and employment planning, as well as an intention to engage in fewer behaviors related to leisure. For example, participants who received information related to Alzheimer disease reported increased intentions related to health-behaviors (e.g., taking supplements to improve memory, exercising) and living arrangements (e.g., downsizing their home, exploring care-home options). This result is consistent with previous research where participants who received "elevated" amyloid PET scan results reported increased desire to engage in behavioral change (like those presented in the current study) compared to participants who received "non-elevated" PET results (Largent et al., 2020). Furthermore, in the REVEAL research, both numeric risk information and *APOE* genotype information were associated with an increase in health-related behavior changes one year following disclosure (Chao et al., 2008).

Among participants in Alzheimer conditions, despite their belief that there is little they can do to affect the disease, participants were still interested in engaging in certain behaviors. It is possible this disjunction between perceived benefits, self-efficacy, and behavioral intentions highlights a diversity of interpretations about what "treatment" may mean in the context of Alzheimer disease. Questions probing benefits and self-efficacy (e.g., "I am able to make differences that will change the risk of developing dementia.") bring to mind pharmacological or lifestyle interventions and their potential for reducing risk or reducing severity of disease.

However, participants in the current study also endorse behaviors related to other facets of quality-of-life changes (e.g., moving closer to or moving in with family) that are distinct from purely clinical interventions. Perceived benefits or feelings of self-efficacy in terms of quality-of-life changes, changes indicated as potentially attractive behaviors, were not captured by the HBM-based questions from Motivation to Change Lifestyle and Health Behaviors for Dementia Risk Reduction Scale used in the current study. The lack of overlap between that particular scale and the reported intentions of participants may reflect a larger disconnect between what participants view as beneficial actions in reaction to Alzheimer risk information (e.g., quality-of-life changes) and what clinicians may deem "actionable treatments" (e.g., pharmacological interventions).

Finally, it is likely that individual perceptions regarding disease risk and severity vary not only by disease but also across other demographic and contextual characteristics. In this vein, the results of the exploratory post-hoc analyses on additional moderating factors suggest that age and disease knowledge may play a role in how participants transform their perceptions of disease into behavioral intentions. For older participants, as well as participants with higher disease, knowledge increased perception of disease risk and was associated with increased behavioral intentions, and for participants with higher disease knowledge, increased perception of disease severity was associated with increased behavioral intentions. These exploratory results underscore the need to take into account preconceptions and misconceptions, as well as to explore demographic factors that may moderate a person's perception and reaction to Alzheimer risk information.

4.2. Preclinical Alzheimer Diagnostic Label Does Not Influence Components of Perceived Threat or Behavioral Intentions

Turning to the results of the mediation models, when participants received the preclinical Alzheimer disease label in addition to their numerical risk information, they did not feel at greater risk for developing symptomatic disease, that it would be more severe, nor did they report any difference in their self-efficacy to do anything about their risk compared to participants who saw numeric risk for Alzheimer disease without the preclinical label. Similarly, the preclinical Alzheimer disease label did not alter how people felt about risk, severity, or self-efficacy in a way that influenced their reported intentions to make changes in their behavior.

In terms of perceived risk for dementia, the addition of a preclinical Alzheimer disease label is not sufficient alone to trigger acute changes in how older adults perceive their risk of progression to clinical symptoms, above and beyond numeric risk information alone. Previous research (Grill et al., 2020) indicates no negative short-term psychological outcomes when biomarkers for Alzheimer disease are disclosed to cognitively normal participants. However, it is worth noting that in all conditions in the current study, participants saw a numeric indicator of their actual risk (25%), and there was no condition in which participants only saw a diagnostic label with no numeric risk information. Indeed, 88% of participants were able to report the exact numeric risk following vignette exposure, and it is possible that any potential variance in perceived risk between conditions was muted because everyone was exposed to the same actual risk information. In other words, when numeric risk information is present it is potent, diverting attention away from other information such as diagnostic terms.

In terms of perceived severity and self-efficacy, here again the preclinical Alzheimer label had no significant impact, in contrast to what would be predicted by the HBM. According

to the HBM, cues to action such as receiving diagnostic or risk information prompt self-reflection and alter perceived risk, perceived severity, and self-efficacy, which in turn lead to intention to change in order to reduce the discomfort caused by those perceptions. Results from the current study, however, suggest that a preclinical Alzheimer diagnosis is not a cue to action in the way conceptualized by the HBM, perhaps for a number of reasons. First, it is possible that the hypothetical online vignette structure was not an effective tool in communicating a preclinical Alzheimer diagnosis. With the hypothetical nature of the vignette structure, people can distance themselves from the diagnosis or risk information provided ("This is not really happening to me.") as a way to reduce negative affect (Erfanian et al., 2020). Even though participants in the study appeared engaged (i.e., could recall and correctly state their disease label and numeric risk), the experience might not have felt real enough to elicit substantial changes.

A second dynamic may be that a preclinical Alzheimer diagnosis is not really a "cue to action" in the way conceptualized by the HBM. In previous studies on HBM and Alzheimer disease, cues to action included *APOE* risk information or a spousal prompting, and these were associated with change in perceived risk, severity, and self-efficacy (Rostamzadeh et al., 2020, Werner & Heinik, 2003). The preclinical label may be less salient or potent than these other cues. Indeed, previous work where researchers used a web-based vignette experiment in which participants differed in their clinical prognosis (improve, worsen, no change) as well as their diagnostic label (Alzheimer disease, traumatic brain injury, no label) found that the Alzheimer disease label was not associated with negative outcomes (e.g., Alzheimer stigma), and prognosis had the greatest influence instead (Johnson et al., 2015). In that case, it was the impending threat of worsening clinical symptoms that functioned as a meaningful cue to action, not the diagnostic

label itself. Therefore, a diagnostic label alone, may not be sufficient to trigger changes in how older adults perceive the severity of their potential disease condition, nor their feelings of being able to handle the disease. This is consistent with previous research where at-risk or prodromal status evoked less stigma than full disease or disorder (Rosin et al., 2020). This may be a benefit to clinicians and researchers who wish to investigate patient and caregivers' understanding of a preclinical Alzheimer label, knowing that the addition of the label to their existing risk-information conversations may not prompt undue stress or modify someone's perception of the disease.

4.3. Disease Type Moderates the Relationship Between Risk Information, Individual Perceptions, and Behavioral Intentions

Taking the full moderated mediation PROCESS outcome into account, where disease condition is the moderating variable, results indicate important differences in the way people view Alzheimer disease relative to heart disease. First, there is support for a moderated effect of diagnostic label on perceived severity in which participants who received the preclinical heart disease diagnostic label reported greater perceived severity than participants who received numeric risk regarding heart disease. Second, there is support for a moderated effect of perceived risk and post-disclosure behavioral intentions such that increased perceived risk was positively associated with increased behavioral intentions, but in the heart disease conditions only. As discussed above, there was no difference in perceived severity between label condition or association between perceived risk and behavioral intentions among participants who received Alzheimer disease information.

One conclusion to draw from these findings is that heart disease follows the expected HBM pathways (Champion & Skinner, 2008), where the addition of a cue to action (heart

disease label) influences an individual perception (perceived severity), and an individual perception (perceived risk) enhances behavioral intention, whereas Alzheimer disease does not follow the expected HBM pathway. In this case, participants interpreted the diagnosis of *preclinical* heart disease as potentially more severe than simply learning they were at increased risk for heart problems, and participants who perceived their heart disease risk information as riskier were more likely to report behavioral intentions. There are two important considerations to note here in regard to how the HBM is usually studied. Previous studies have traditionally looked at individual pieces of the model, such as the effect of a cue to action on an individual perception *or* the effect of an individual perception on a behavioral intention or change. In the current study, several components of the HBM are explored and analyzed at once, and the pathways that emerge are not always consistent with the model. Specifically, in the current study, the individual perception (perceived severity) that is influenced by a cue to action is not the same perception (perceived risk) that is associated with behavioral intention. Furthermore, previous studies often combine the individual perceptions of perceived risk, severity, and self-efficacy into one construct called perceived threat (Champion & Skinner, 2008). Results from this current study suggest that perceived risk and perceived severity, and to a lesser extent, self-efficacy, may be correlated, but they are also distinct constructs with differential effects. Similarly, participants in Alzheimer disease conditions report reduced benefits compared to heart disease, whereas the perception of barriers is the same in both disease conditions. These results suggest that these constructs may operate differently in the context of preclinical Alzheimer disease, given the uncertain progression from the at-risk state (positive biomarker status) to dementia, as well as the differences between Alzheimer and other diseases in terms of what a lack of available pharmacological treatments means for people's perception of self-efficacy and

their perception of barriers and benefits. Future researchers should take caution to a) fully specify their model and adequately power analysis of the collective HBM pathways, and b) exercise caution when combining individual perceptions into a unitary construct.

4.4 Limitations

4.4.1 Demographic Diversity of the Sample and Methodological Limits to Generalizability

An obvious limitation of the current study is the limited generalizability of results based on sample characteristics. The demographics of the sample approximate those of a specialty tertiary memory clinic (e.g., White, formally educated, knowledgeable about dementia), rather than the general population, and the current sample may have had pre-existing familiarity with concepts such as amyloid, tau, and Alzheimer risk reduction strategies. Exploratory post-hoc analyses suggest that disease knowledge may moderate the relationship between individual perceptions like perceived risk and severity and their reported behavioral intentions. This matters because in the current research landscape, the majority of biomarker disclosure projects happen in tertiary memory clinics, and the high level of Alzheimer knowledge in this sample may not mirror the myths and misinformation regarding Alzheimer disease and dementia that are still common in other groups. For instance, in a recent study of rural and underserved older adults, more than 30% of the sample answered the item, "Nothing can be done to reduce the risk of AD" incorrectly (Wiese et al., 2019). Sample differences in variables such as pre-disclosure disease knowledge and understanding of Alzheimer risk reduction methods may increase a person's perception of Alzheimer biomarker risk information signaling "the beginning of the end" instead of an opportunity to engage in adaptive planning and risk reduction strategies.

Furthermore, the current study excluded people who self-reported concern about their memory. In practice, the population of people who are most likely to be told they have

preclinical Alzheimer disease are also likely to believe they have a memory problem. However, by definition, they will *not* have objective evidence of cognitive issues if they receive a preclinical Alzheimer disease label. However, they are unlikely to be as unsuspecting of any problem as the sample in the current study. Relatedly, attempts to more fully interpret results of the current study in terms of heart disease are limited by methodological oversight wherein explicit personal history of heart disease or other heart problems was not captured. Participants were asked, generally, about their health, but the current study neglected to include an analogue question of "Do you have memory and thinking problems?" for heart disease. Discussion about how the constructs of the HBM are potentially influenced by a preclinical heart disease diagnosis should be tempered by this limitation.

4.4.2 Hypothetical Vignette Design May Underestimate Findings in Clinical Practice

A second limitation of this study is the hypothetical nature of the vignette and the subsequent risk information disclosed. When best practices are followed, vignettes are generally effective methods to research ethically sensitive topics (such as the diagnosis of preclinical Alzheimer disease) (Aguinis & Bradley, 2014), and vignettes have been used effectively in a wide range of Alzheimer research investigating quality of life decision-making, perceptions of Alzheimer disease, and Alzheimer stigma, among other topics (Herrmann et al., 2018, Randhawa, Jiwa, & Oremus, 2015). While the current study took great care to craft engaging, realistic vignettes, and while it appears that participants paid attention to and were affected by the vignettes given their ability to recall information and their free-response reports of emotions following the vignette, the fact remains that vignettes are a hypothetical approximation of receiving disease risk information. As such, it is possible that the current findings underestimate effects that would appear in actual research settings or clinical practice.

4.4.3 Lack of a Pure Control Condition Sacrifices Experimental Clarity for Ecological Validity

The last group of limitations concerns the development of the measures and their use in the moderated mediation model. As discussed above, it is possible that the presentation of numeric risk across all conditions may have overshadowed the influence of the preclinical diagnostic label. A true control condition in which a preclinical label is given without corresponding numeric risk information would have enabled a more pure test of the experimental manipulations. The rationale *for* the inclusion of such a control condition like that is experimental rigor, and the rationale for its *absence* is ecological. It would be unlikely (and perhaps unethical) for a clinician to provide *just* a diagnostic label, with limited information regarding how the label translates into risk of symptom development. Current disclosure protocols for Alzheimer biomarkers (Harkins et al., 2015; Largent et al., 2020) include educational sessions where participants receive verbal and written information covering what is known and unknown about amyloid imaging, including possible results and their meaning, implications of results for risk of future cognitive decline, and information about Alzheimer risk factors. It is possible that presenting a preclinical Alzheimer label without additional information regarding risk and implications would increase participants perception of risk and severity, potentially motivating them to engage in more risk-reducing behaviors. A future direction for research would be to examine how Alzheimer risk information is currently presented in large-scale disclosure studies such as A4 and SOKRATES in order to create a true control condition and tease apart the effect of a preclinical Alzheimer diagnostic label from numeric information regarding risk of progression.

