RUNNING HEAD: Expected vs. Experienced AD Stigma

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Learning about a heightened genetic risk for dementia: Expected stigma is greater than experienced stigma

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Abstract

What social repercussions do older adults expect to experience if they learn they are at heightened genetic risk for Alzheimer's disease (AD)? We compared these individuals' hypothetical expectations to the actual experiences of AD stigma reported by those who knew their *APOE ε4* genotype, a key genetic risk factor for AD dementia. As part of a multi-session study, participants aged 60-85 completed a 23-item modified Social Impact Scale (mSIS) to assess AD stigma. At Time 1, participants who knew their *APOE* genotype were divided into two experiential groups: *APOE ε4* carriers (n = 65) and *ε4* non-carriers (n = 46). Experiential group participants reported their experiences of stigma. Participants unaware of their *APOE* genotype (n=180) formed the hypothetical group and reported the level of stigma they expected if they were to learn they had an elevated risk for AD. Results showed that expected stigma was significantly greater than experienced stigma. At Time 1, mean agreement with mSIS statements was 26.1% in the hypothetical group compared with only 2.3% in the *ε4* carrier experiential group. The largest expectation–experience gaps concerned competence and social belonging. These findings suggest that older adults overestimate the social consequences of learning they are at genetic risk for AD. Theoretically, the results add to our understanding of the disability paradox, which refers to outsiders predicting worse life outcomes for people with chronic conditions than those individuals report themselves. Our findings show similar mispredictions occur even in the absence of symptoms.

Keywords: Alzheimer's disease stigma, *APOE* genotype, genetic risk perception

Public Health Significance Statement

APOE genetic testing provides information about a person's risk for developing dementia due to Alzheimer's disease. Our study found that while older adults expect to face significant stigma if they learn they are at a heightened genetic risk, those who know their *APOE* genotype report far fewer experiences of stigma. Clinicians can use this information to address patients' concerns about the social repercussions of *APOE* testing.

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Expectations about the future have an important role in mental and physical health (Constantino et al., 2011; Mondloch et al, 2001). For example, treatment expectations contribute to placebo and nocebo effects and moderate the efficacy of active medical treatments (Petrie & Rief, 2019). Expectations about future feelings also impact people's health-related decision making (Halpern & Arnold, 2008). When people expect that engaging in exercise will lead to positive feelings, they are subsequently more likely to begin and maintain regular physical activity (Dunton & Vaughn, 2008). Conversely, when people with cancer expect that a chemoprevention medication will increase their health-related stress, they have weaker intentions to take the medication (Hoerger et al., 2016).

Because people make decisions based on their expectations about the future, it is concerning that these expectations are often inaccurate. In health contexts, a striking example of this is the *disability paradox* (Albrecht & Devlieger, 1999; Ubel et al., 2005), in which members of the public frequently assume that individuals with chronic health conditions experience a lower quality of life than what these individuals themselves report (Peeters & Stiggelbout, 2010). This mismatch between the "haves" and "have nots" has been documented across a wide range of conditions, including asthma, diabetes, epilepsy, hemophilia, kidney disease (Walsh & Ayton, 2009), acne, arthritis (Baron et al., 2003), colostomy (Boyd et al., 1990), hemodialysis (Sackett & Torrance, 1978), and chronic lung disease (Lacey et al., 2013).

The disability paradox demonstrates that people living with serious and persistent disabilities often report good or excellent quality of life, but outsiders assume their lives are undesirable. Many explanations have been put forward to explain this phenomenon (for a review,

see Ubel et al., 2003). One possibility is that patients evaluate their quality of life relative to others with similar conditions, rather than in comparison to "healthy" individuals, which could inflate their self-assessments. Another possibility is that the public underestimates patients' ability to adapt to their disabilities or reprioritize their values following onset of disability. The focusing illusion (Wilson et al., 2000) may also play a role, such that the public narrowly focuses on the aspects of life that are impacted by the patient's condition, while overlooking areas that remain unaffected. Finally, some scholars have argued that this disability paradox reflects a logical fallacy such that the public equates physical normalcy with higher life quality and mistakenly assumes that physical differences will inherently lead to a lower quality of life (Koch, 2000).

A key feature these explanations share is the assumption that the disability paradox occurs in the evaluation of people who are understood to have limitations or impairments in their daily functioning. But what happens when a person faces a *heightened risk* of developing a debilitating disease but has no actual disability? If expectations and experiences diverge even in this case, it would suggest that the paradox is not solely about adaptation to disability but also reflects general cognitive biases in how people anticipate the consequences of health conditions. People may overestimate how much a condition, or even the risk of a condition, will impact daily life. The current research addresses this possibility by examining the expectations versus experiences of individuals who know they have a genetic risk for Alzheimer's disease (AD) dementia, but who do not (yet) have any impairments associated with the condition. In doing so, we focus specifically on expectations versus experiences of stigma.

Stigma and Genetic Risk for AD

Stigma occurs when people are labeled as different, associated with negative stereotypes, and socially excluded or devalued as a result (Link & Phelan, 2001). Importantly, stigma includes

not only the negative reactions of others (public stigma) but also individuals' own anticipation of rejection and discrimination (internalized stigma). When a person is aware that they have been labeled as a current or future member of a stigmatized group it can lead them to expect devaluation, monitor for signs of discrimination, and even internalize negative stereotypes, ultimately shaping their self-concept and behavior in harmful ways (Link et al., 1989).

Perception of genetic information often contains essentialist beliefs, such that people view genes as central to identity and strongly deterministic of behavior (Dar-Nimrod & Heine, 2011). As a result, asymptomatic carriers of risk-conferring genetic alleles can internalize these beliefs in the form of self-stigma, in which being labeled with a specific genotype leaves them feeling fundamentally different and permanently "at risk". This perception can trigger stereotyping and loss of social status, even in the absence of any symptoms or current impairment (Billings et al., 1992; Taylor et al., 2008). Evidence of genetic risk stigma has now been reported for multiple conditions. For example, adults who learn they carry the Huntington's-disease mutation often report negative social interactions, employment discrimination, and heightened concerns about future discrimination specifically because of their genetic risk (Erwin et al., 2010). Comparable experiences of stigma have also been documented among BRCA mutation carriers who are at increased risk of developing breast and ovarian cancer (Wauters & Van Hoyweghen, 2018) and among at-risk relatives of colorectal patients (Apse et al., 2004).

In the context of AD, people can also experience stigma when they carry apolipoprotein (*APOE*) *ε4* alleles. Of the three major *APOE* alleles (*ε2, ε3,* and *ε4*), carrying one, or especially two, copies of *ε4* confers a higher risk for developing AD dementia (Qian et al., 2017). Consistent with broader findings on genetic risk stigma, asymptomatic individuals who learn they are *ε4* carriers report concerns about stigma and discrimination, worrying that if others learned of their

genetic status they would be viewed or treated differently (Largent et al., 2021). Related work demonstrates that the public stigmatizes cognitively unimpaired individuals when they are described as having an elevated risk for AD based on biomarker test results (Stites, Gill, et al., 2022). Together, these findings highlight that stigma can occur based upon AD risk, even when there are no observable impairments based upon that risk.

Anticipated versus Experienced Stigma

Although prior work documents experiences of stigma for people who have learned they have an increased AD risk, far less is known about the stigma people *expect* to experience *before* learning this information. However, some recent research shows that some cognitively unimpaired adults expect to experience stigma in these cases. Clark et al. (2022), for instance, found that roughly one-quarter of respondents feared that an elevated AD biomarker result would cause their doctor, family, friends, or coworkers to treat them differently. Subsequent research showed that these AD stigma expectations are especially common among individuals with a lower internal health locus of control and those without a family history of AD (Clark et al., 2023).

Prior studies have confirmed the safety of returning *APOE* genotype results to individuals screened for psychological readiness (Ashida et al., 2010; Green et al., 2009). However, we are aware of only one study that assessed stigma perceptions before and after disclosure of *APOE* test results. Christensen et al. (2011) found that worries about employment discrimination were greater 12-months post-disclosure than at baseline (pre-disclosure). However, this sample was relatively young (Median age = 57 years), mostly still employed, and all participants were relatives of family members with AD dementia. In contrast, older individuals undergoing screening for an AD prevention trial may have more immediate concerns about stigma.

Current Study

In this study, we compared the expected and experienced stigma associated with knowledge of a heightened risk for AD dementia, such as the risk conveyed by an *APOE ε4* genotype test result. To do so, we recruited older adults who all underwent *APOE* testing, and either knew or did not know the test results. Participants who knew their *APOE* genotype reported on the actual stigma they experienced due to this knowledge whereas those who did not know their *APOE* genotype reported on the stigma they expected to face if they were found to be at an elevated risk for AD. We tested two competing hypotheses regarding the relationship between experienced and expected AD stigma. On the one hand, based upon the results reported by Christensen et al. (2011), it is possible that people underestimate AD stigma, such that experienced AD stigma is greater than expected AD stigma. On the other hand, based upon numerous studies documenting the disability paradox (for reviews, see Peeters & Stiggelbout, 2010; Ubel et al., 2005), it is possible that expected stigma is substantially higher than what individuals report experiencing. We tested these predictions both cross-sectionally and longitudinally. In doing so, this study advances our understanding of the effects of genetic risk disclosure and evaluates whether the disability paradox may extend to individuals who are at risk for disease and disability, even in the absence of current impairments.