4.5 Clinical Implications and Future Directions for Research

4.5.1 Preclinical Alzheimer Diagnosis Label: Support for Patient Understanding

Results of this study suggest that telling an older adult that they are in the preclinical stage of Alzheimer disease may not result in harmful misunderstandings or anxiety, despite some previously expressed concerns (Grill, Johnson, & Burns, 2013; Sperling, Karlawish, & Johnson, 2013). Granted, this was a hypothetical vignette study, but the results lend some support to the idea that if the uncertainty inherent in preclinical risk information is acknowledged, and if information is provided to people about potential risk and actionable steps to reduce that risk, patients and families may be able to understand and act upon a preclinical Alzheimer disease diagnosis.

Inherent in the claim above is the assumption that most people will prefer risk information disclosed and modeled in a certain way. The results described here indicate associations between demographic and contextual information included in the current models as covariates, such as age, baseline behavioral engagement, and disease knowledge, and components of the HBM. The current study was focused on the effect of the preclinical Alzheimer disease label and is limited in ability to fully explore these relationships and their interactions. Exploratory post-hoc analyses in the current study identified age and disease knowledge as potential moderators of interest that may influence how an older adult receiving Alzheimer risk information transforms their beliefs about risk information into behavioral intentions. These covariates warrant intentional exploration from future studies to inform more precise and informed models of diagnostic delivery, given that preclinical diagnoses are likely to emerge soon in clinical practice. A future direction for research is the development of an evidence-based preclinical Alzheimer disease disclosure protocol, similar to those developed for

Alzheimer biomarkers, utilizing different forms and methods for presenting risk information. For example, perhaps instead of presenting a "best-guess" numeric risk, researchers could present a gradient of risk or uncertainty (e.g., "You are *very likely* to develop dementia.") and measure how people understand, feel about, and act on that information. The first step in the development of such a protocol would be to examine individual perceptions and behavioral outcomes longitudinally, in a sample of cognitively normal individuals who receive genuine, personal risk information related to preclinical Alzheimer disease. While currently uncommon, investigation of biomarker risk disclosure to cognitively normal people is in its nascent stages, with calls from prominent researchers to extend disclosure of biomarker results (Grill & Karlawish, 2022) and preliminary research indicating a lack of negative short-term psychological outcomes of such disclosures (Grill et al., 2020).

4.5.2 Motivation to Act: Need for Longitudinal Study of Alzheimer Risk-Reduction Behaviors

The results of the study also suggest that older adults are generally interested in pursuing behavioral change in response to a preclinical Alzheimer disease disclosure. Alerting people to their at-risk state may motivate them to action, action that may be more likely to be effective if completed before symptoms emerge. The current study identified an association between receiving Alzheimer information and increased intentions towards health behaviors and planning future living arrangements. Health behaviors, such as diet and exercise, may reduce risk, although meta-analyses looking at randomized controlled trials indicate mixed results in terms of effectiveness (Bartochowski et al., 2020; Kelly et al., 2014; Northey et al., 2018). And living arrangements often have wait periods on the scale of years, so early action is likely to be beneficial. In response to the development of a recent FDA-approved drug for the treatment of Alzheimer disease, asymptomatic, amyloid positive patients are asking questions regarding their

condition and possible treatment options (Mozersky et al., 2022). A preclinical Alzheimer label is likely to prompt similar questions, and the current study suggests that it may be helpful to reframe treatment from "prevention" towards "risk reduction," with an emphasis on actionable avenues such as planning and lifestyle adjustments in order to improve future quality of life.

Future research should study how aspects of the Alzheimer risk disclosure process may facilitate behavior change. According to one prominent meta-analysis, medium-to-large changes (d = .66) in behavioral intentions are associated with smaller effects (d = .36) in terms of actual behavioral change (Webb & Sheeran 2006). Therefore, it can be assumed that the behavioral intentions reported in the current study may not translate into actual behavioral change, leaving questions of how to best facilitate behavior change following Alzheimer risk disclosure. A recently published editorial (Ketchum et al., 2022) argued for the adoption of a Huntington disease framework for Alzheimer disease, including research at multiple phases of disclosure (e.g., pre-disclosure, disclosure, and post-disclosure). The current study focused on just one phase of the disclosure process (e.g., disclosure of tests and results) and also point toward a need for research in other phases of the process (e.g., post-disclosure longitudinal risk management). Current disclosure protocols for Alzheimer biomarkers (Erickson et al., 2021, Harkins et al., 2015) emphasize the critical need for longitudinal follow-up, with a diverse demographic sample, both for continued monitoring of psychological reactions and motivation toward long-term planning and health behaviors.

4.6 Conclusion

Results of this study suggest that telling an older adult that they are in the preclinical stage of Alzheimer disease may not influence their perceptions of disease nor influence their desire to engage in health and planning behaviors. That said, the current study provides evidence

that Alzheimer disease differs from other medical conditions, like heart disease, in ways that confirm older adults' fear regarding development of Alzheimer disease and anxiety regarding lack of treatment options. And despite the increased perception of severity and lowered self-efficacy, older adults who received risk information for Alzheimer disease maintained interest in undertaking behavioral changes that may improve their quality of life. The current study highlights potential caveats and pitfalls of adopting the Health Belief Model for Alzheimer disease. As anti-amyloid drugs come to market, available for the treatment of Alzheimer disease, continued exploration of older adults' understanding and perceptions regarding disease, biological markers, and risk is imperative.

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Table 1

Descriptive nomenclature under the revised research criteria

	Clinical Stage		
Biomarker	Cognitively unimpaired	Mild cognitive impairment	Dementia
A-T-N-	Normal AD biomarkers, cognitively unimpaired	Normal AD biomarkers with MCI	Normal AD biomarkers with dementia
A+T-N-	Preclinical Alzheimer pathologic change	Alzheimer pathologic change with MCI	Alzheimer pathologic change with dementia
A+T+N- A+T+N+	Preclinical Alzheimer disease	Alzheimer disease with MCI	Alzheimer disease with dementia
A+T-N+	Alzheimer AND concomitant suspected non-Alzheimer pathologic change, cognitively unimpaired	Alzheimer AND concomitant suspected non-Alzheimer pathologic change with MCI	Alzheimer AND concomitant suspected non-Alzheimer pathologic change with dementia
A-T+N- A-T-N+ A-T+N+	Non-Alzheimer pathologic change, cognitively unimpaired	Non-Alzheimer pathologic change with MCI	Non-Alzheimer pathologic change with dementia

Note. Adapted from "NIA-AA Research Framework: Toward a biological definition of Alzheimer's disease," by Jack et al. (2018). *Alzheimer's & Dementia*, *14*(4), 535-562. A = amyloid, T = tau, N = neurodegeneration, AD = Alzheimer disease, MCI = mild cognitive impairment.

Table 2

Demographic and contextual characteristics of the sample (N = 300)

	Total		MTurk (*n* = 200)		Department subject pool (*n* = 100)	
	M/n	*SD/%*	*M/n*	*SD/%*	*M/n*	*SD/%*
Age (yrs)	64.1	7.41	63.1**	5.32	66.1**	10.1
Female	189	63%	125	62.5%	63	63%
Cis-gender	296	98.7%	197	98.5%	99	99%
Racial identity						
American Indian or Alaska Native	1	0.33%	0	0%	1	1%
Asian	4	1.33%	2	1%	2	2%
Black or African American	15	5.0%	9	4.5%	6	6%
Native Hawaiian or Pacific Islander	1	0.33%	0	0%	1	1%
Multiple racial identities selected	10	3.33%	7	3.5%	3	3%
White	269	89.7%	182	91%	87	87%
Hispanic or Latino	11	3.7%	6	3%	5	5%
Non-Hispanic or Latino	289	96.3%	194	97%	95	95%
Highest grade completed						
High school or GED	24	8.0%	21	10.5%	3	3%
Some college	47	15.7%	32	16%	15	15%
Associate degree	35	11.7%	27	13.5%	8	8%
College degree	113	37.7%	79	39.5%	34	34%
Graduate degree	81	27.0%	41	20.5%	40	40%
Self-reported memory issues						
None	253	84.3%	165	82.5%	88	88%
Unsure	47	15.7%	35	17.5%	12	12%
Self-reported health						
Poor	7	2.3%	6	3%	1	1%
Fair	37	12.3%	26	13%	11	11%
Good	113	37.7%	80	40%	33	33%
Very good	92	39.7%	54	27%	38	385
Excellent	51	17.0%	34	17%	17	17%
Pre-disclosure behaviors	10.3	3.73	10.1	3.53	10.8	4.07
Experience with disease						

Genetic	130	43.3%	84	42.0%	46	46%
Non-genetic	72	24.0%	44	22.0%	28	28%
No experience	98	32.6%	72	36.0%	26	26%
List-learning						
Immediate recall	8.35	3.16	8.25	3.14	8.54	3.20
Delayed recall	7.11	3.29	7.14	3.35	7.07	3.20
Alzheimer disease knowledge[a]	22.7	4.12	22.8	3.94	22.6	4.49
Heart disease knowledge[a]	22.4	4.03	22.3	3.97	22.6	4.18
Neuroticism	10.25	2.20	10.0*	2.30	10.7*	1.93

[a] Total sample size for knowledge measures = 150 (MTurk sample = 100, Department subject pool sample = 50)

*$p < .05$. **$p < .001$.

Table 3

Descriptive statistics for demographic and contextual variables by condition (N = 300)

	Total		Preclinical Alzheimer disease label (n = 75)		Alzheimer disease numeric risk (n = 75)		Preclinical heart disease label (n = 75)		Heart disease numeric risk (n = 75)	
	M/n	*SD/%*	*M/n*	*SD/%*	*M/n*	*SD/%*	*M/n*	*SD/%*	*M/n*	*SD/%*
Age (yrs)	64.1	7.41	64.28	6.77	64.07	7.10	64.24	6.57	63.88	9.08
Female	189	63.0%	54	72.0%	50	66.7%	39	52.0%	46	61.3%
Cis-gender	296	98.7%	74	98.7%	73	97.3%	74	98.7%	75	100.0%
Racial identity										
American Indian or Alaska Native	1	0.3%	0	0.0%	0	0.0%	0	0.0%	1	1.3%
Asian	4	1.3%	0	0.0%	3	4.0%	0	0.0%	1	1.3%
Black or African American	15	5.0%	4	5.3%	3	4.0%	4	5.3%	4	5.3%
Native Hawaiian or Pacific Islander	1	0.3%	1	1.3%	0	0.0%	0	0.0%	0	0.0%
Multiple racial identities selected	10	3.3%	2	2.7%	1	1.3%	2	2.7%	5	6.7%
White	269	89.7%	68	90.7%	68	90.7%	69	92.0%	64	85.3%
Hispanic or Latino	11	3.7%	1	1.3%	3	4.0%	2	2.7%	5	6.7%
Non-Hispanic or Latino	289	96.3%	74	98.7%	72	96.0%	73	97.3%	70	93.3%
Highest grade completed										
High school or GED	24	8.0%	8	10.7%	4	5.3%	6	8.0%	6	8.0%
Some college	47	15.7%	12	16.0%	11	14.7%	12	16.0%	12	16.0%
Associate degree	35	11.7%	8	10.7%	13	17.3%	8	10.7%	6	8.0%
College degree	113	37.7%	29	38.7%	24	32.0%	29	38.7%	31	41.3%
Graduate degree	81	27.0%	18	24.0%	23	30.7%	20	26.7%	20	26.7%
Self-reported memory issues										

None	253	84.3%	58	77.3%	64	85.3%	66	88.0%	65	86.7%
Unsure	47	15.7%	17	22.7%	11	14.7%	9	12.0%	10	13.3%
Self-reported health										
Poor	7	2.3%	3	4.0%	0	0.0%	3	4.0%	1	1.3%
Fair	37	12.3%	11	14.7%	13	17.3%	7	9.3%	6	8.0%
Good	113	37.7%	29	38.7%	20	26.7%	31	41.3%	33	44.0%
Very good	92	30.7%	22	29.3%	25	33.3%	20	26.7%	25	33.3%
Excellent	51	17.0%	10	13.3%	17	22.7%	14	18.7%	10	13.3%
Pre-disclosure behaviors	10.3	3.73	10.6	2.89	10.3	3.98	9.45	3.61	10.9	4.22
Experience with disease										
Genetic	130	43.3%	27	36.0%	29	38.7%	35	46.7%	39	52.0%
Non-genetic	72	24.0%	20	26.7%	212	282.7%	14	18.7%	17	22.7%
No experience	98	32.7%	28	37.3%	25	33.3%	26	34.7%	19	25.3%
List-learning										
Immediate recall	8.35	3.16	8.2	2.89	8.6	3.32	7.8	3.35	8.81	3.0
Delayed recall	7.11	3.29	7.03	3.49	7.35	3.22	6.60	3.46	7.48	2.97
Alzheimer disease knowledge[a]	22.69	4.12	23.2	4.07	22.2	4.14				
Heart disease knowledge[a]	22.41	4.03					22.64	4.27	22.19	3.79
Neuroticism	10.25	2.20	10.21	2.13	10.28	1.99	10.24	2.40	10.25	2.31

[a] Total sample size for knowledge measures = 150

Table 4

Descriptive statistics for study outcome variables by condition (N = 300).