Methods

Transparency and Openness

All procedures were approved by the Western Institutional Review Board (Protocol #20180837), but study procedures and analyses were not pre-registered. The data reported here were collected as part of the Cognition Across Time (CAT) Study. No findings from the CAT Study have been previously published. The study materials and the data that support the findings

of this study are available from the corresponding author upon reasonable request from any qualified investigator.

Sample

The data come from the CAT Study, a multi-session online study conducted between July 2018 and December 2019. The primary objective of the CAT Study was to examine the impact of *APOE* genotype, and knowledge of that genotype, on cognition across time. A total of 404 older adults (ages 60-75) participated. All participants lived in the United States, were fluent in English, and were required to have at least 6 years of regular schooling.

Participant Recruitment and *APOE* Genotyping

CAT Study participants were recruited from the Alzheimer's Prevention Initiative's GeneMatch program, which is a registry of individuals interested in enrolling in AD-focused studies (Langbaum et al., 2019). As part of GeneMatch enrollment, participants provided a cheek swab for *APOE* genotyping by a Clinical Laboratory Improvement Amendments certified lab (clinicaltrials.gov NCT02564692). Participants did not receive their *APOE* results from GeneMatch, but they consented to allow their genotype to be shared with the CAT Study research team.

The CAT Study itself did not disclose *APOE* results to participants. However, the CAT Study was conducted in parallel with the Generation Program clinical trials (clinicaltrials.gov NCT02565511 and NCT03131453), which did provide disclosure of *APOE* status as part of eligibility screening (Lopez Lopez, et al., 2019). All CAT Study participants had expressed interest in the Generation Program, and some underwent its eligibility screening before or during their participation in the CAT Study. As a result, some CAT Study participants learned their *APOE* test results through the Generation Program clinical trials. These results were disclosed by

a trained and licensed genetic counselor, physician, or healthcare provider, who also explained the heritability of *APOE* genotypes and provided probabilistic estimates of developing AD dementia based on *APOE* genotype (Langlois et al., 2019). Other CAT Study participants either did not complete the Generation Program screening or completed it only after finishing all CAT Study procedures and thus remained unaware of their *APOE* genotype throughout their participation in the CAT Study.

Measure

We used a modified version of the Social Impact Scale (SIS) to assess expected and experienced AD stigma. The SIS is a self-report questionnaire that measures the social impact of stigmatization (Fife & Wright, 2000). This conceptualization of stigma is based on modified labelling theory (Link et al., 1989). A key component of this theory is internalized stigma, which is a sociological concept that explains how individuals can internalize negative societal beliefs. Items on the SIS assess internalized shame, social rejection, social isolation, and financial insecurity, with responses contributing to a unidimensional stigma construct (Fife & Wright, 2000). Responses to SIS items are given on a 4-point scale from strongly disagree to strongly agree, with scores of 3 and 4 indicating levels of agreement. Higher scale scores indicate more severe adverse social consequences.

In this study, we focused on AD stigma, and how it may emerge due to knowledge of a genetic test result associated with heightened risk for AD. To adapt the original scale to the context of AD stigma, we modified the SIS (mSIS) by dropping one item ("*Changes in my appearance have affected my social relationships*") and tailored the language of the items to AD dementia. The mSIS included 23 items. Factor loadings are shown in Supplemental Table 1, and internal consistency reliability (Cronbach's alpha) is 0.93 (see also Supplemental Table 2).

We varied the instructions for completing the mSIS based upon participants' self-reported knowledge of their *APOE* genotype. Participants who reported knowing their *APOE* genotype were assigned to the *experiential group* and indicated their level of agreement that each mSIS statement reflected their own experiences since learning their risk of developing AD dementia. Participants who reported not knowing their *APOE* genotype were assigned to the *hypothetical group*. These participants were asked to imagine learning that they were at risk for AD dementia and indicated their level of agreement that each mSIS statement would reflect their experiences in this scenario. The mSIS scale and its instructions are shown in the Appendix.

CAT Study Procedures

Participants completed online surveys, administered on the following schedule:

- Time 0 (baseline)
- Time 1 (around 6 to 9 weeks after baseline)
- Time 2 (around 6 months after baseline)

All participants provided informed consent. At each timepoint, participants were asked whether they knew their *APOE* genotype.[1] For those that answered affirmatively, they were asked to report the result. At each timepoint participants also completed cognitive assessments and questionnaires, including a demographic questionnaire (Time 0 only). The current study focused specifically on AD stigma. This was assessed via the mSIS (see Measures above), which was included as part of the study questionnaires administered at Times 1 and 2, administered at the end of each of these study sessions. As compensation, participants received an electronic $10 Amazon gift card after completing each administration.

[1] Some of the clinical trial protocols also involved disclosure of brain amyloid results, and CAT Study participants were also asked to report whether they knew these results. As shown in Table 1, only 6 participants were aware of these results at Time 0, and knowledge of brain amyloid results was therefore not considered in the current research.

Group Assignment for Analyses

Study analyses use data from the 291 CAT Study participants who completed the mSIS at Time 1. Of these, 180 participants reported not knowing their *APOE* test result at Time 1, and they were assigned to the *hypothetical* group. The remaining 111 participants reported knowing their *APOE* test result at Time 1 and were assigned to one of two *experiential groups* based on their test result. One experiential group (n=65) was comprised of *APOE ε4* carriers and will be referred to as the *ε4 carrier experiential group*. The other experiential group (n=46) was comprised of *APOE ε4* non-carriers and will be referred to as the *ε4 non-carrier experiential group*.

Among the experiential group participants, the majority (n = 68) learned their *APOE* genotype between Time 0 and Time 1 (n = 40 the *ε4 carrier experiential group* and n = 28 in the *ε4 non-carrier experiential group*). The remaining participants (n = 43) already knew their *APOE* genotype before beginning the Time 0 session (n = 25 in the *ε4 carrier experiential group* and n = 18 in the *ε4 non-carrier experiential group*).

Of the 291 participants who completed the mSIS at Time 1, 150 also completed the mSIS at Time 2, which allowed us to analyze change in mSIS endorsement over time. In analyses comparing mSIS between Time 1 and 2, we excluded three participants who knew their *APOE* result at Time 1 but no longer remembered it at Time 2, resulting in a final Time 2 sample of 147. Of these 147 participants, 19 learned their *APOE* test result between the Time 1 and Time 2 assessment. The flowchart (Figure 1) illustrates these group assignments.

Power Analyses

Sensitivity power analyses were conducted using Stata to determine the minimum detectable effect sizes given our sample size. These analyses indicated that the study had 80%

power to detect a standardized mean difference of .339 on the mSIS when comparing the hypothetical group to the full experiential group, and 80% power to detect a standardized mean difference of .407 on the mSIS when comparing the hypothetical group specifically to the *ε4* carrier experiential group. The mSIS scores were also compared at Time 1 (6 to 9 weeks after baseline) and Time 2 (6 months after baseline), with participants serving as their own controls. Within these longitudinal analyses, we compared participants who were in the same study group at both time points, as well as a small subgroup (n = 19) who converted from the hypothetical group to the experiential group. For this smallest subgroup, the sensitivity analysis indicated 80% power to detect a standardized mean difference of at least .636 on the mSIS.

Results

We considered mean differences to be statistically significant when the 95% confidence interval did not include zero, which is equivalent to $p < .05$. All analyses were conducted in Stata v 17.0 and R v 1.4.

Sample Characteristics

Sample characteristics were similar in the hypothetical and experiential groups. The hypothetical group was an average of 68 years old and majority women (62%, Table 1). Most participants in the hypothetical group were at least college graduates (69%), married (72%), retired (74%) and self-identified as White (96%). Similarly, the experiential group was an average of 69 years old and about half women (52%). Most participants in the experiential group were at least college graduates (77%), married (80%), retired (77%) and self-identified as White (96%). Demographic characteristics were also similar between the *ε4* carrier and *ε4* non-carrier experiential groups (Table 1).

Expected versus Experienced AD Stigma: Study Group Comparisons at Time 1

To examine how expectations of AD stigma compared with actual experiences, we compared mean mSIS scores at Time 1 between the hypothetical group and the *ε4* carrier experiential group. This analysis tested whether participants imagining the impact of elevated AD risk differed from those who knew they were at heightened risk for dementia due to their *APOE ε4* status.

As shown in Figure 2, the distribution of mean mSIS scores differed between the hypothetical and *ε4* carrier experiential groups. Scores in the hypothetical group were fairly normally distributed, whereas scores in the *ε4* carrier experiential group clustered heavily at the lowest scale value, consistent with a zero-inflation distribution. Visual inspection suggested that compared with the hypothetical group, participants in the *ε4* carrier experiential group were more likely to give very low ratings, indicating little endorsement of AD stigma. This difference was confirmed in between-group comparisons. At Time 1, the mean mSIS score was 1.83 points (95% CI [1.67, 1.98]) in the hypothetical group and 1.13 points (95% CI [0.90, 1.36]) in the *ε4* carrier experiential group (Table 2). The non-overlapping confidence intervals indicated a statistically significant difference ($p < .05$), which was corroborated by a Kruskal-Wallis test that accounted for the non-normal score distribution, $X^2 = 93.14$, $p < .0001$.[2] Thus, although hypothetical participants anticipated moderate AD stigma, the *ε4* carriers aware of their *APOE* genotype reported much lower levels of experienced AD stigma.[3]

Even though the mean mSIS scores significantly differed between the two groups, both fell below a rating of 2, reflecting a general tendency toward disagreement with the mSIS statements. To better capture the extent to which participants in the two groups agreed with the

[2] All subsequent group comparisons were also confirmed using Kruskal–Wallis tests and the conclusions were consistent across analytic approaches.
[3] In analyses stratified by self-reported sex and age, patterns of data were similar for men and women and between those who were younger and older than the median sample age (Supplemental Table 3).

mSIS items, we next dichotomized responses as "agree" versus "disagree" and calculated percent agreement across items. This complementary approach quantifies the magnitude of group differences in affirmation of the mSIS items. This approach also enhances the clinical interpretability of the findings as affirmation (e.g., agree vs. disagree) is typically easier to identify and act upon in clinical settings as compared to fine gradations of disagreement (e.g., disagree vs. strongly disagree). It also sets a higher threshold and is suggestive of differences that may be more likely to reflect concerns warranting clinical attention. The dichotomized analysis again revealed differences in AD stigma between the groups. Participants in the hypothetical group agreed with 26.1% of the mSIS statements (95% CI [23.0, 29.1]), compared with only 2.3% (95% CI [1.1, 3.6]) in the *ε4* carrier experiential group. These findings indicate that anticipated AD stigma in the hypothetical group was substantially greater than the AD stigma experienced by *APOE ε4* carriers aware of their genotype. The full tabled data using the dichotomized scores are shown in Supplemental Table 3.

Item-Level Differences in mSIS Responses at Time 1

The largest discrepancies in mSIS responses between the hypothetical group and the *ε4* carrier experiential group centered on competence and social belonging (Table 3). Specifically, mean differences were greatest for the following three items: "*Some people act like I am less competent*" (Mean difference = 1.35 points, 95% CI [1.14, 1.55]), "*I have a greater need than usual for reassurance that others care about me*" (Mean difference = 1.02 points, 95% CI [0.75, 1.17]), and "*I feel set apart from others who are well*" (Mean difference = 0.96 points, 95% CI [0.75, 1.17]). In each case, the expected AD stigma in the hypothetical group exceeded the experienced AD stigma in the *ε4* carrier experiential group. Importantly, the pattern of items with the largest discrepancies was generally consistent across analytic approaches (mean ratings and

dichotomized agreement; see Supplemental Figure 1). A similar distribution of agreement was also observed in the *ε4* carrier experiential group as with the full experiential sample, which combined both *ε4* carriers and non-carriers (see Supplemental Table 3).

Comparison of Study Groups Between Time 1 (6-Weeks) and Time 2 (6-Months)

A small group of 19 individuals in the hypothetical group at Time 1 learned their *APOE* test result before the Time 2 assessment. All learned that they were *ε4* non-carriers. These individuals were therefore in the hypothetical group at Time 1, but in the *ε4* non-carrier experiential group at Time 2 (see Figure 1 for a flowchart). Among these individuals, expected AD stigma at Time 1 was greater than experienced AD stigma at Time 2. At Time 1, this group had a mean mSIS score of 1.89 points (95% CI [1.66, 2.13]), and this agreement decreased by 0.7 points (95% CI [-0.82, -0.35]) at Time 2.

For the remaining 128 participants who completed the mSIS at both Time 1 and Time 2 group assignment remained unchanged (i.e., participants remained in either the hypothetical or experiential group at both timepoints). For these participants, we examined how agreement with mSIS statements varied over time and tested whether this differed for those in the experiential (*ε4* carriers: n = 36, *ε4* non-carriers: n = 27) and hypothetical (n = 65) groups. At Time 1, the mean mSIS score in the hypothetical group was 1.88 points (95% CI [1.76, 1.99]), which increased by 0.11 points (95% CI [0.002, 0.21]) at Time 2. In the *ε4* carrier and *ε4* non-carrier experiential groups at Time 1, overall agreement with mSIS items was 1.15 points (95% CI [1.09, 1.21]) and 1.11 points (95% CI [1.00, 1.22]), respectively (Table 4). Change in mSIS scores from Time 1 to Time 2 in the *ε4* carrier and *ε4* non-carrier experiential groups did not reach statistical significance, with numerical increases of only 0.11 points (95% CI [-0.03, 0.12]) and 0.04 points (95% CI [-0.02, 0.11]), respectively.

Comparisons at Time 1 in the Experiential Study Group by Time 0 Genotype Knowledge

In this study, we did not specifically assess when participants learned their *APOE* genotype. However, some individuals knew their *APOE* status at Time 0 (upon entry into the study; n = 68) and some individuals only found out this information between Time 0 and Time 1 (n = 43). We tested whether experienced AD stigma reported at Time 1 differed between these two experiential groups. Comparison between the mean mSIS scores in these two groups at Time 1 was statistically significant (mean difference = 0.10, 95% CI [0.01, 0.21]) with higher AD stigma among those who had known their *APOE* genotype for longer. This pattern was also present, but not statistically significant (mean difference = 0.06, 95% CI [-0.02, 0.08], when restricting analyses to the small subgroup of ε4 carriers. Among these individuals, experiences of AD stigma at Time 1 were numerically greater among individuals who had known they were *APOE ε4* carriers for longer. The group of *ε4* carriers who already knew their genetic status at Time 0 (n = 25) had a mean mSIS score of 1.28 points (95% CI [1.09, 1.47]), compared to the group of *ε4* carriers who learned their genetic status in the few weeks prior to the first mSIS assessment (n = 40), who had a mean mSIS score of 1.11 points (95% CI [1.03 to 1.19]).

Discussion and Implications

This study examined the relationship between expected and experienced AD stigma. We recruited older adults who either knew their *APOE* genotype (experiential group) or did not know their *APOE* genotype (hypothetical group). The experiential group reported actual stigma experienced due to their risk for AD dementia, while the hypothetical group reported the stigma they anticipated if found to be at risk for AD dementia. Our primary finding was that anticipated stigma exceeded experienced stigma by a wide margin, with mean agreement with the mSIS

statements in the hypothetical and *ε4* carrier experiential groups of *APOE ε4* carriers at 26.1% and 2.3%, respectively.

Beyond overall differences in stigma, it is also informative to consider where specific expectations and experiences most diverged between the groups. In the hypothetical group, the highest-rated concern was "*some people would act as though I am less competent than usual*," reflecting anticipated negative judgments from others. By contrast, among ε4 carriers in the experiential group, the highest-rated concern was "*I feel less competent than I did before*," reflecting a more internalized, self-directed worry. Competence-related concerns thus emerged as the most common issue overall, but their focus shifted: individuals unaware of their *APOE* genotype anticipated external stigma tied to heightened AD risk, whereas those aware that they were *ε4* carriers were most likely to report concerns related to self-perceptions of competence.

Theoretical Implications: The Disability Paradox

The findings from this study are consistent with prior research on the disability paradox and extend it in important ways. Prior work shows that the public often anticipates a much lower quality of life for people with chronic health conditions than those individuals report experiencing (for reviews, see Peeters & Stiggelbout, 2010; Ubel et al., 2005). In the present study, a similar discrepancy emerged between the "haves" (those who knew they carried a heightened genetic risk for AD) and the "have nots" (those who only imagined being at risk for AD) even in the absence of any functional impairment among the "haves". This pattern suggests that the disability paradox cannot be explained solely by the public underestimating patients' capacity to adapt once illness occurs. Instead, it points to a broader cognitive bias in which people assume that the mere possibility of future impairment diminishes current life outcomes, even when symptoms are absent.

Our findings also support another explanation of the disability paradox, which is that people imagining life with a condition often lack the detailed knowledge needed to predict its actual impact. In our study, participants in the hypothetical group imagined learning they were at risk for AD dementia but were not given concrete probability information about what this risk entailed. As a result, they may have assumed that having a heightened risk was equivalent to an almost certain diagnosis in the near future, thereby inflating their stigma expectations. In contrast, participants in the experiential condition responded based upon the concrete risk information they learned. For example, the *ε4* heterozygotes were likely told that their risk of developing dementia was 20-25% through age 85 (Stites, Vogt, et al., 2022). Asymmetry in risk understanding between the hypothetical and experiential groups may also have contributed to differences between expected and experienced stigma.