	Total		Preclinical Alzheimer disease label (n = 75)		Alzheimer disease numeric risk (n = 75)		Preclinical heart disease label (n = 75)		Heart disease numeric risk (n = 75)	
	M/n	*SD/%*	*M/n*	*SD/%*	*M/n*	*SD/%*	*M/n*	*SD/%*	*M/n*	*SD/%*
Recall										
Recalled both	205	68%	65	87%	45	60%	62	83%	33	44%
Numeric risk recall	265	88%	69	92%	68	91%	64	85%	64	85%
Label recall	220	73%	69	92%	46	61%	70	93%	35	47%
Recalled neither	20	7%	2	3%	6	8%	3	4%	9	12%
Individual Perceptions										
Anxiety	2.17	0.92	2.15	1.00	2.37	0.98	2.09	0.79	2.05	0.87
Perceived risk	11.75	3.53	11.71	3.35	11.88	3.92	11.57	3.43	11.84	3.46
Perceived severity	16.28	3.43	16.37	3.23	17.28	3.18	16.17	3.45	15.28	3.63
Self-efficacy	7.71	1.41	7.43	1.43	7.51	1.53	7.85	1.33	8.05	1.29
Perceived benefits	15.53	2.48	14.69	2.54	14.81	2.71	16.32	2.19	16.31	1.96
Perceived barriers	8.61	3.35	8.73	3.13	8.72	3.90	8.20	3.08	8.80	3.29
Behavior										
Post-disclosure behavior	12.59	6.37	13.69	6.26	13.10	6.81	11.61	5.97	11.97	6.34

Table 5

Comparison of pre-disclosure and post-disclosure behaviors (N = 300)

	Alzheimer disease (n = 150)			Heart disease (n = 150)			
	M	*SD*	*Range*	*M*	*SD*	*Range*	*t*
Pre-disclosure							
Health Behaviors	3.46	1.57	0 – 8	3.23	1.40	0 – 7	1.32
Financial Planning	1.57	.94	0 – 4	1.63	.92	0 – 5	-.56
Living Arrangements	.89	.57	0 – 3	.85	.70	0 – 3	.54
Leisure Time & Activities	2.82	1.40	0 – 6	2.74	1.24	0 – 6	.53
Medical & Legal Planning	.59	.82	0 – 4	.63	.93	0 – 4	-.33
Employment	1.11	1.01	0 – 6	1.13	.91	0 - 4	-.18
Post-disclosure							
Health Behaviors	4.57	2.13	1 – 8	3.43	1.65	0 – 8	5.18***
Financial Planning	1.62	1.16	0 – 5	1.51	1.16	0 – 5	.78
Living Arrangements	1.21	.93	0 – 4	.96	.93	0 – 4	2.29*
Leisure Time & Activities	2.28	1.90	0 – 6	2.41	1.80	0 – 6	-.59
Medical & Legal Planning	2.35	1.50	0 – 4	2.03	1.50	0 – 4	1.81*
Employment	1.37	1.38	0 - 6	1.45	1.51	0 - 6	-.48

*$p < .05$. **$p < .01$. ***$p < .001$.

Table 6

Correlations among components of the Health Belief Model (N = 300)

	1	2	3	4	5
Total sample (n = 300)					
1. Perceived Risk	-				
2. Perceived Severity	.50***	-			
3. Self-Efficacy	.16**	.14*			
4. Perceived Benefits	.19***	.18**	.57***		
5. Perceived Barriers	.20***	.25***	-.30***	-.11	-
6. Behavioral Intentions	.17**	.24***	.19***	.18**	-.11
Alzheimer disease (n = 150)					
1. Perceived Risk	-				
2. Perceived Severity	.45***	-			
3. Self-Efficacy	.11	.22**	-		
4. Perceived Benefits	.04	.23**	.56***	-	
5. Perceived Barriers	.33***	.22**	-.21**	-.02	-
6. Behavioral Intentions	.07	.17*	.15	.16	-.16
Heart disease (n = 150)					
1. Perceived Risk	-				
2. Perceived Severity	.56***	-			
3. Self-Efficacy	.24**	.13			
4. Perceived Benefits	.43***	.28***	.55***		
5. Perceived Barriers	.05	.28***	-.40***	-.21**	-
6. Behavioral Intentions	.29***	.27***	.30***	.33***	-.07

*$p < .05$. **$p < .01$. ***$p < .001$.

Table 7

Moderated mediation analysis with perceived risk as mediator

Predictors	Perceived Risk			Behavioral Intentions		
	b	SE	95% CI	b	SE	95% CI
Constant	19.97	2.21	[15.62, 24.31]	17.24	4.31	[8.77, 25.72]
Age	-.12**	.03	[-.85, -.07]	-.20**	.05	[-.29, -.11]
Pre-Vignette Behaviors	.07	.05	[-.04, .18]	.66**	.09	[.48, .84]
Neuroticism	.13	.09	[-.04, .31]	-.03	.15	[-.33, .26]
Experience	-.16	.23	[-.61, .29]	.21	.39	[-.55,.97]
Knowledge	-.10*	.04	[-.18, -.01]	.09	.07	[-.05, .24]
Label	-.01	.56	[-1.10, 1.09]	-.31	.94	[-2.15, 1.53]
Disease	-.17	.56	[-1.26, .93]	-5.53*	2.37	[-10.20, -.86]
Label x Disease	.08	.79	[-1.47, 1.64]	-.44	1.33	[-3.05, 2.17]
Perceived Risk				-.001	.13	[-.26, .26]
Perceived Risk x Disease				.37*	.19	[.002, .74]
R^2	.11**			.23**		
F	4.48			8.78		

Note: Analysis conducted using PROCESS Model #59 in Hayes 2018. Age, pre-vignette reported behaviors, neuroticism, disease experience, and disease knowledge are included as covariates.
*$p < .05$. **$p < .001$.

Table 8

Moderated mediation analysis with perceived severity as mediator

Predictors	Perceived Severity			Behavioral Intentions		
	b	SE	95% CI	b	SE	95% CI
Constant	19.10	2.10	[15.01, 23.19]	14.08	4.51	[5.21, 22.95]
Age	-.09***	.03	[-.14, -.04]	-.20***	.05	[-.29, -.11]
Pre-Vignette Behaviors	.15**	.05	[.05, .25]	.63***	.09	[.45, .81]
Neuroticism	.31***	.08	[.14, .47]	-.10	.15	[-.40, .20]
Experience	.13	.22	[-.29, .56]	.15	.39	[-.61, .91]
Knowledge	-.08*	.04	[-.16, .00]	.11	.07	[-.04, .25]
Label	.79	.52	[-.24, 1.82]	-.52	.95	[-2.38, 1.34]
Disease	.10	.52	[-1.13, .93]	-1.96	3.36	[-8.57, 4.66]]
Label x Disease	-1.93**	.74	[-3.39, -.47]	.16	1.34	[-2.48, 2.81]
Perceived Severity				.25	.15	[-.05, .54]
Perceived Severity x Disease				.05	.20	[-.35, .44]
R^2	.17***			.23***		
F	7.29			8.73		

Note: Analysis conducted using PROCESS Model #59 in Hayes 2018. Age, pre-vignette reported behaviors, neuroticism, disease experience, and disease knowledge are included as covariates. *p < .05. **p < .01. ***p <.001.

Table 9

Moderated mediation analysis with self-efficacy as mediator

Predictors	Self-Efficacy			Behavioral Intentions		
	b	SE	95% CI	B	SE	95% CI
Constant	9.05	.90	[7.27, 10.83]	14.95	4.58	[5.94, 23.96]
Age	-.03**	.01	[-05, -.01]	-.20***	.05	[-.29, -.11]
Pre-Vignette Behaviors	.04	.02	[-.01, .08]	.65***	.09	[.47, .82]
Neuroticism	-.04	.04	[-.11, .03]	.02	.15	[-.27, .31]
Experience	-.04	.09	[-.23, .14]	.24	.39	[-.52, 1.00]
Knowledge	.02	.02	[-.02, .05]	.06	.07	[-.08, .21]
Label	.11	.23	[-.34, .56]	-.40	.93	[-2.23, 1.43]
Disease	.47*	.23	[.03, .92]	-7.24	3.77	[-14.66, .17]
Label x Disease	.02	.32	[-.61, .66]	-.46	1.32	[-3.05, 2.13]
Self-Efficacy				.39	.32	[-.23, 1.01]
Self-Efficacy x Disease				.74	.48	[-.20, 1.67]
R^2	.07**			.24***		
F	2.63			9.33		

Note: Analysis conducted using PROCESS Model #59 in Hayes 2018. Age, pre-vignette reported behaviors, neuroticism, disease experience, and disease knowledge are included as covariates.
*$p < .05$. **$p < .01$.

Table 10

Summary of study hypotheses and results

Study Hypotheses	Results
H1.A. Participants in the Alzheimer disease condition will report higher levels of perceived risk, higher levels of perceived severity, and lower levels of self-efficacy compared to participants in the heart disease conditions.	Participants in the Alzheimer disease condition reported higher levels of perceived severity and lower levels of self-efficacy than participants in the heart disease condition. There was no difference between disease conditions in terms of perceived risk. (Section 3.2.2)
H1.B. There will be no differences in recall of label and numeric risk information between the disease conditions.	Participants had generally good recall. There were no differences in recall between disease conditions, but there were differences in recall between label conditions. (Section 3.2.1)
H1.C. There will be higher behavioral intentions in response to heart disease information than Alzheimer disease information.	Participants in the Alzheimer disease condition reported more overall behavioral intentions than participants in the heart disease condition. (Section 3.2.3)
H2.A. Participants who receive a diagnostic label of preclinical Alzheimer disease will report higher perceived risk, higher perceived severity, and lower self-efficacy than participants who receive a numeric risk alone.	Receiving a preclinical Alzheimer disease label was not associated with differences in perceived risk, perceived severity, or self-efficacy compared to participants who received numeric risk information for Alzheimer disease. (Section 3.3)
H2.B. Participants who report higher perceived risk, higher perceived severity, or lower self-efficacy will report more behavioral intentions. Compared to participants in the numeric risk condition, participants in the preclinical Alzheimer disease condition will report the most behavioral intentions.	Receiving a preclinical Alzheimer disease label was not associated, either directly or indirectly through an individual perception-mediated pathway, with differences in behavioral intentions compared to participants in the numeric risk condition. (Section 3.3)
H3.A. Explore moderating effects of disease condition on the relationship between label condition, individual perceptions, and behavioral intentions.	Disease condition was a significant moderator of the relationship between perceived risk and behavioral intentions. (Section 3.3.1) Disease condition was also a significant moderator of the relationship between label condition and perceived severity. (Section 3.3.2)
H3.B. Use post-hoc analyses to explore moderating effects of additional demographic and contextual variables on the relationship between label condition, individual perceptions, and behavioral intentions.	Age and disease knowledge were identified as potential moderators of interest based on initial results. Age and disease knowledge were significant moderators of the relationship between perceived risk and behavioral intentions. Disease knowledge was a significant moderator of the relationship between perceived severity and behavioral intentions. (Section 3.3.4)

Figure 1

The Health Belief Model (Janz & Becker, 1984)