Longitudinal Trends in AD Stigma

In this study, we also examined changes in AD stigma over time. Among the small subgroup of 19 participants who transitioned from the hypothetical group at Time 1 to the ε4 non-carrier experiential group at Time 2, stigma decreased. This pattern is unsurprising, as at Time 1 these participants imagined facing stigma if they had a heightened AD risk but later reported their actual experiences of stigma after learning they were not at heightened risk.

More interesting were the changes in AD stigma over time among participants whose group membership remained stable across assessments. In the hypothetical group (n = 65), mean mSIS scores showed a small but statistically significant increase over six months. In contrast, mean mSIS scores in both the *ε4* carrier (n = 36) and non-carrier (n = 27) experiential groups showed only slight increases over time that did not reach statistical significance. Together, these findings suggest that repeatedly imagining being at risk may amplify concerns about stigma,

whereas knowing one's *APOE* genotype does not appear to worsen stigma over short intervals, even among *ε4* carriers.

However, a different pattern emerged in our cross-sectional analyses. At Time 1, the *ε4* carriers who knew their genetic status longer (i.e., knew their test result before entering the study at Time 0) had higher scores on the mSIS than *ε4* carriers who more recently learned their genetic status (i.e., learned their test result between Time 0 and Time 1). This could suggest that concerns about stigma may build over time as individuals have more opportunities to reflect on or encounter situations where their genetic risk could become salient. Another possibility is that over time, even in the absence of clinical impairment, some carriers begin attributing everyday memory lapses or interpersonal experiences to their genetic status, heightening perceived vulnerability. It is also possible that this trend reflects unmeasured differences between those who sought out testing earlier versus more recently, rather than the passage of time itself.

When considered together, the longitudinal findings suggest that in the short term, stigma among *ε4* carriers is relatively stable. However, the cross-sectional findings suggest that over longer periods, concerns may accumulate. Additional research is needed to clarify these trajectories and mechanisms. This line of research may aid in supporting efforts to guide care for individuals learning their risk of AD dementia.

Clinical Considerations

The findings from this study are informative for clinical discussions with individuals considering learning their *APOE* status. *APOE* testing in clinical contexts is becoming increasingly common as it can determine entry into AD prevention trials (Langlois et al., 2019). In addition, following the recent Food and Drug Administration's approvals of new drugs for early AD treatment expert groups now recommend *APOE* genotyping and disclosure to guide

clinical treatment decisions, since *APOE ε4* carriers are at heightened risk of medication-related adverse events (Cummings et al., 2023; Rabinovici et al., 2025; van Dyck et al., 2023). Efforts are underway to help guide clinicians in these conversations (Stites et al., 2022), and this current study contributes to those efforts.

Our results suggest that, particularly prior to *APOE* testing, individuals may have concerns about AD stigma. Clinicians may find it helpful to address these concerns during pre-test discussions, by correcting misinformation, setting realistic expectations, and referring individuals to mental health or social support resources as needed (Stites & Karlawish, 2018).

For individuals who had already learned their *APOE* test results, we found that experienced AD stigma was low, but it was not absent. Regardless of *APOE ε4* carrier status, the most common concerns in the experiential group included feeling less competent, needing to keep their risk secret, and not feeling open about their risk. While the overall base rates were low, these issues may be beneficial topics for follow-up discussions with individuals who have learned their genetic results.

Comparison of the Current Results to Christensen et al. (2011)

The key finding in this study was that anticipated stigma exceeded experienced stigma. However, this contrasts with results reported by Christensen et al. (2011), who instead observed increases in fears of discrimination post-*APOE* disclosure. Several factors may explain this discrepancy.

First, it is important to note that the two studies measured different constructs. Our study directly compared expected versus experienced AD stigma, whereas Christensen et al. focused on the perceived pros and cons of AD genetic testing more broadly. As a result, their participants'

responses likely reflected general concerns about how genetic testing is viewed in society, rather than their own lived experiences of stigma.

Second, the studies differed in timing. Christensen et al. (2011) compared perceptions before *APOE* disclosure with those 12-months after disclosure. Although we did not assess when participants in the current study learned their *APOE* result, 65% of participants in the experiential groups became aware of their result between Time 0 and Time 1 of the CAT Study, meaning they had only known their result for a few weeks. If stigma experiences evolve over time, this could explain the difference in findings between the two studies.

Third, the participant samples differed. Christensen et al.'s (2011) sample consisted of adults aged 33-86, with 66% of their participants currently employed. In contrast, our sample was relatively older (ages 60-75) and largely retired (only 25% currently employed). Because Christensen et al. found significant post-disclosure increases only in employment-related discrimination fears, this effect may not have been detectable in our primarily retired sample.

Finally, the broader context of genetic testing and AD research has shifted over the past decade. Public awareness of genetic testing has increased sharply, rising from approximately 57% in 2017 to 81% in 2022 (Makhoon et al., 2024; Tiner et al., 2022). The use of genetic tests has also grown. In a 2022 nationally representative U.S. survey, 40% of adults reported having completed at least one genetic test (Makhoon et al., 2024). This greater familiarity and acceptance of genetic testing may have normalized *APOE* disclosure, making it less socially threatening today than when Christensen et al. (2011) conducted their study.

Limitations

Several limitations of this study should also be acknowledged. This study used a convenience sample of individuals who registered to participate in AD research and underwent

APOE testing. High endorsement of anticipated AD stigma is therefore somewhat unexpected, as stigma is a known barrier to research participation (e.g., Garand et al., 2009). Many participants expected that being found to have an elevated AD dementia risk would mean being treated as less competent, personally feel less competent, and be set apart from others. Nonetheless, these individuals agreed to learn their *APOE* test result as part of the screening process for the Generation Program clinical trials, suggesting that these participants were willing to confront negative expectations to be part of AD research. The finding also raises an important question for future research: what amount of anticipated stigma deters individuals from participating?

As noted previously, another limitation is that we did not assess how or when participants learned their *APOE* result. Most participants in the two experiential groups (65%) acquired this information between Time 0 and Time 1 of the CAT Study. We assume this knowledge was obtained through the formal disclosure process in the Generation Program clinical trials, but because we did not ask, we cannot know this for certain. The disclosure process in the Generation Program trials is a tested, evidence-based process, where individuals receive counseling and education by trained experts (Langlois et al., 2019). We do not know whether experienced AD stigma would be low in individuals who learn their *APOE* result through other methods (e.g., direct-to-consumer services) that lack this scaffolding.

Most participants in this study were at least college graduates, married, retired and self-identified as White. These characteristics are fairly consistent with those of individuals participating in observational studies and AD prevention trials but they are not representative of the populations most affected by AD. It is unknown whether this study's results would generalize to populations with different characteristics or over longer periods.

Additionally, our study groups that did and did not know their *APOE* test result were similar on all but one assessed characteristic. Those who knew their *APOE* result rated their health status, on average, better than those who did not know their result (see Table 1). However, it is unclear whether the average difference of 0.02 points in self-rated health (on a 1 to 9 scale) is clinically meaningful, and the underlying reason for the difference is unknown. Possible explanations may relate to the study's context, as individuals with worse health may have self-selected out of participating in the Generation Program clinical trials, or may have been screened out, and hence may not have learned their *APOE* test result. It is also possible that *ε4* carriers aware of their *APOE* status evaluated their current health relative to expectations of future decline, leading them to rate their current health somewhat more favorably. This issue requires further investigation.

Finally, it should also be noted that the mSIS was administered at the end of each study session, following a battery of cognitive assessments. We cannot rule out the possibility that performance on these assessments may have influenced participants' responses on the mSIS. However, this procedure was consistent across all participants, including those in both the hypothetical and experiential groups, so any such effects would have applied equally across study conditions.

Conclusion

This study compared the AD stigma that people *expected* to experience upon learning they were at a heightened risk for dementia with the experience of AD stigma *actually reported* by people who knew they had a heightened risk for dementia based upon their *APOE* test results. Across analyses, stigma expectations were consistently higher than reported experiences. These findings suggest that the disability paradox is not only a product of individuals adapting to life

with illness but also of observers misjudging what such risks entail. Clinically, these findings highlight opportunities to support people considering *APOE* testing by addressing how people anticipate and experience stigma, which could help guide pre-test counseling and informed decision-making.