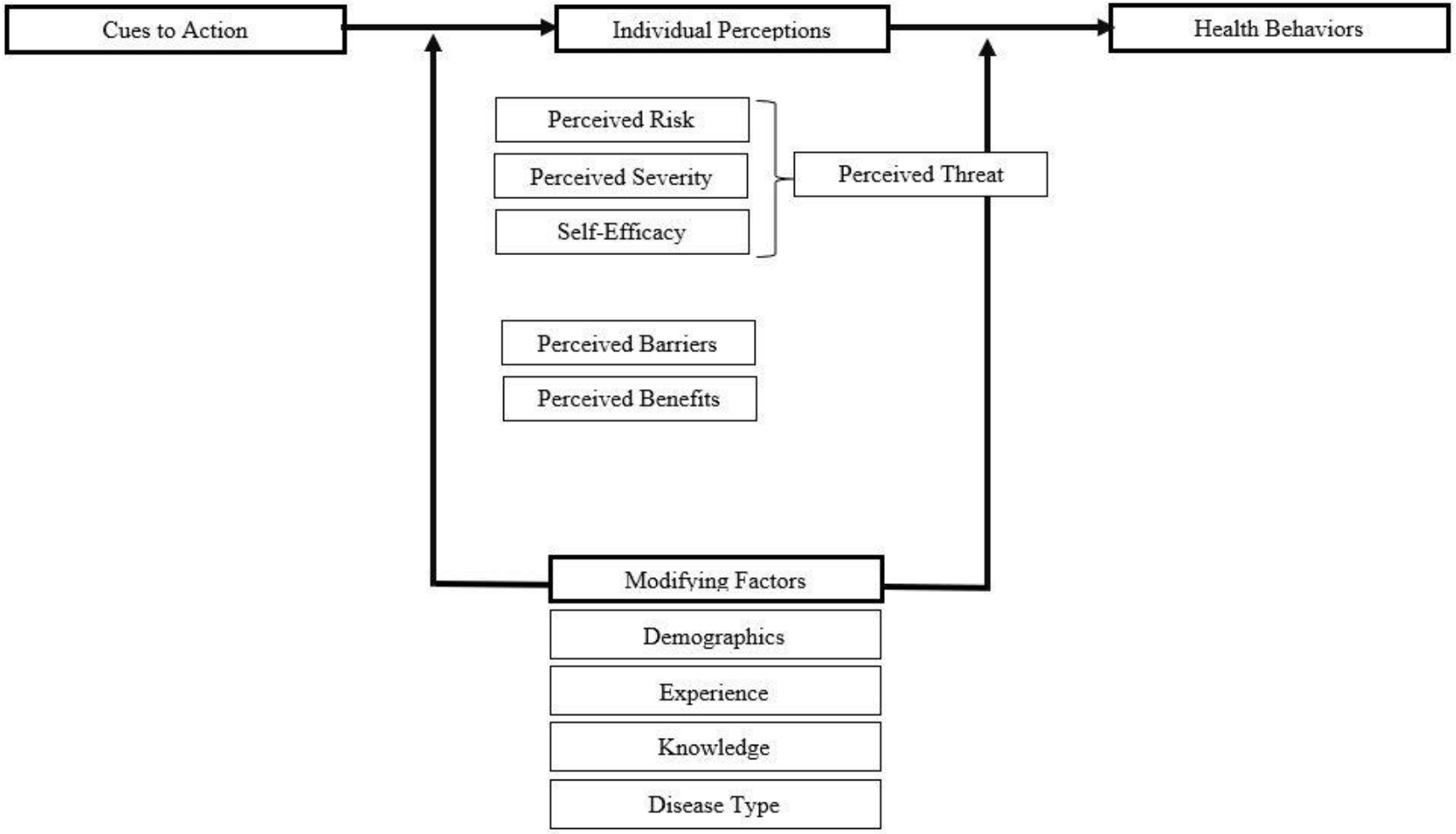
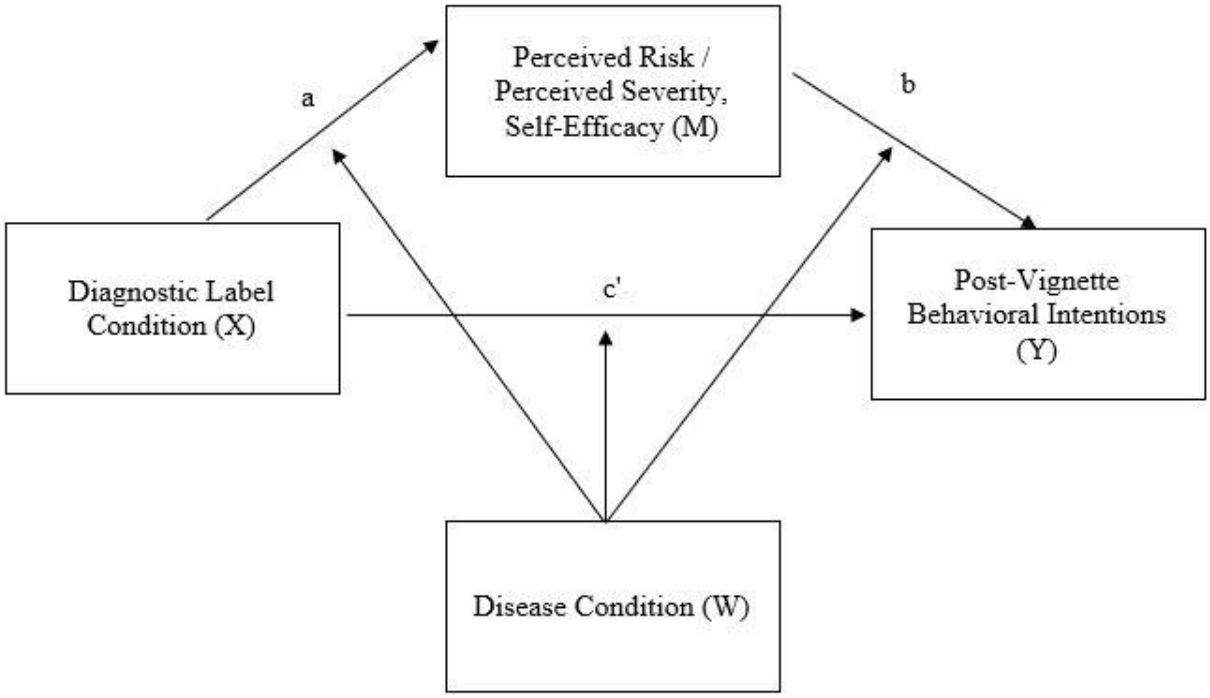


Figure 2

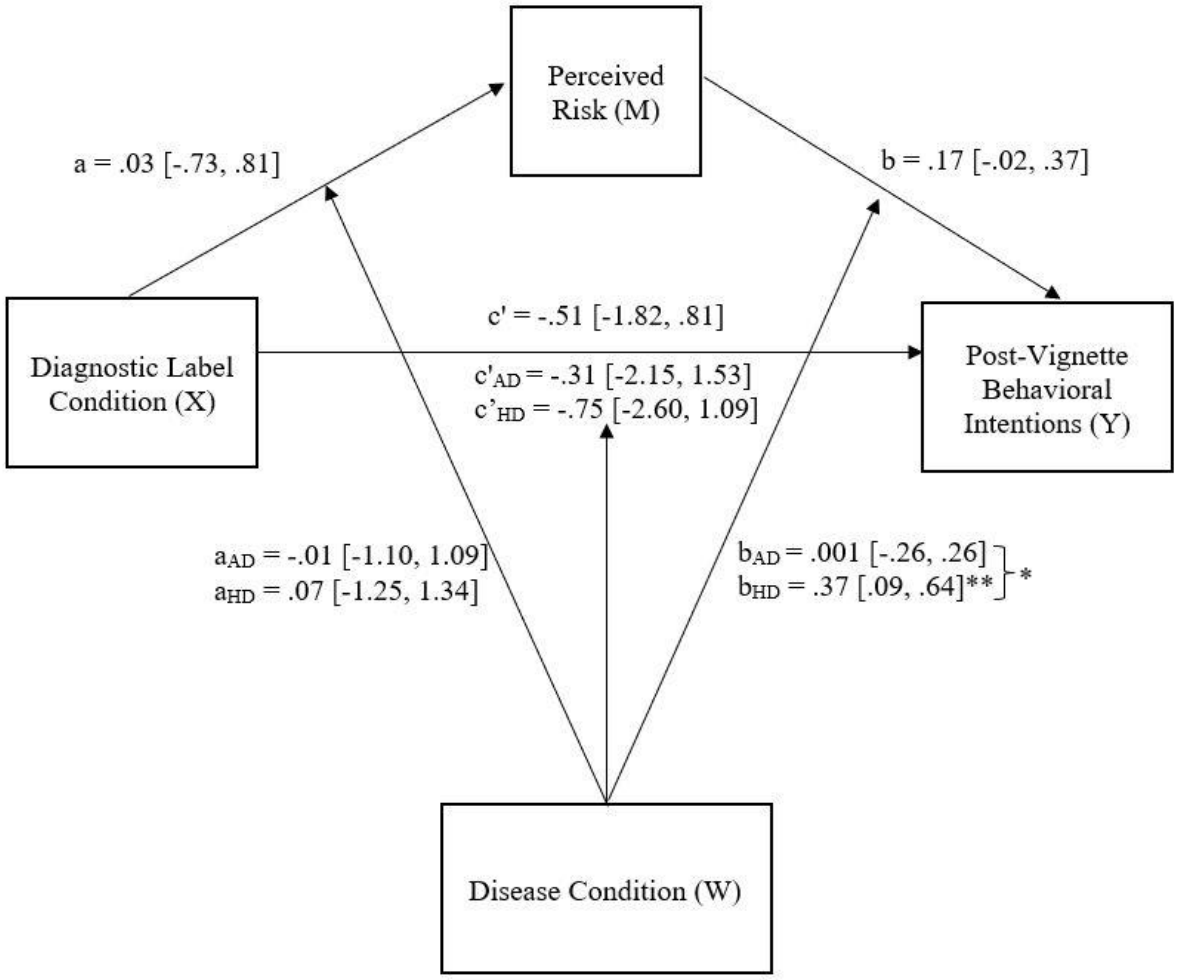
PROCESS moderated mediation model



Note: Model adapted from Model #59 in Hayes (2018).

Figure 3

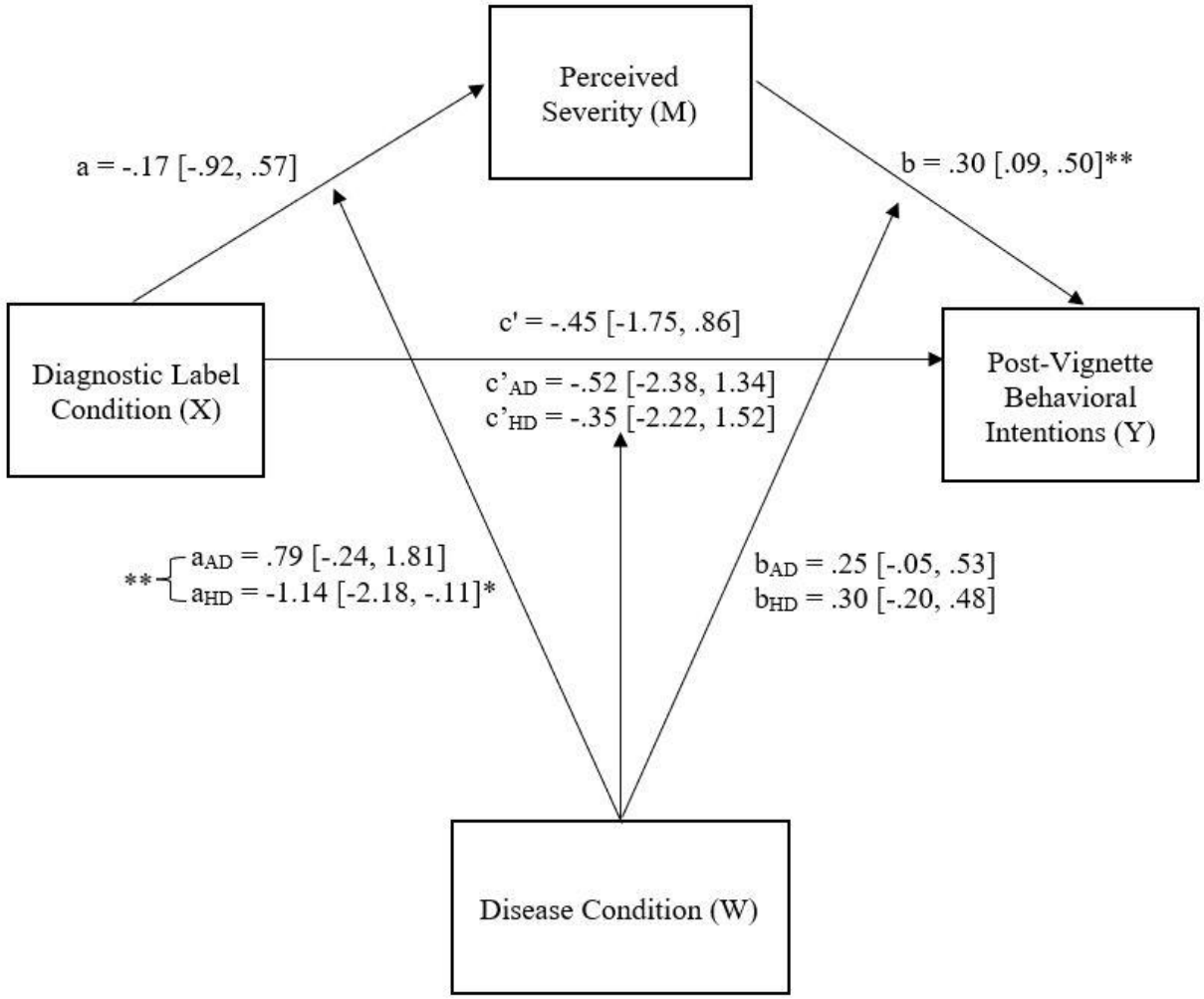
PROCESS moderated mediation model using perceived risk as mediator