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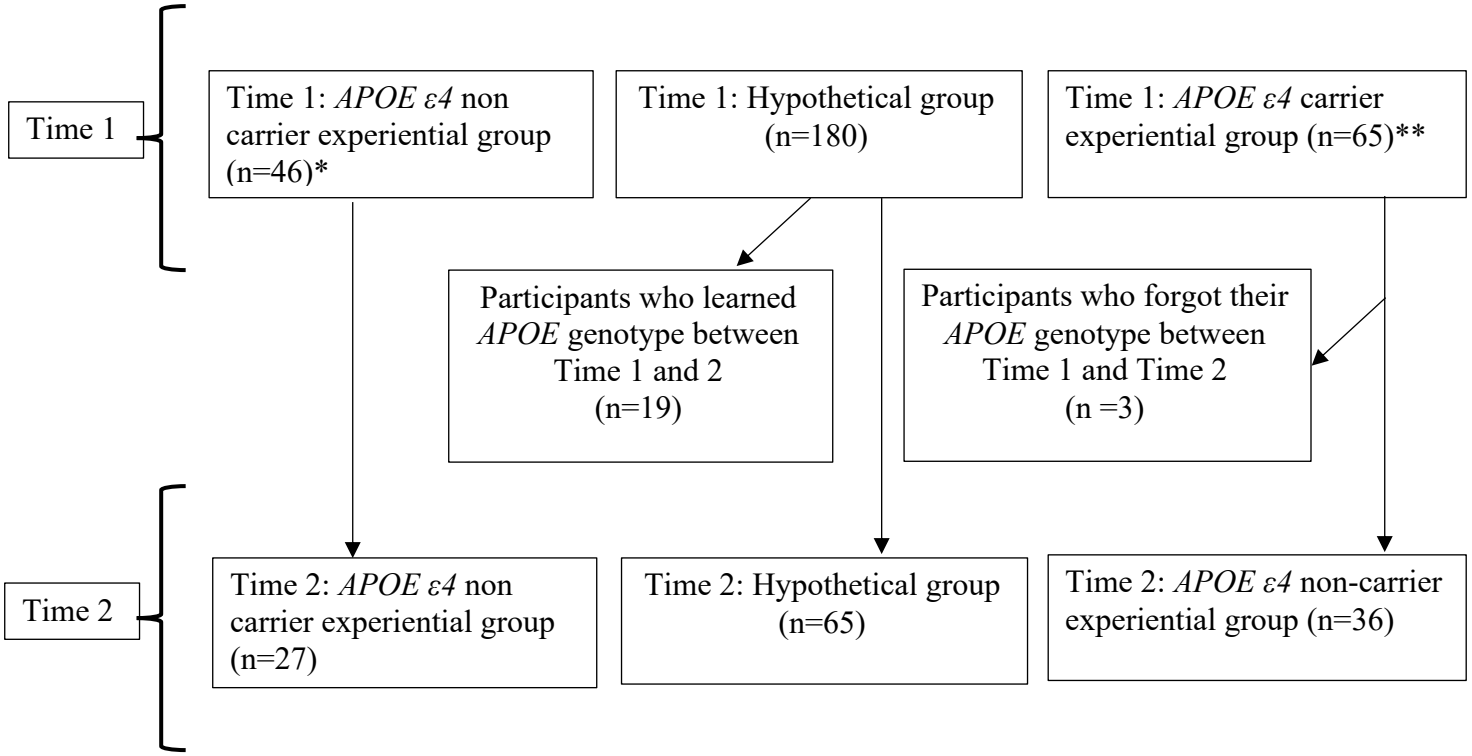
Tables & Figures

Figure 1

Assignment of Study Groups and Timeline of Data Collection of the Modified Social Impact Scale (mSIS)



Note. The CAT Study involved multiple online sessions. Time 1 occurred 6-9 weeks after the baseline Time 0 assessment and Time 2 occurred about 6 months after the baseline Time 0 assessment. The mSIS was collected at Times 1 and 2**.** Time 0 is not represented here as the mSIS was not collected at this visit.

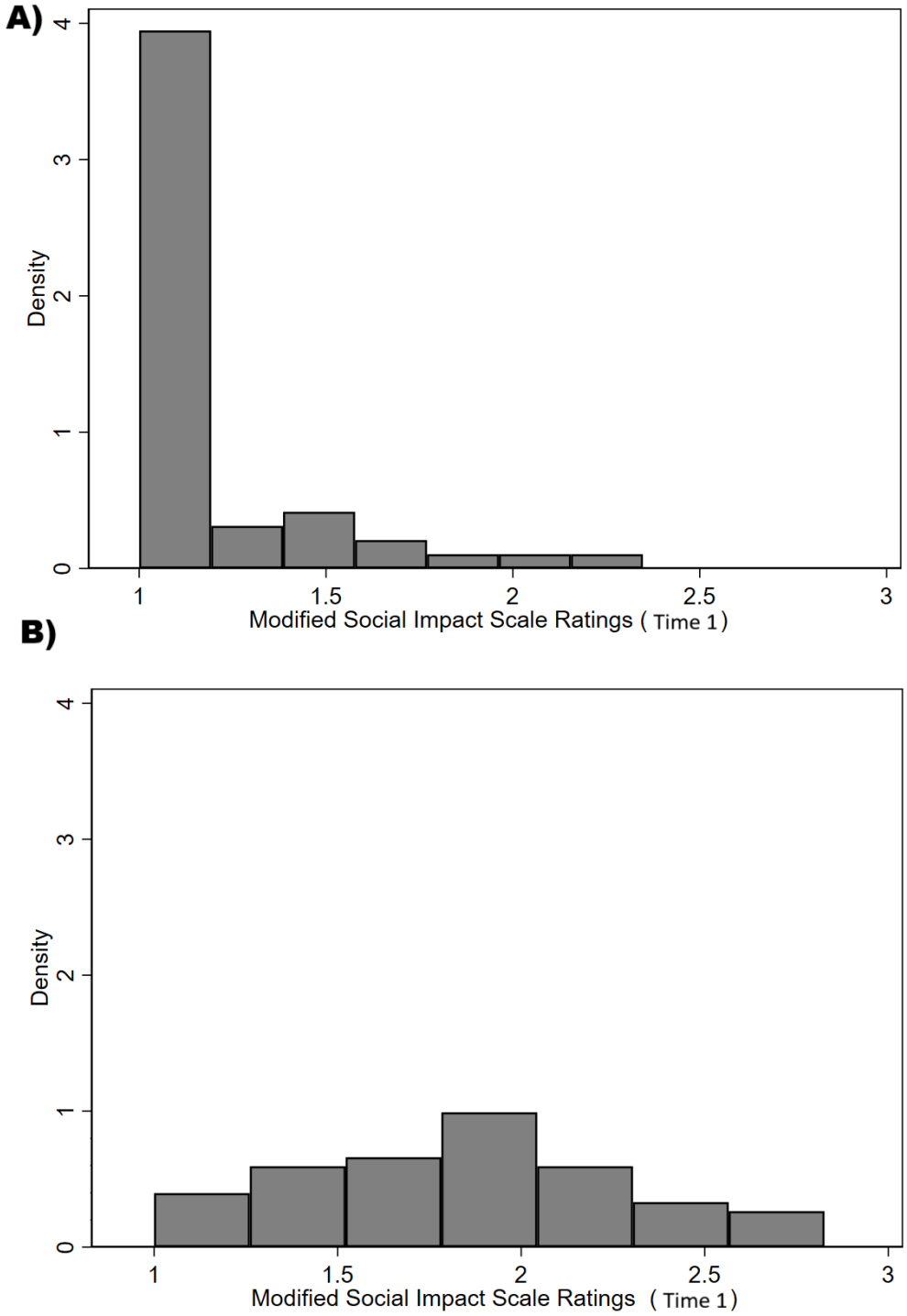
*18 of 46 knew their APOE test result at Time 0.
** 25 of 65 knew their APOE test result at Time 0.

Table 1.
Cognition Across Time (CAT) Study Sample Characteristics by Study Groups

Demographic and clinical characteristics	Experiential group All (n=111)	*ε4* Carriers (n=65)	*ε4* Non-carriers (n=46)	Hypothetical group (n=180)	*p*-value[a]	*p*-value[b]
Demographic characteristics						
Age, mean (SD)	68.7 (2.97)	69.0 (2.60)	68.2 (3.44)	68.4 (3.33)	0.17	0.14
Women, % (n)	52.2 (58)	50.8 (33)	54.3 (25)	61.7 (110)[c]	0.72	0.11
White, % (n)	96.3 (107)	98.5 (64)	93.4 (43)	95.6 (172)	0.16	0.49
Retired, % (n)	77.4 (86)	78.5 (51)	76.1 (35)	73.9 (133)	0.76	0.57
Education, % (n)						
High school	3.6 (4)	6.2 (4)	0 (0)	3.3 (6)	0.09	0.54
Some college/2-year degree	18.9 (21)	13.9 (9)	26.1 (12)	26.7 (48)	0.11	0.05
4-year degree or greater	77.4 (86)	80.0 (52)	73.9 (34)	69.4 (125)	0.44	0.14
Marital status [d]						
Married, % (n)	80.2 (89)	84.6 (55)	73.9 (34)	72.2 (130)	0.16	0.07
Divorced, % (n)	11.7 (13)	9.2 (6)	15.2 (7)	17.8 (32)	0.33	0.15
Widowed % (n)	5.4 (6)	6.2 (4)	4.4 (2)	5.6 (10)	0.68	>0.99
Clinical characteristics						
Family history of AD, % (n)	78.4 (87)	80.0 (52)	76.1 (35)	77.2 (139)	0.62	0.07
Overall health,[e] mean (SD)	7.67 (0.93)	7.75 (0.94)	7.62 (0.83)	7.40 (1.17)	0.45	0.04[x]
Knowledge at Time 0						
APOE result, % (n)	38.7 (43)	38.5 (25)	39.1 (18)	0	<0.001[z]	<0.001[z]
Amyloid result,[f] % (n)	2.7 (3)	3.1 (2)	2.2 (1)	0	0.77	<0.01[z]
Knows APOE result at Time 1						
ε4 homozygote, % (n)	9.9 (11)	16.9 (11)	0	0	0.003[y]	<0.001[z]
ε4 heterozygote, % (n)	48.6 (54)	83.1 (54)	0	0	<0.001[z]	<0.001[z]
ε4 non-carrier, % (n)	41.4 (46)	0	100 (46)	0	<0.001[z]	<0.001[z]