Note: Model adapted from Model #59 in Hayes (2018). Coefficients appearing on the lines from X to M, M to Y, and X to Y represent unmoderated effects. Coefficients appearing on the lines from W represent moderated effects. Model presented is adjusted for age, neuroticism, pre-vignette reported behaviors, disease experience, and disease knowledge.
* = p <.05, ** = p < .01

Figure 4

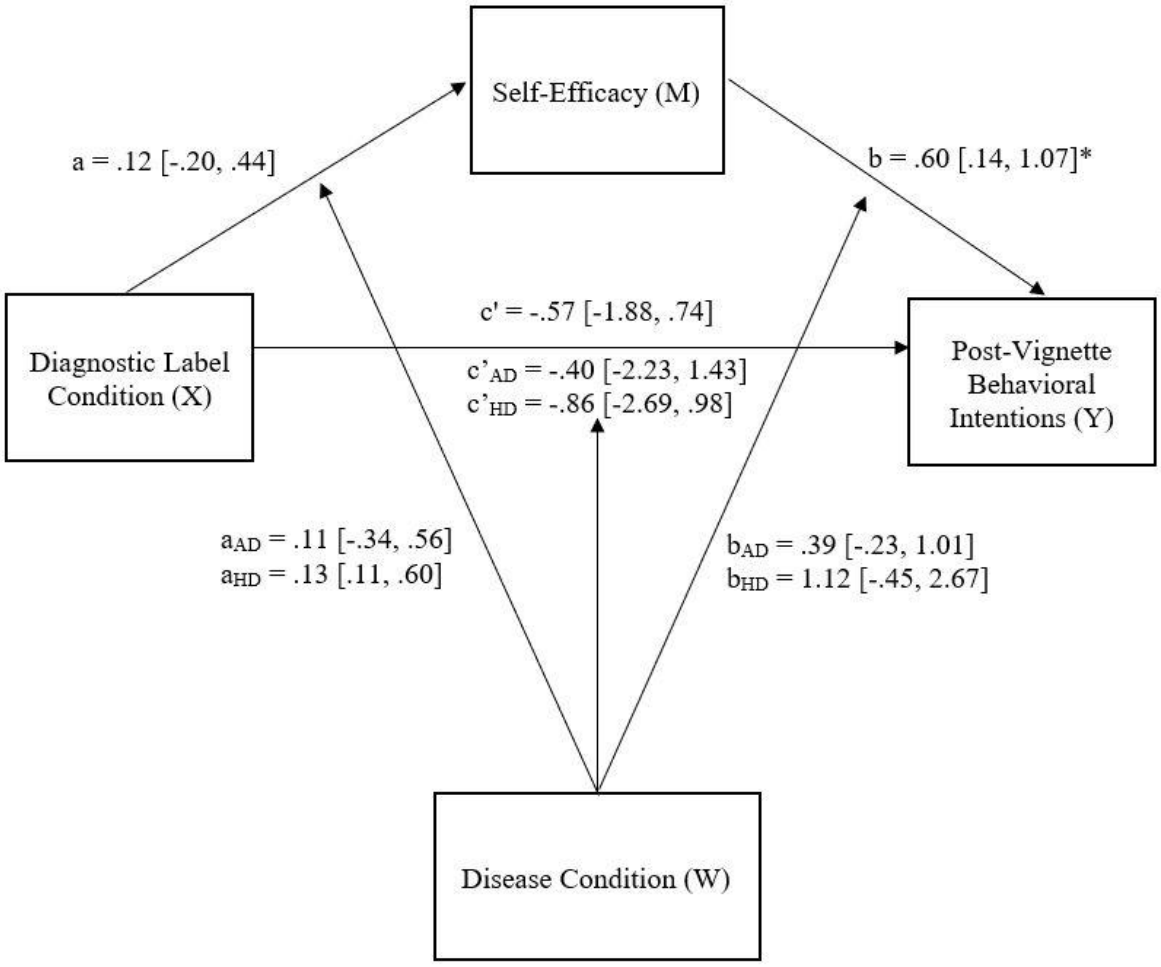
PROCESS moderated mediation model using perceived severity as mediator



Note: Model adapted from Model #59 in Hayes 2018. Coefficients appearing on the lines from X to M, M to Y, and X to Y represent unmoderated effects. Coefficients appearing on the lines from W to X, M, and Y represent moderated effects. Model presented is adjusted for age, neuroticism, pre-vignette reported behaviors, disease experience, and disease knowledge.
* = p <.05, ** = p < .01

Figure 5

PROCESS moderated mediation model using self-efficacy as mediator



Note: Model adapted from Model #59 in Hayes 2018. Coefficients appearing on the lines from X to M, M to Y, and X to Y represent unmoderated effects. Coefficients appearing on the lines from W to X, M, and Y represent moderated effects. Model presented is adjusted for age, neuroticism, pre-vignette reported behaviors, disease experience, and disease knowledge.
* = p <.05

Appendix A: Vignette Materials

Imagine you have enrolled in a research study regarding dementia. Today is your first visit with the researcher.

"Hello! Thank you for participating in the research study. Today I'll have you do several tests and procedures."

"First, I would like to learn a little more about you. Click the arrow when you're ready to answer some questions about yourself."

Dr. Jones, Ph.D.

Slide 1A: Introduction to the hypothetical research study (Alzheimer disease conditions)

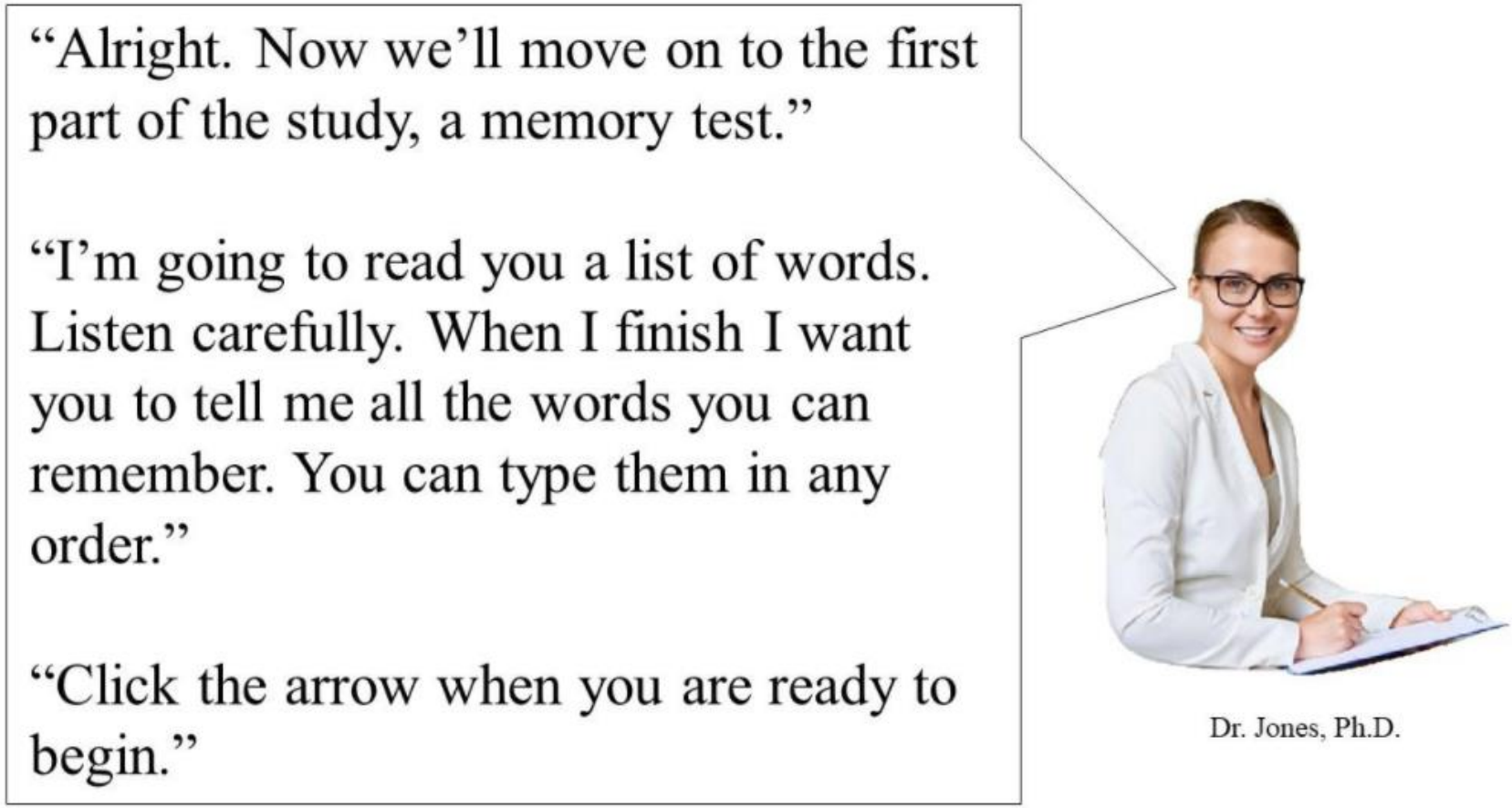
Imagine you have enrolled in a research study regarding heart disease. Today is your first visit with the researcher.

"Hello! Thank you for participating in the research study. Today I'll have you do several tests and procedures."

"First, I would like to learn a little more about you. Click the arrow when you're ready to answer some questions about yourself."

Dr. Jones, Ph.D.

Slide 1B: Introduction to the hypothetical research study (heart disease conditions)



Slide 2: Introduction to the memory test (all conditions)

"Next, I'd like to get a sense of the types of things you've been doing recently."

"I will present lists with activities that people sometimes do. Please mark all the things that you consider to be part of your daily life, or that you have done at least once in the past 30 days."

"Click the arrow when you are ready to begin."

Dr. Jones, Ph.D.

Slide 3: Asking about current behaviors (all conditions)

"Finally, we're going to scan your brain. This will conclude your participation in the research study."

"You will hear some loud noises as the machine works, but the scan will only last about one minute."

"Click the arrow when you are ready to scan your brain."

Dr. Jones, Ph.D.

Slide 4A: Introduction to brain scan (Alzheimer disease conditions)

"Finally, we're going to scan your heart. This will conclude your participation in the research study."

"You will hear some loud noises as the machine works, but the scan will only last about one minute."

"Click the arrow when you are ready to scan your heart."

Dr. Jones, Ph.D.

Slide 4B: Introduction to heart scan (heart disease conditions)

Slide 5: Inside of MRI machine shown during hypothetical brain or heart scan (all conditions)

"Before you go, I'm going to test your memory one more time."

"A few minutes ago, I read you a list of words and asked you to remember them. Type as many of the words you can remember now in the boxes below."

Dr. Jones, Ph.D.

Slide 6: Introduction to delayed recall of previously shown word list (all conditions)

A couple of days after your research visit, you receive a phone call from the researcher.

"Hi! Thank you again for completing the research study. We'd like to share some of the results with your physician. They will be able to discuss these results with you in more detail."

"When you are ready, click the arrow to talk to your physician."

Dr. Jones, Ph.D.

Slide 7: Transition slide from hypothetical research study to disclosure of test results and diagnosis (all conditions)

"The researcher has asked me to share some results from your recent research visit."

"First, I'll explain your baseline risk for dementia based on your biological sex, race, and age."

"When you're ready, press the arrow to learn about your baseline risk."

Dr. Watson, M.D.