Note. Hypothetical group = participants who did not know their *APOE* status; Experiential group = participants who knew their APOE carrier status. Group comparisons were conducted using chi-square tests for categorical variables, Kruskal–Wallis tests for ordinal variables, and *t*-tests for continuous variables.
[a] *p*-value for *ε4* carriers vs non-carriers
[b] *p*-value for experiential vs hypothetical group
[c] Two participants in the hypothetical group did not report sex
[d] Two participants reported never being married. One participant reported being separated.
[e] Participants were asked to describe their overall health on a scale of 1 to 9, where higher scores indicated better health.
[f] Knowledge derived from either cerebrospinal fluid (CSF) or positron emission tomography (PET) scan data.
[x] <0.05 [y]<0.01 [z]<0.001

Figure 2.
Histograms of Average mSIS Scores at Time 1 for the Hypothetical Group (Panel A) and the ε4 Carrier Experiential Group (Panel B)



Note. The CAT Study included multiple online sessions; Time 1 was conducted 6–9 weeks after the baseline (Time 0) assessment.

Table 2
Modified Social Impact Scale (mSIS) Scores by Study Group at Time 1

Study group	mSIS Score (1-4 scale)	mSIS Percent Agreement Score (dichotomized responses)
	Mean (95%CI)	Mean (95%CI)
Hypothetical group (n=180)	1.83[w,x] (1.67 to 1.98)	22.7[y,z] (19.7 to 30.0)
Experiential group (n=111)	1.04[w] (0.99 to 1.10)	2.3[y] (1.1 to 3.6)
ε4 Carriers (n=65)	1.13[x] (0.90 to 1.36)	2.3[z] (0.1 to 3.8)
ε4 Non-carriers (n=46)	1.0 (0.95 to 1.05)	2.4 (0.1 to 4.6)

Note. The *mSIS Score* column presents the mean across the full 1–4 response scale, with higher scores indicating greater agreement with AD stigma-related statements. The *mSIS Percent Agreement Score* column presents the proportion of items endorsed after dichotomizing responses (agree vs. disagree) and averaging across items. The experiential group (EG) refers to participants who knew their APOE test result, whereas the hypothetical group (HG) refers to participants who underwent APOE testing but did not know their result. The CAT Study included multiple online sessions; Time 1 was conducted 6–9 weeks after the baseline (Time 0) assessment. 95% CI = 95% confidence interval.

[w]p-value for experiential vs hypothetical group, $p < .001$
[x]p-value for ε4 carriers vs hypothetical group, $p < .001$
[y]p-value for experiential vs hypothetical group, $p < .001$
[z]p-value for ε4 carriers vs hypothetical group, $p < .001$

Table 3

Modified Social Impact Scale (mSIS) Items Showing the Six Largest Differences Between the ε4 Carrier Experiential Group and the Hypothetical Group

mSIS Scale Item	*ε4* EG Mean Rating (95%CI)	HG Mean Rating (95%CI)	Mean difference
People act like I am less competent	1.25 (1.20 to 1.45)	**2.60[a] (2.36 to 2.84)**	1.35 1.14 to 1.55
Feel set apart from others who are well	1.18 (1.14 to 1.39)	2.14 (1.93 to 2.35)	0.96 (0.75 to 1.17)
Have a greater need than usual for reassurance	1.23 (1.19 to 1.45)	2.21 (2.00 to 2.42)	1.02 (0.81 to 1.22)
Others feel awkward and tense around me.	1.05 (1.01 to 1.15)	1.97 (1.75 to 2.18)	0.92 (0.72 to 1.11)
Feel lonely more often than usual.	1.21 (1.12 to 1.40)	2.14 (1.93 to 2.34)	0.93 (0.73 to 1.14)
Feel less competent than I did before	**1.58[b] (1.38 to 1.69)**	2.36 (2.17 to 2.56)	0.78 (0.57 to 0.99)

Note. Hypothetical group (HG) = participants do not know their *APOE* status; n = 180. *ε4* Experiential group (EG) = participants know their *APOE ε4* carrier status; n = 65. 95% CI = normal 95% confidence interval.

[a] Highest mean rating in HG group

[b] Highest mean rating in *ε4* EG group

[c] Estimated from item with highest percent agreement in HG group

[d] Estimated from item with highest percent agreement in *ε4* EG group

Table 4

Mean Ratings on the Modified Social Impact Scale (mSIS) at Time 1 and Change From Time 1 to Time 2 Between the Experiential Group (EG) and Hypothetical Group (HG)

Study group	Average mSIS Score (1-4 scale) at Time 1	Change in mSIS Scores (1-4 scale)	Change in mSIS Percent Agreement Scores (dichotomized responses)
	Time 1 Mean (95%CI)	Paired mean difference (95%CI)	Paired mean difference (95%CI)
Hypothetical group (n=65)	1.88 (1.76 to 1.99)	0.11 (0.002 to 0.21)	5.5 (0.5 to 10.6)
Experiential group (n=63)	1.13 (1.07 to 1.19)	0.08 (0.03 to 0.14)	1.4 (0.3 to 2.5)
ε4 Carriers (n=36)	1.15 (1.09 to 1.21)	0.11 (-0.03 to 0.12)	1.7 (-0.0 to 3.4)
ε4 Non-carriers (n=27)	1.11 (1.00 to 1.22)	0.04 (-0.02 to 0.11)	1.0 (-0.0 to 2.2)
HG to EG Conversion (n=19)	1.89 (1.66 to 2.13)	-0.70 (-0.82 to -0.35)	-19.8 (-28.8 to -10.8)

Note. The *Change in mSIS Scores* column presents the paired mean difference on the full 1–4 response scale, with higher scores indicating greater agreement with AD stigma-related statements. The *Change in mSIS Percent Agreement Scores* column presents the paired mean difference in the proportion of items endorsed after dichotomizing responses (agree vs. disagree) and averaging across items. The experiential group (EG) refers to participants who knew their *APOE* test result, whereas the hypothetical group (HG) refers to participants who underwent *APOE* testing but did not know their result. Change values represent within-group differences between Time 1 (6–9 weeks after the baseline [Time 0] assessment) and Time 2 (approximately 6 months after baseline). All HG-to-EG converters were *APOE ε4* non-carriers. The Time 1 *Average mSIS Score* values reported in this table are based only on participants included in the longitudinal analyses and therefore may not perfectly match the Time 1 values reported in Table 2. 95% CI = 95% confidence interval.

Appendix

List of Statements from Modified Social Impact Scale (mSIS) by Study Group

Item No.	Experiential Group	Hypothetical Group
1	Some people act as though I am less competent than usual.	Some people would act as though I am less competent than usual.
2	I feel I have been treated with less respect than usual by others	I would be treated with less respect than usual by others.
3	I feel others are concerned they could "catch" my risk for Alzheimer's disease dementia through contact like a handshake or eating food I prepare.	Others would be concerned they could "catch" my risk for Alzheimer's disease dementia through contact like a handshake or eating food I prepare.
4	I feel others avoid me because of my risk for Alzheimer's disease dementia.	Others would avoid me because of my risk for Alzheimer's disease dementia.
5	Some family members have rejected me because of my risk for Alzheimer's disease dementia	Some family members would reject me because of my risk for Alzheimer's disease dementia.
6	I feel some friends have rejected me because of my risk for Alzheimer's disease dementia.	Some friends would reject me because of my risk for Alzheimer's disease dementia.
7	I encounter embarrassing situations as a result of my risk for Alzheimer's disease dementia.	I would encounter embarrassing situations as a result of my risk for Alzheimer's disease dementia.
8	Others seem to feel awkward and tense when they are around me due to my risk for Alzheimer's disease dementia.	Others would feel awkward and tense when they are around me due to my risk for Alzheimer's disease dementia.
9	I have experienced financial hardship that has affected how I feel about myself.	I would experience financial hardship that would affect how I feel about myself.
10	My job security has been affected by my risk for Alzheimer's disease dementia.	My job security would be affected by my risk for Alzheimer's disease dementia.
11	I have experienced financial hardship that has affected my relationship with others.	I would experience financial hardship that would affect my relationship with others.
12	I feel others think I am to blame for my risk for Alzheimer's disease dementia.	Others would think I am to blame for my risk for Alzheimer's disease dementia.
13	My employer/ co-workers have discriminated against me.	My employer/ co-workers would discriminate against me.
14	I feel less competent than I did before.	I would feel less competent than I did before.
15	I fear someone telling others about my risk for Alzheimer's disease dementia without my permission	I would fear someone telling others about my risk for Alzheimer's disease dementia without my permission.
16	I feel I need to keep my risk for Alzheimer's disease dementia a secret	I would feel I need to keep my risk for Alzheimer's disease dementia a secret

17	I do not feel I can be open with others about my risk for Alzheimer's disease dementia	I would not feel I can be open with others about my risk for Alzheimer's disease dementia
18	I feel I am at least partially to blame for my risk for Alzheimer's disease dementia.	I would feel I am at least partially to blame for my risk for Alzheimer's disease dementia.
19	I feel set apart from others who are well.	I would feel set apart from others who are well.
20	I have a greater need than usual for reassurance that others care about me.	I would have a greater need than usual for reassurance that others care about me.
21	I feel lonely more often than usual	I would feel lonely more often than usual
22	I have a sense of being unequal in my relationships with others due to my risk for Alzheimer's disease dementia	I would have a sense of being unequal in my relationships with others due to my risk for Alzheimer's disease dementia
23	I sometimes feel useless due to my risk for Alzheimer's disease dementia.	I would sometimes feel useless due to my risk for Alzheimer's disease dementia.

Note. Instructions for the experiential group were: "*Please read each statement below and consider how accurately it reflects your experiences since learning your risk for developing Alzheimer's disease dementia. On a scale from 1 to 4, please indicate how strongly you agree or disagree with each.*"
Instructions for the hypothetical group were: "*Please read each statement below and answer based on how accurately you believe it would reflect your experiences after learning you are at risk for developing Alzheimer's disease dementia. On a scale from 1 to 4, please indicate how strongly you agree or disagree with each."*

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Contributions

SDS conceived of the study idea; SDS and KH modified the SIS; SDS, MD and SJB analyzed the data; SDS and SJB prepared the first draft of this manuscript; all authors interpreted results and contributed to revising the writing of the manuscript.

Supplemental Materials

Supplemental Table 1

Factor Loadings for the Modified Social Impact Scale (mSIS)

Item No.	Item	Factor 1 Loading
1	People act like I am less competent.	0.7856
2	Feel I been treated with less respect.	0.7719
3	Feel others are concerned they could catch my AD risk.	0.3456
4	Feel others avoid me.	0.7220
5	Family members have rejected me.	0.5245
6	Some friends have rejected me.	0.7271
7	Encounter embarrassing situations.	0.8188
8	Others feel awkward and tense around me.	0.8339
9	Experienced financial hardship that has affected how I feel about myself.	0.7273
10	Job security has been affected.	0.7452
11	Experienced financial hardship that has affected my relationship with others.	0.7688
12	Feel others think I am to blame for my AD risk.	0.7053
13	Employer/ co-workers have discriminated against me.	0.7030
14	Feel less competent than I did before.	0.7403
15	Fear someone telling others about my AD risk without my permission.	0.7586
16	Feed I need to keep my risk a secret.	0.6753
17	Do not feel I can be open with others about my risk.	0.6849
18	Feel I am at least partially to blame for my risk	0.3384
19	Feel set apart from others who are well.	0.8890
20	Have a greater need than usual for reassurance.	0.8038
21	Feel lonely more often than usual.	0.8932
22	Have a sense of being unequal in my relationships.	0.8898
23	Feel useless due to my risk for AD dementia.	0.8153

Note. For the full wording of all items, see the Appendix.

Supplemental Table 2

Reliability Coefficients for the Modified Social Impact Scale (mSIS) by Scoring Method and Study Group

Scale	Cronbach's α (95% CI)
mSIS Scores [a]	
Experiential Group	0.95 (.90 to .99)
Hypothetical Group	0.93 (.91 to .96)
mSIS Percent Agreement Scores [b]	
Experiential Group	0.91 (.50 to .99)
Hypothetical Group Agreement Percentage	0.87 (.83 to .92)

[a] Mean of mSIS item ratings on the full 1-4 response scale (1 = strongly disagree, 4 = strongly agree).
[b] Mean of mSIS items after responses were binarized as disagree (0) or agree (1).

Supplemental Table 3

Percentages of Participants Agreeing with Modified Social Impact Scale (mSIS) Statements in the Hypothetical Group and Experiential Group at Time 1

	Experiential Group			Hypothetical Group	*p*-value[a]	*p*-value[b]
	All (n=111) % (95%CI)	***ε4* Carriers (n=65) % (95%CI)**	***ε4* Non-Carriers (n=46) % (95%CI)**	**(n=180) % (95%CI)**		
mSIS Scale Score (Total)	2.3 (1.1 to 3.6)	2.3 (0.1 to 3.8)	2.4 (0.1 to 4.6)	26.1 (23.0 to 29.1)	<0.001[z]	<0.001[z]
mSIS Scale Items						
People act like I am less competent.	2.6 (-0.3 to 5.6)	3.1 (-1.1 to 7.3)	2.2 (-2.1 to 6.5)	65.6 (58.6 to 72.5)	<0.001[z]	<0.001[z]
Have a greater need than usual for reassurance.	5.3 (1.2 to 9.4)	4.6 (-0.5 to 9.7)	6.7 (-0.6 to 14.0)	46.7 (39.4 to 54.0)	<0.001[z]	<0.001[z]
Feel less competent than I did before.	8.8 (3.6 to 14.0)	7.7 (1.2 to 14.2)	8.9 (0.6 to 17.2)	42.2 (35.0 to 49.4)	<0.001[z]	<0.001[z]
Feel set apart from others who are well.	1.8 (-0.7 to 4.2)	3.1 (-1.1 to 7.3)	0.0 (0.0 to 0.0)	41.1 (33.9 to 48.3)	<0.001[z]	<0.001[z]
Encounter embarrassing situations.	2.6 (-0.3 to 5.6)	1.5 (-1.5 to 4.5)	2.2 (-2.1 to 6.5)	40.6 (33.4 to 47.7)	<0.001[z]	<0.001[z]
Fear someone telling others about my AD risk without my permission.	2.6 (-0.3 to 5.6)	3.1 (-1.1 to 7.3)	2.2 (-2.1 to 6.5)	39.4 (32.3 to 46.6)	<0.001[z]	<0.001[z]
Feel I been treated with less respect.	0.9 (-0.8 to 2.6)	0.0 (0.0 to 0.0)	2.2 (-2.1 to 6.5)	38.9 (31.8 to 46.0)	<0.001[z]	<0.001[z]
Feel lonely more often than usual.	2.6 (-0.3 to 5.6)	1.5 (-1.5 to 4.5)	4.4 (-1.6 to 10.5)	36.7 (29.6 to 43.7)	<0.001[z]	<0.001[z]
Have a sense of being unequal in my relationships.	2.6 (-0.3 to 5.6)	3.1 (-1.1 to 7.3)	2.2 (-2.1 to 6.5)	35.0 (29.6 to 42.0)	<0.001[z]	<0.001[z]
Do not feel I can be open with others about my risk.	7.0 (2.3 to 11.7)	7.7 (1.2 to 14.2)	6.7 (-0.6 to 14.0)	29.1 (22.4 to 35.7)	<0.001[z]	<0.001[z]