Slide 8A: Introduction to baseline risk information (Alzheimer disease conditions)

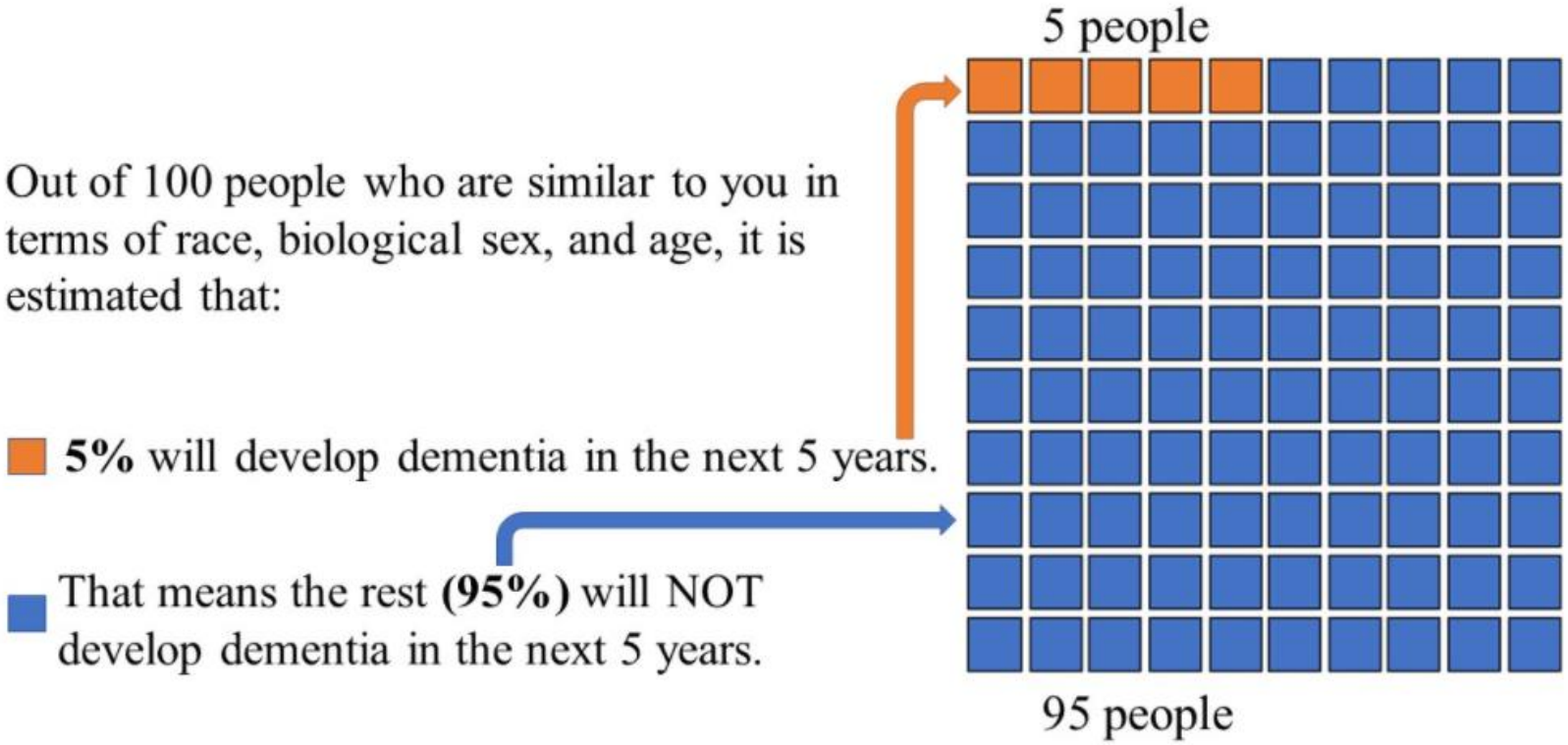
"The researcher has asked me to share some results from your recent research visit."

"First, I'll explain your baseline risk for heart attack based on your biological sex, race, and age."

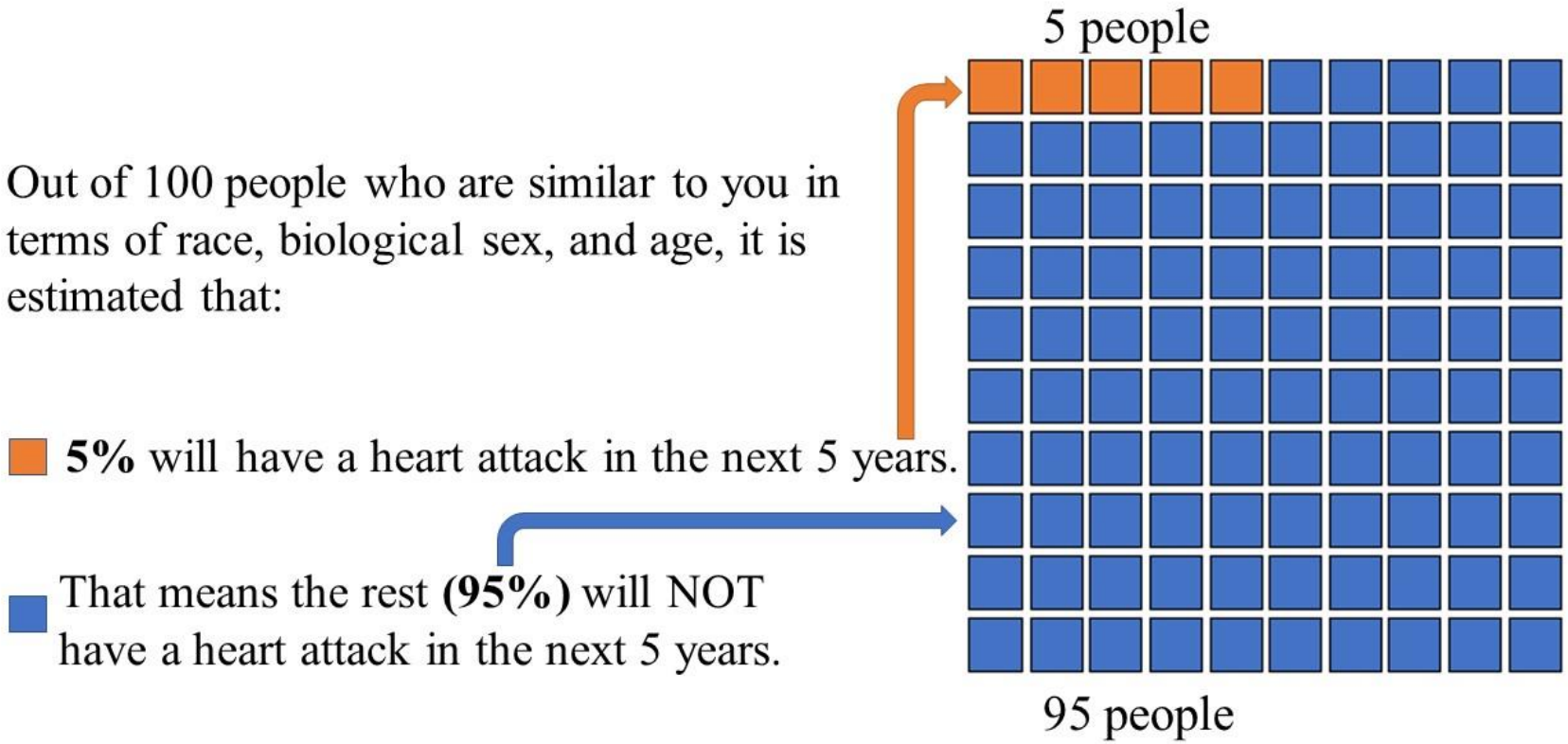
"When you're ready, press the arrow to learn about your baseline risk."

Dr. Watson, M.D.

Slide 8B: Introduction to baseline risk information (heart disease conditions)



Slide 9A: Baseline risk information (Alzheimer disease conditions)



Slide 9B: Baseline risk information (heart disease conditions)

"During the study, you underwent brain scans that let us take a look at your brain."

"Sometimes, what we see on the scan can affect how we think about your risk for developing dementia."

"When you're ready, press the arrow to learn about your scan results."

Dr. Watson, M.D.

Slide 10A: Introduction to biomarker test results (Alzheimer disease conditions)

"During the study, you underwent heart scans that let us take a look at your heart."

"Sometimes, what we see on the scan can affect how we think about your risk for having a heart attack."

"When you're ready, press the arrow to learn about your scan results."

Dr. Watson, M.D.

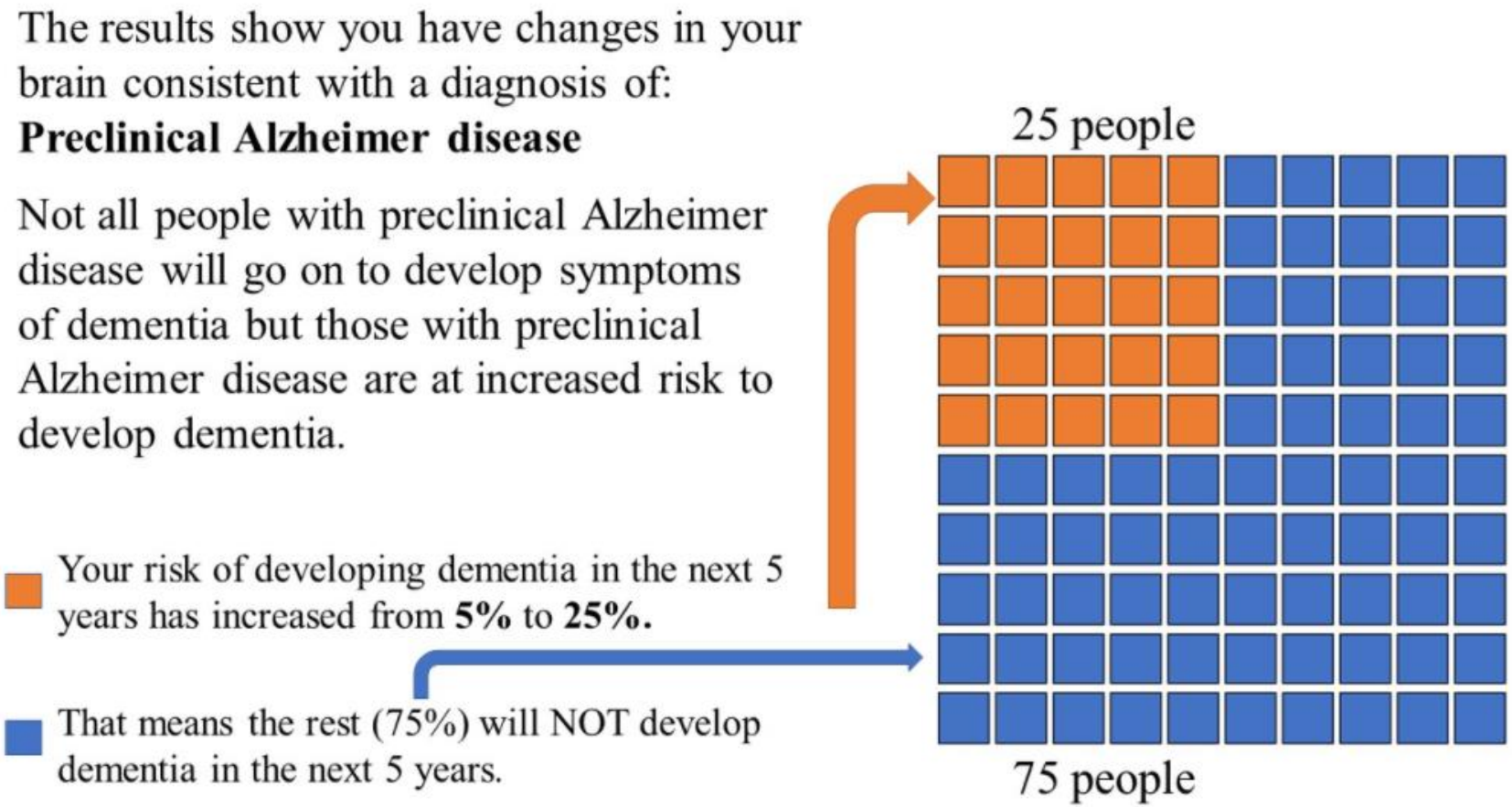
Slide 10B: Introduction to biomarker test results (heart disease conditions)

Amyloid brain scan	**Your test result**
This brain scan measures the amount of amyloid in a person's brain. Amyloid is a protein that is higher in the brains of people with Alzheimer dementia.	Your amyloid score is **elevated**. This means you have a higher amount of amyloid in your brain compared to other people your age.
Tau brain scan	**Your test result**
This brain scan measures the amount of tau in a person's brain. Tau is a protein that is higher in the brains of people with Alzheimer dementia.	Your tau score is **elevated**. This means you have a higher amount of tau in your brain compared to other people your age.

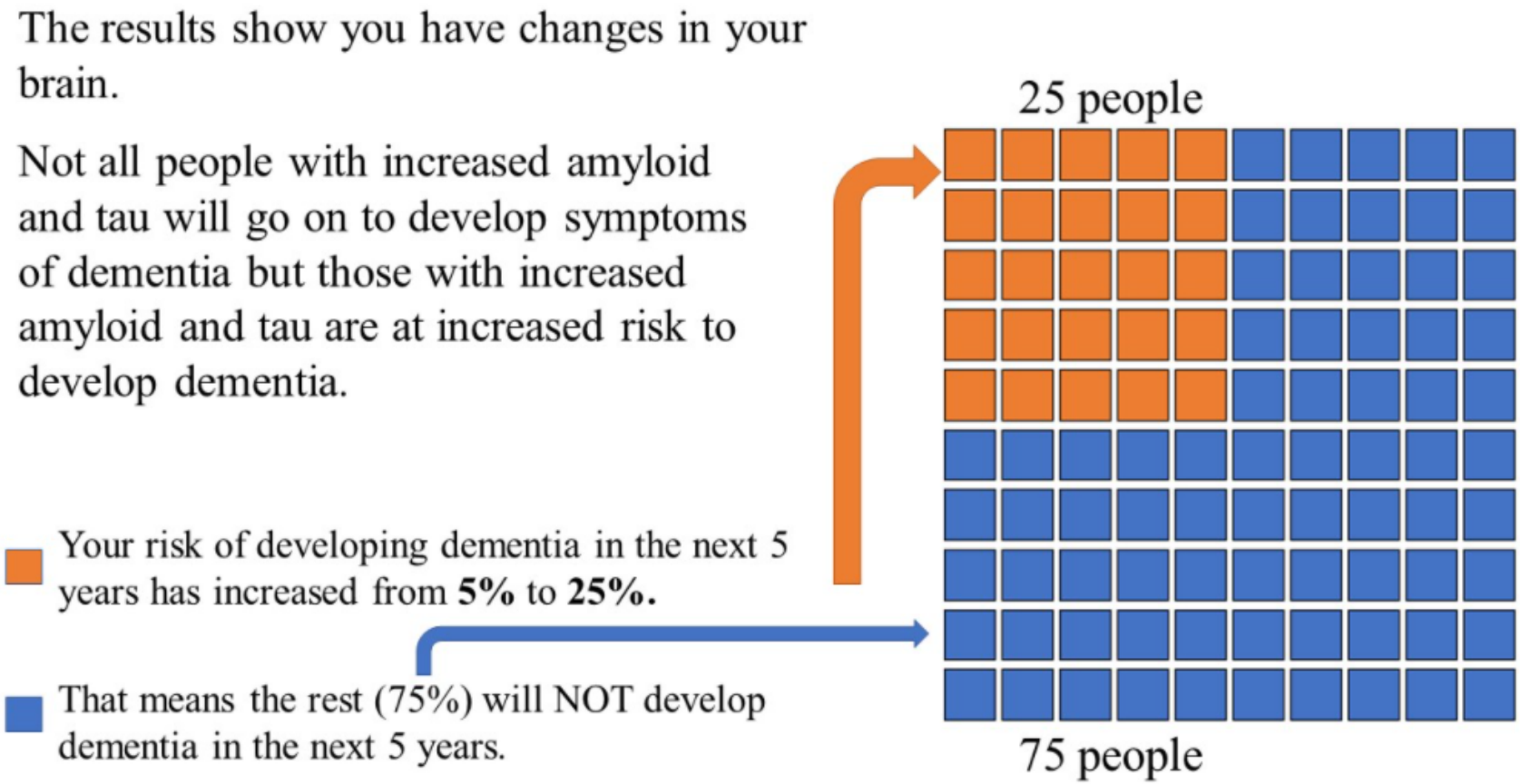
Slide 11A: Biomarker test results (Alzheimer disease conditions)

Coronary calcium scan	**Your test result**
This scan measures the amount of calcium in a person's heart. Deposits of calcium in the arteries can make a heart attack more likely.	Your coronary calcium score is **elevated**. This means you have a higher amount of calcium in your heart compared to other people your age.
CT angiography	**Your test result**
This scan measures the amount of plaque buildup in a person's heart. Plaque in the arteries can make a heart attack more likely.	Your angiography score is **elevated**. This means you have a higher amount of plaque in your heart compared to other people your age.

Slide 11B: Biomarker test results (heart disease conditions)



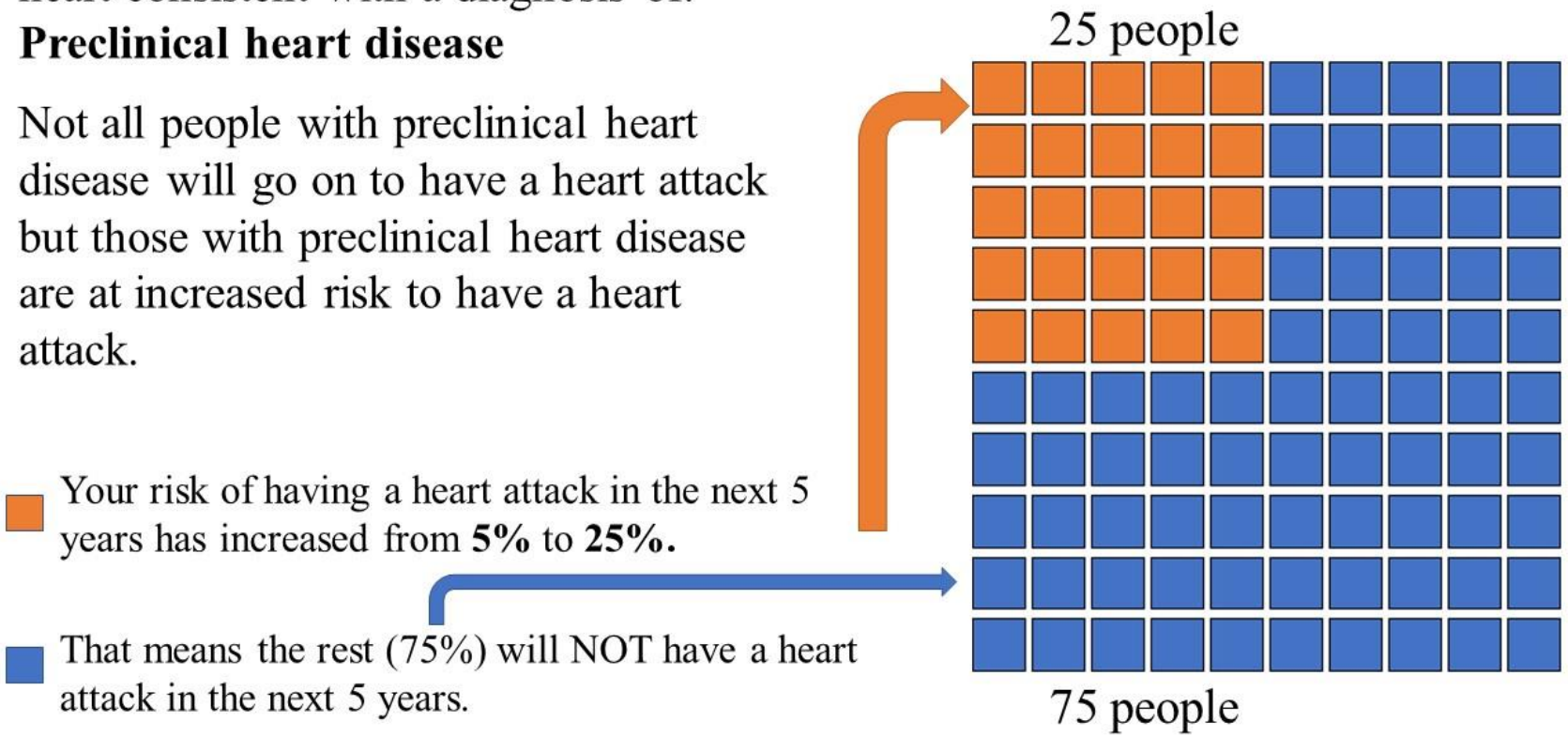
Slide 12A: Updated risk information (preclinical Alzheimer disease condition)



Slide 12B: Updated risk information (numeric risk for dementia condition)

The results show you have changes in your heart consistent with a diagnosis of:
Preclinical heart disease

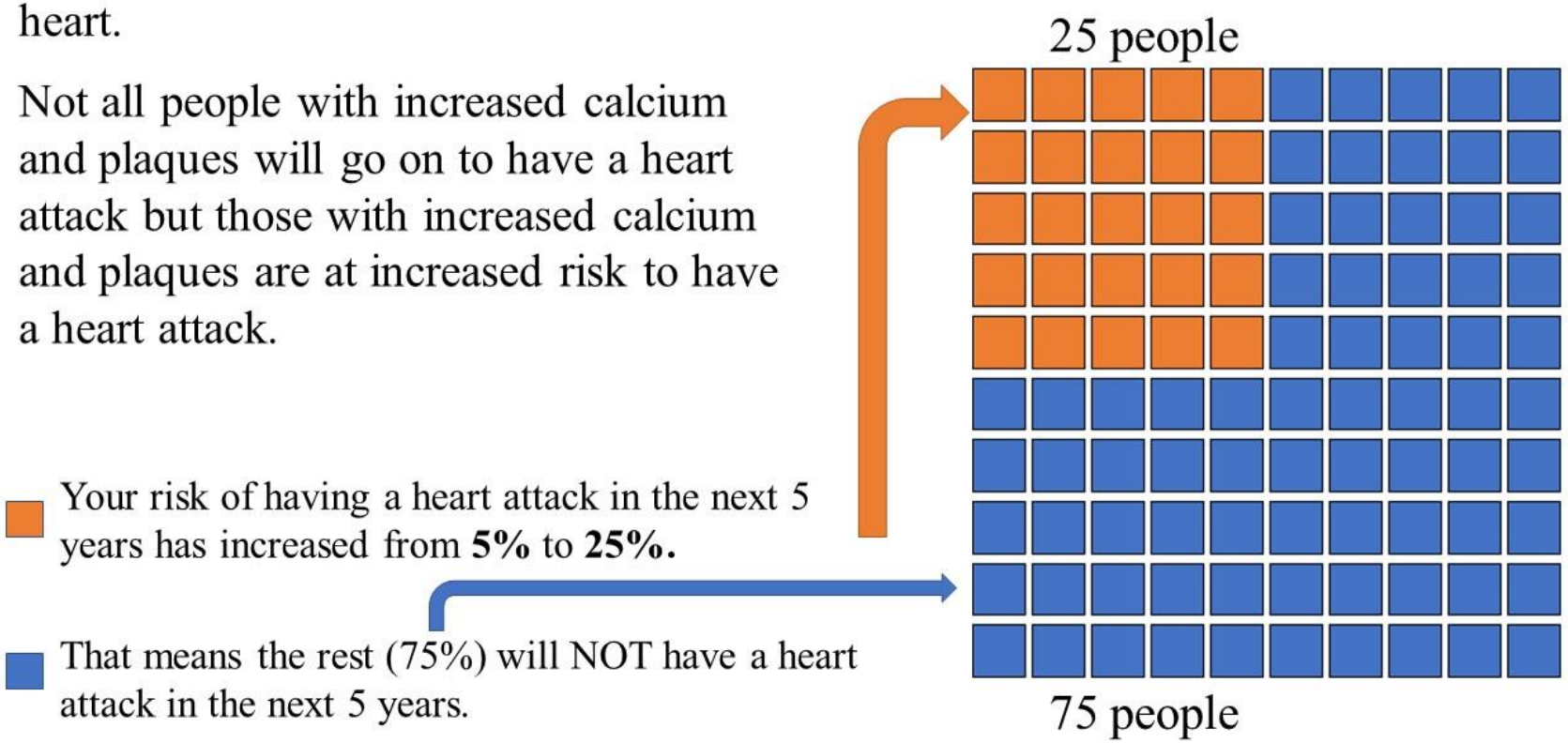
Not all people with preclinical heart disease will go on to have a heart attack but those with preclinical heart disease are at increased risk to have a heart attack.



Slide 12C: Updated risk information (preclinical heart disease condition)

The results show you have changes in your heart.

Not all people with increased calcium and plaques will go on to have a heart attack but those with increased calcium and plaques are at increased risk to have a heart attack.



Slide 12D: Updated risk information (numeric risk for heart disease condition)

A couple of days after your talk with the physician, you receive another phone call from the researcher.

"Hi! Thank you again for completing the research study. We'd like to check in and ask a few questions about the information you discussed with your physician."

"When you are ready, click the arrow to answer the questions."

Dr. Jones, Ph.D.

Slide 14: Introduction to post-disclosure questions (all conditions)

Appendix B: Measures

A. Screening questions and demographics

1. What is your age?

    [enter a number]

2. What was your sex assigned at birth?

    Female/Male

3. What is your gender?

    Female/Male/Nonbinary or third gender/Prefer to self-describe/Prefer not to say

4. Do you identify as transgender?

    Yes/No/Prefer not to say

5. What is your race? (select all that apply)

    American Indian or Alaska Native/Asian/Black or African American/
    Native Hawaiian or Pacific Islander/White

6. What is your ethnicity?

    Hispanic or Latino or Spanish Origin/Not Hispanic or Latino or Spanish Origin

7. Are you fluent in English?

    Yes/No

8. What is the highest grade of school you finished?

    Some high school/High school or GED/ Some college/Associate degree/
    College degree/Graduate degree

9. Do you have problems with memory or thinking?

    Yes/No

10. Would you say your health is excellent, very good, good, fair, or poor?

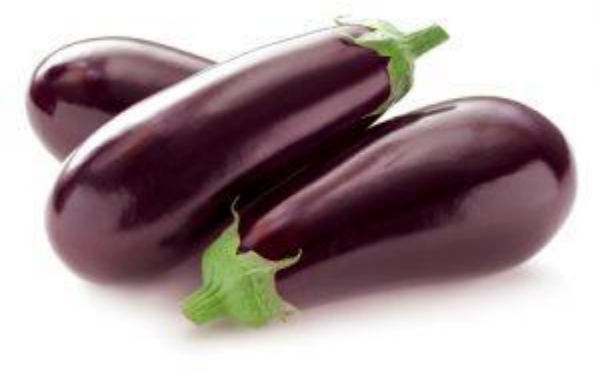
    Excellent/Very good/Good/Fair/Poor

11. Please type out your answer to question 10 in the box below

[free response]

12. What is the common “every day” name of the vegetable/fruit below?

[free response]



B. Experience with Alzheimer disease

1. Do you know or have you known someone with Alzheimer disease?

Yes/No

1a. How frequently do you see/did you see them?