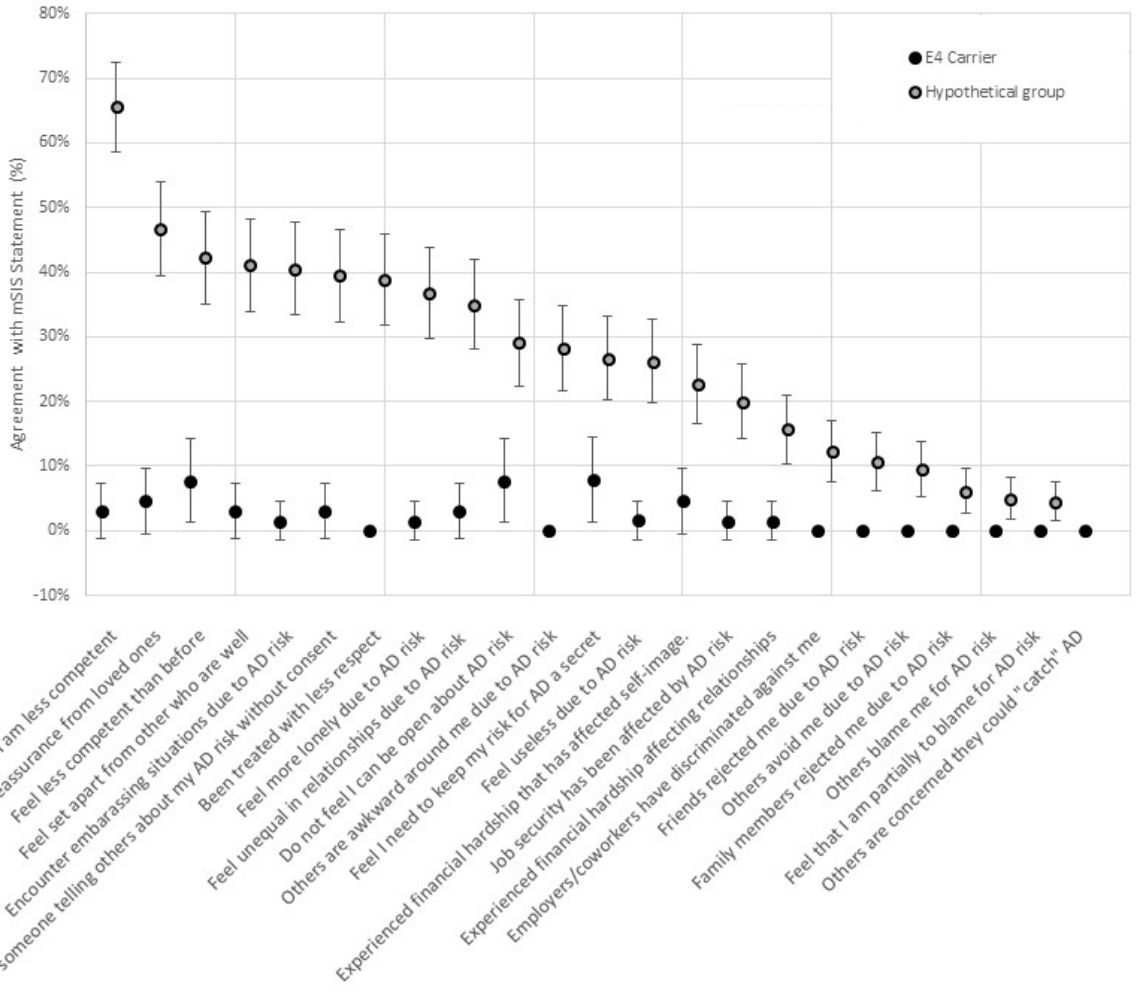
Others feel awkward and tense around me.	0.0 (0.0 to 0.0)	0.0 (0.0 to 0.0)	0.0 (0.0 to 0.0)	28.3 (21.7 to 34.9)	<0.001[z]	<0.001[z]
Feed I need to keep my risk a secret.	7.1 (2.4 to 11.8)	7.8 (1.2 to 14.4)	6.7 (-0.6 to 14.0)	26.7 (20.2 to 33.1)	<0.001[z]	0.003[y]
Feel useless due to my risk for AD dementia.	1.8 (-0.7 to 4.2)	1.6 (-1.5 to 4.6)	2.2 (-2.1 to 6.5)	26.3 (19.8 to 32.7)	<0.001[z]	<0.001[z]
Experienced financial hardship that has affected how I feel about myself.	3.5 (0.1 to 6.9)	4.6 (-0.5 to 9.7)	2.2 (-2.1 to 6.5)	22.8 (16.7 to 28.9)	<0.001[z]	0.002[y]
Job security has been affected.	2.6 (-0.3 to 5.6)	1.5 (-1.5 to 4.5)	4.4 (-1.6 to 10.5)	20.0 (14.2 to 25.8)	<0.001[z]	<0.001[z]
Experienced financial hardship that has affected my relationship with others.	0.9 (-0.8 to 2.6)	1.5 (-1.5 to 4.5)	0.0 (0.0 to 0.0)	15.6 (10.3 to 21.0)	<0.001[z]	0.006[y]
Employer/ co-workers have discriminated against me.	0.9 (-0.8 to 2.6)	0.0 (0.0 to 0.0)	2.2 (-2.1 to 6.5)	12.3 (7.5 to 17.1)	<0.001[z]	0.007[y]
Some friends have rejected me.	0.0 (0.0 to 0.0)	0.0 (0.0 to 0.0)	0.0 (0.0 to 0.0)	10.7 (6.1 to 15.2)	<0.001[z]	0.01[x]
Feel others avoid me.	0.0 (0.0 to 0.0)	0.0 (0.0 to 0.0)	0.0 (0.0 to 0.0)	9.4 (5.2 to 13.7)	0.002[y]	0.02[x]
Family members have rejected me.	0.0 (0.0 to 0.0)	0.0 (0.0 to 0.0)	0.0 (0.0 to 0.0)	6.1 (2.6 to 9.6)	0.02[x]	0.09
Feel others think I am to blame for my AD risk.	0.0 (0.0 to 0.0)	0.0 (0.0 to 0.0)	0.0 (0.0 to 0.0)	5.0 (1.8 to 8.2)	0.04[x]	0.15
Feel I am at least partially to blame for my risk.	0.0 (0.0 to 0.0)	0.0 (0.0 to 0.0)	0.0 (0.0 to 0.0)	4.4 (1.4 to 7.4)	0.06	0.19
Feel others are concerned they could catch my AD risk.	0.0 (0.0 to 0.0)	0.0 (0.0 to 0.0)	0.0 (0.0 to 0.0)	2.2 (0.1 to 4.4)	0.28	0.52

[a]p-value for experiential vs hypothetical group
[b]p-value for ε4 carriers vs hypothetical group

Note. 95%CI = 95% confidence interval. AD = Alzheimer's disease. The experiential group includes those who reported knowing their *APOE* test result, and responses are tabled separately by *APOE ε4* carrier status. The hypothetical group includes participants who underwent *APOE* testing but did not know their *APOE ε4* carrier status. The mSIS items are listed here in descending order from highest to lowest agreement in the hypothetical group.

Supplemental Figure 1

Percentages of Participants Endorsing Agreement on Modified Social Impact Scale (mSIS) Statements by Study Group (ε4 Carrier Experiential versus Hypothetical Groups) at Time 1 (N = 245).



Note. The experiential group of *APOE ε4* carriers includes participants who knew their *APOE* test result and were *APOE ε4* carriers. The hypothetical group includes participants who underwent *APOE* testing but did not know their *APOE* test result. Values reflect dichotomized data (percent of participants endorsing agreement with each statement). Error bars represent normal 95% confidence intervals. For items with 0% reported, no participants endorsed agreement.

Supplemental Table 4

Percent Agreement Scores on the Modified Social Impact Scale (mSIS) at Time 1 and Within-Group Change from Time 1 to Time 2 by Study Group, Sex, and Age

Study Group	mSIS Percent Agreement Scores Time 1 % (95%CI)	Change in mSIS Agreement Rating from Time 1 to Time 2 Paired Mean Difference (95%CI)
Sex		
Female		
Experiential Group (n=31)	1.11 (1.05 to 1.17)	-0.11 (-0.19 to -0.03)
ε4 Carriers (n=20)	1.14 (1.06 to 1.23)	0.12 (-0.22 to -0.01)
ε4 Non-Carriers (n=11)	1.05 (-0.98 to 1.11)	-0.09 (-0.25 to 0.07)
Hypothetical Group (n=36)[a]	1.92 (1.78 to 2.06)	-0.13 (-0.28 to 0.03)
HG to EG Convertors (n=13)	1.89 (1.59 to 2.20)	-0.68 (-0.99 to -0.37)
Male		
Experiential Group (n=32)	1.15 (1.05 to 1.25)	-0.06 (-0.14 to 0.02)
ε4 Carriers (n=16)	1.14 (0.96 to 1.33)	-0.10 (-0.25 to 0.05)
ε4 Non-Carriers (n=16)	3.5 (-3.1 to 10.2)	0.01 (0.08 to 0.05)
Hypothetical Group (n=27)[a]	1.80 (1.66 to 1.95)	-0.10 (-0.25 to 0.06)
HG to EG Convertors (n=6)	1.89 (1.37 to 2.41)	-0.46 (-0.92 to -0.01)
Age		
Below median age of 69 years		
Experiential Group (n=34)	1.11 (1.01 to 1.21)	-0.10 (-0.19 to -0.02)
ε4 Carriers (n=18)	1.09 (1.01 to 1.17)	-0.10 (-0.19 to 0.003)
ε4 Non-Carriers (n=16)	1.13 (0.94 to 1.32)	-0.11 (-0.27 to 0.04)
Hypothetical Group (n=38)	1.97 (1.80 to 2.14)	-0.06 (-0.23 to 0.12)
HG to EG Convertors (n=6)	1.87 (1.31 to 2.43)	-0.80 (-1.35 to -0.25)
At and above median age of 69		
Experiential Group (n=29)	1.15 (1.08 to 1.22)	-0.06 (-0.14 to 0.01)
ε4 Carriers (n=18)	1.19 (1.09 to 1.28)	-0.11 (-0.21 to -0.003)
ε4 Non-Carriers (n=11)	1.08 (0.96 to 1.19)	0.03 (-0.06 to 0.11)
Hypothetical Group (n=27)	1.81 (1.68 to 1.93)	-0.16 (-0.28 to -0.03)
HG to EG Convertors (n=13)	1.90 (1.61 to 2.20)	-0.52 (-0.81 to -0.24)

Note. Results are shown separately by study group, stratified by sex (female, male) and age (below vs. at/above the median age of 69 years). The experiential group (EG) includes those who

knew their *APOE* test result. The hypothetical group (HG) includes those who did not know their *APOE* test result.

[a] Two participants in the HG did not report sex