1 – very rarely, 2 – rarely, 3 – occasionally, 4 – frequently, 5 – very frequently

1b. How emotionally close do you feel/did you feel to them?

1 – not at all, 2 – slightly, 3 – moderately, 4 – very, 5 – extremely

1c. How related are you/were you to them genetically?

1 –parent, sibling, or child 2 – other relative 3 – not genetically related

2a. Have you ever provided care for a family member with Alzheimer disease?

Yes/No

2b. Have you ever provided care for a friend with Alzheimer disease?

Yes/No

C. Experience with heart disease

1. Do you know or have you known someone with heart disease?

Yes/No

1a. How frequently do you see/did you see them?

1 – very rarely, 2 – rarely, 3 – occasionally, 4 – frequently, 5 – very frequently

1b. How emotionally close do you feel/did you feel to them?

1 – not at all, 2 – slightly, 3 – moderately, 4 – very, 5 – extremely

1c. How related are you/were you to them genetically?

1 – first degree relatives 2 – second degree relatives 3 – not genetically related

2a. Have you ever provided care for a family member with heart disease?

Yes/No

2b. Have you ever provided care for a friend with heart disease?

Yes/No

D. Knowledge of Alzheimer disease

Alzheimer's Disease Knowledge Scale (Carpenter et al., 2008)
Below are some statements about Alzheimer's disease. Please read each statement carefully and circle whether you think the statement is True or False. If you aren't sure of the right answer, make your best guess. It's important to circle an answer for every statement, even if you're not completely sure of the answer.

True	False	1.	People with Alzheimer's disease are particularly prone to depression.
True	False	2.	It has been scientifically proven that mental exercise can prevent a person from getting Alzheimer's disease.
True	False	3.	After symptoms of Alzheimer's disease appear, the average life expectancy is 6 to 12 years.
True	False	4.	When a person with Alzheimer's disease becomes agitated, a medical examination might reveal other health problems that caused the agitation.
True	False	5.	People with Alzheimer's disease do best with simple, instructions given one step at a time.
True	False	6.	When people with Alzheimer's disease begin to have difficulty taking care of themselves, caregivers should take over right away.
True	False	7.	If a person with Alzheimer's disease becomes alert and agitated at night, a good strategy is to try to make sure that the person gets plenty of physical activity during the day.
True	False	8.	In rare cases, people have recovered from Alzheimer's disease.
True	False	9.	People whose Alzheimer's disease is not yet severe can benefit from psychotherapy for depression and anxiety.
True	False	10.	If trouble with memory and confused thinking appears suddenly, it is likely due to Alzheimer's disease.
True	False	11.	Most people with Alzheimer's disease live in nursing homes.
True	False	12.	Poor nutrition can make the symptoms of Alzheimer's disease worse.
True	False	13.	People in their 30s can have Alzheimer's disease.

True	False	14.	A person with Alzheimer's disease becomes increasingly likely to fall down as the disease gets worse.
True	False	15.	When people with Alzheimer's disease repeat the same question or story several times, it is helpful to remind them that they are repeating themselves.
True	False	16.	Once people have Alzheimer's disease, they are no longer capable of making informed decisions about their own care.
True	False	17.	Eventually, a person with Alzheimer's disease will need 24-hour supervision.
True	False	18.	Having high cholesterol may increase a person's risk of developing Alzheimer's disease.
True	False	19.	Tremor or shaking of the hands or arms is a common symptom in people with Alzheimer's disease.
True	False	20.	Symptoms of severe depression can be mistaken for symptoms of Alzheimer's disease.
True	False	21.	Alzheimer's disease is one type of dementia.
True	False	22.	Trouble handling money or paying bills is a common early symptom of Alzheimer's disease.
True	False	23.	One symptom that can occur with Alzheimer's disease is believing that other people are stealing one's things.
True	False	24.	When a person has Alzheimer's disease, using reminder notes is a crutch that can contribute to decline.
True	False	25.	Prescription drugs that prevent Alzheimer's disease are available.
True	False	26.	Having high blood pressure may increase a person's risk of developing Alzheimer's disease.
True	False	27.	Genes can only partially account for the development of Alzheimer's disease.
True	False	28.	It is safe for people with Alzheimer's disease to drive, as long as they have a companion in the car at all times.

True False 29. Alzheimer's disease cannot be cured.

True False 30. Most people with Alzheimer's disease remember recent events better than things that happened in the past.

E. Knowledge of heart disease

Heart Disease Knowledge Questionnaire (Bergman et al., 2011)
Below are some statements about heart disease. Please read each statement carefully and circle whether you think the statement is True or False. If you aren't sure of the right answer, make your best guess. It's important to select an answer for every statement, even if you're not completely sure of the answer.

True	False	1.	Polyunsaturated fats are unhealthier for the heart than saturated fats.
True	False	2.	Women are less likely to get heart disease after menopause than before.
True	False	3.	Having had chicken pox increases the risk of getting heart disease.
True	False	4.	Eating a lot of red meat increases heart disease risk.
True	False	5.	Most people can tell whether or not they have high blood pressure.
True	False	6.	Trans-fats are healthier for the heart than most other kinds of fats.
True	False	7.	The most important cause of heart attacks is stress.
True	False	8.	Walking and gardening are considered types of exercise that can lower heart disease risk.
True	False	9.	Most of the cholesterol in an egg is the white part of the egg.
True	False	10.	Smokers are more likely to die of lung cancer than heart disease.
True	False	11.	Taking an aspirin each day decreases the risk of getting heart disease.
True	False	12.	Dietary fiber lowers blood cholesterol.
True	False	13.	Heart disease is the leading cause of death in the United States.
True	False	14.	The healthiest exercise for the heart involves rapid breathing for a sustained period of time.
True	False	15.	Turning pale or gray is a symptom of having a heart attack.
True	False	16.	A healthy person's pulse should return to normal within 15 minutes after exercise.
True	False	17.	Sudden trouble seeing in one eye is a common symptom of having a heart attack.

True	False	18.	Cardiopulmonary resuscitation (CPR) helps to clear clogged blood vessels.
True	False	19.	HDL refers to "good" cholesterol and LDL refers to "bad" cholesterol.
True	False	20.	Atrial defibrillation is a procedure where hardened arteries are opened to increase blood flow.
True	False	21.	Feeling weak, lightheaded, or faint is a common symptom of having a heart attack.
True	False	22.	Taller people are more at risk for getting heart disease.
True	False	23.	"High" blood pressure is defined as 110/80 (systolic/diastolic) or higher.
True	False	24.	Most women are more likely to die from breast cancer than heart disease.
True	False	25.	Margarine with liquid safflower oil is healthier than margarine with hydrogenated soy oil.
True	False	26.	People who have diabetes are at higher risk of getting heart disease.
True	False	27.	Men and women experience many of the same symptoms of a heart attack.
True	False	28.	Eating a high fiber diet increases the risk of getting heart disease.
True	False	29.	Heart disease is better defined as a short-term illness than a chronic long-term illness.
True	False	30.	Many vegetables are high in cholesterol.

F. Recall, understanding, and emotional perceptions of Alzheimer disease and heart disease risk information

1. While receiving your test results, which of the following terms did you see?
    a. Preclinical Alzheimer disease
    b. Preclinical heart disease
    c. Both
    d. Neither

2. Based on your results, what is your risk of developing dementia/heart disease over the next 5 years?
    a. 5%
    b. 15%
    c. 25%
    d. 40%

3. Your physician told you about changes in your brain. In your own words, describe what your results mean in terms of risk of developing dementia/heart disease.

[Free response]

4. The risk information you received can sometimes make people feel differently about their health or their future. In your own words, describe how the risk information you received made you feel.

[Free response]

5. I feel anxious, upset, or worried.
    a. Not at all
    b. Somewhat
    c. Moderately so
    d. Very much so

G. Individual Perceptions

Motivation to Change Lifestyle and Health Behavior for Dementia Risk Reduction Scale (Kim, Sargent-Cox, Cherbuin & Anstey, 2014)

All questions are answered using a 5-point Likert scale

1 – strongly disagree 2 – disagree 3 – neither agree nor disagree 4 – agree 5 – strongly agree

Perceived risk

1. My chances of developing dementia/heart disease are great

2. I feel that my chances of developing dementia/heart disease in the future are high

3. There is a strong possibility that I will develop dementia/heart disease

4. Within the next 10 years I will develop dementia/heart disease

Perceived severity

5. The thought of dementia/heart disease scares me

6. When I think about dementia/heart disease my heart beats faster

7. My feelings about myself would change if I develop dementia/heart disease

8. When I think about dementia/heart disease I feel nauseous

9. It would be more serious for me to develop dementia/heart disease than if I developed other diseases

Perceived benefits

10. Information and advice from experts may give me something that I never thought of, and may reduce my chance of developing dementia/heart disease

11. Changing my lifestyle and health habits can help me reduce my chance of developing dementia/heart disease

12. I have a lot to gain by changing my lifestyle and health behavior

13. Adapting to a healthier lifestyle and behavior would prevent dementia/heart disease for me

Perceived barriers

14. I am too busy to change my lifestyle and health habits

15. My financial situation does not allow me to change my lifestyle and behavior

16. Family responsibilities make it hard for me to change my lifestyle and behavior

17. Changing lifestyle and behavior interferes with my schedule

Self-efficacy

18. I am certain that I can change my lifestyle and behavior so I can reduce the risk of developing dementia/heart disease

19. I am able to make differences that will change the risk of developing dementia/heart disease

I. Pre-disclosure engagement in health-related and other behaviors

Below is a list of behaviors related to health. Choose all the behaviors that are part of your daily life, that you have done at least once in the past 30 days.

Health Behaviors

- Exercising
- Improving diet
- Seeking out cognitive activity (e.g., brain training games; crosswords)
- Taking medication for your memory or thinking
- Taking vitamins or supplements for your memory or thinking
- Improving sleep
- Drinking alcohol
- Smoking tobacco
- Drinking less alcohol
- Smoking less

Leisure Time and Activities

- Socializing
- Traveling
- Volunteering
- Meditating
- Playing or listening to music
- Engaging in religious or spiritual activities

Financial Planning

- Meeting with a financial planner
- Reviewing accounts or investments
- Spending more money
- Saving more money
- Considering long-term care insurance

Medico-Legal Planning

- Reviewing or updating your will
- Reviewing your power of attorney documents
- Having a conversation about medical wishes
- Having a conversation about end of life wishes

Living Arrangements

- Downsizing or selling property
- Considering a housing option with more support (e.g., assisted living, nursing home)
- Moving closer or moving in with family
- Engaging in home repairs or renovations

Employment

- Balancing work and leisure
- Making attempts to reduce workload
- Considering switching careers
- Considering retirement
- Switching careers
- Retiring

I. Postdisclosure engagement in health-related and other behaviors

Please mark any of the following behaviors you would consider changing (if any) based on the results you were given:

Health Behaviors

- Exercising
- Improving diet
- Seeking out cognitive activity (e.g., brain training games; crosswords)
- Taking medication for your memory or thinking
- Taking vitamins or supplements for your memory or thinking
- Improving sleep
- Drinking less alcohol
- Smoking less

Leisure Time and Activities

- Socializing
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- Balancing work and leisure
- Making attempts to reduce workload
- Considering switching careers
- Considering retirement
- Switching careers
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J. DIAN 16-item list learning task.

"I am going to show you a list of words. Look carefully. When I finish I want you to type in all the words you can remember. You can type them in any order. Ready?

List 1
Mammal
Deluge
Sonata
Piston
Residue
Agility
Interim
Algebra
Circle
Doctor
Mother
Length
History
Product
Engine
Thought
Recall

A few minutes ago, I read you a list of words and asked you to remember them. Type as many of the words as you can remember now in the boxes below.

K. Mini-IPIP Personality Measure

Rate how well each of the following statements describe you on a scale from 1 (Strongly Disagree) to 5 (Strongly Agree).
1 – strongly disagree 2 – disagree 3 – neither agree nor disagree 4 – agree 5 – strongly agree

1. I am the life of the party
2. I sympathize with other's feelings
3. I get chores done right away
4. I have frequent mood swings
5. I have a vivid imagination
6. I don't talk a lot
7. I am not interested in other peoples' problems
8. I often forget to put things back in their proper place
9. I am relaxed most of the time
10. I am not interested in abstract ideas
11. I talk to a lot of different people at parties
12. I feel others' emotions
13. I like order
14. I get upset easily
15. I have difficulty understanding abstract ideas
16. I keep in the background
17. I am not really interested in others
18. I make a mess of things
19. I seldom feel blue
20. I do not have a good imagination