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Public Perceptions of Presymptomatic Testing for Alzheimer's Disease

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Abstract

Objective—To explore, among online visitors to an Alzheimer's disease (AD) website, the self-expressed desire for, envisioned reaction to, and basic understanding of presymptomatic AD-related genetic and biomarker tests.

Patients and Methods—Information about presymptomatic testing, and an online multiple choice format survey were posted from November 1, 2012 through June 20, 2013 on the AD Prevention Registry website (www.endALZnow.org).

Results—Of 4036 respondents, 80.8% wanted genetic testing if paid by insurance; 58.7% if it would cost them at least $100. 80.2% wanted biomarker testing. If found to be at high risk for AD, 90.5% endorsed that they would "pursue a healthier lifestyle," but 11.6% endorsed "seriously consider suicide." The implication of a positive genetic test was incorrectly understood by 13.1%, and 32.6% failed to view a positive biomarker test as evidence of either increased risk for or the presence of AD.

Conclusion—Despite efforts to increase public awareness of AD, our survey results suggest that greater education of the public is needed. Interested patients should probably undergo

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psychological screening to identify those at high risk of adverse psychological outcomes, and disclosure of presymptomatic test results should be anchored to tangible constructive action plans such as healthy lifestyle changes, long term care planning, and when available and appropriate, participation in research trials.

The proper role for presymptomatic genetic and biomarker tests marketed directly to consumers is not yet clear yet the practice is growing and may find a ready customer base among those concerned about their risk for Alzheimer's disease (AD). There are risks attendant to such tests (1), and presymptomatic screening for AD is of particular concern because AD is prevalent and lacks effective prevention therapy (the implicit purpose of presymptomatic testing). Hence the number of people potentially seeking such testing is likely to be high even though there are still no proven disease modifying interventions to offer those disclosed to be at high risk or to harbor early stage AD. Insights gained regarding the effects of apolipoprotein E (APOE) genotype disclosure (the most prevalent genetic risk factor for AD [2,3]) derive primarily from the Risk Evaluation and Education for Alzheimer's Disease (REVEAL) study, a carefully executed entry into the impending world of personalized medicine that focused on a small subset of carefully screened and counseled research participants whose main message has been interpreted to be that disclosure can be done safely (4). Such screening and followup is unlikely to accompany widespread clinical practice, however, and does not now routinely accompany direct to consumer marketing. There remains, therefore, a need to explore the perspectives of unscreened and unsheltered individuals who are likely to seek presymptomatic testing for AD so as to better prepare healthcare providers and policy makers to anticipate and address the questions and consequences that may arise from this rapidly growing practice. To address this, we administered a questionnaire through an online website dedicated to AD to specifically assess: 1) the desire for preclinical testing in the absence of effective interventions, 2) possible reactions to such information, and 3) how well the results of such testing would be understood.

Methods

Development of the Questionnaire

To develop this survey we conducted a 2 part interview: in part 1, 20 members of the Arizona APOE cohort (5) were initially interviewed with open ended questions to get a sense of what features of presymptomatic AD testing seemed most relevant to them (for example, whether they felt any form of predictive testing for AD was appropriate, if so how they would like to see such testing offered, and how they might handle such information if it were disclosed to them). This cohort is comprised of cognitively healthy Maricopa County residents who have undergone genetic screening for APOE (the results of which have not been disclosed to them) and who undergo longitudinal neuropsychological and related testing every one to two years. Guided by their responses, in part 2 an information sheet describing presymptomatic biomarker and genetic testing and a self-completed questionnaire was provided by a genetics counselor (KH) to 12 different members of this cohort whose verbatim responses were transcribed and analyzed. A final draft of the questionnaire comprised of yes/no and multiple choice questions addressing demographics, genetic

testing, biomarker testing, and possible reactions to such information was then posted on the Alzheimer's Prevention Registry website. A copy of the questionnaire is included in the supplementary materials, eAppendix 1.

Study population

The Alzheimer's Prevention Initiative (6) launched the online Alzheimer's Prevention Registry in 2012. This registry is an online community of people at least 18 years of age who are interested in Alzheimer's disease prevention research, either for purely informational purposes or to be considered for possible research participation in future studies. The survey was posted on the Alzheimer's Prevention Registry Website (www.endALZnow.org), and was completed online by visitors who registered with this website. If a survey was completed once by a registrant, it was no longer available after that. The survey was posted and offered to all registry members between November 1, 2012 and June 30, 2013. All parts of this study were approved by the Mayo Clinic Institutional Review Board.

Data analysis

Descriptive statistics included unpaired t-tests (two-tailed) for continuous data and chi-square for categorical data. Continuous data were summarized using mean +/− standard deviation and categorical variables were summarized using frequency (%). Univariate regression of responses to questions regarding perceptions of, desire for, and reactions to presymptomatic testing, as well as responses to two basic questions testing understanding of presymptomatic testing was performed for each of eight demographic variables (age, sex, years of formal education, self-reported racial/ethnic background, previous or current role as a caregiver for a dementia patient, first degree relative with dementia, total number of family members known to have/had dementia, and whether current residence is within same geographic region as where respondent was raised) were performed. Multivariate regressions of all eight demographic variables were then performed from which odds ratios (O.R.) and 95% confidence intervals (C.I.) were calculated.

Results

There were 4036 website respondents, mean age 58.0+/−12.2 years, mean education 16.1+/−3.9 years (95% were high school graduates and 66% were college graduates), 82.1% women, of whom 61.3% reported a first degree relative with dementia (table one). 78.3% perceived themselves to be at higher than average risk for AD. In a multivariate analysis (table two; see eTable 1 for univariate analyses and specific n for each analysis), younger age (O.R. 0.95 per year, 95% C.I. 0.93–0.96, $P<.001$), male sex (O.R. 2.4., 95% C.I. 1.27–4.60, $P=.007$), having a first degree relative with dementia (O.R. 12.76, 95% C.I. 7.28–22.36, $P<.001$), and a greater number affected family members (O.R. 4.89 per member, 95% C.I. 3.59–6.67, $P<.001$) were significantly associated with a higher likelihood of perceiving oneself to be at higher than average risk for AD. 82% of respondents indicated their greatest disease related fear was AD (and not cancer, heart attack or stroke), and in multivariate analyses, having a first degree relative with dementia O.R. 3.52, 95% C.I. 2.46–5.05, $P<.001$, the number of relatives with dementia (O.R. 1.37, 95% C.I. 1.20–1.57 per relative, $P<.$

001) and residing in a region other than where raised (O.R. 1.41, 95% C.I. 1.05–1.90, *P*=.02) were significantly associated with their greatest disease related fear of AD.

Regarding their willingness to undergo presymptomatic testing, 70.4% felt genetic testing for APOE was important even in the absence of any effective intervention. 94.9% of respondents would be willing to have APOE genetic results disclosed to them if it were required for participation in a research study, and 88.7% would actually want such results. Clinically, 80.8% would have genetic testing if it were paid for by insurance but this dropped to 58.7% if there was at least a $100 out of pocket cost for testing. Among those not wanting genetic testing even if free, the most common reasons were personal fear of the possible results (28.2%) and fear it might hurt their insurability (16.8%). Male gender (O.R. 1.63, 95% C.I. 1.23–2.16, *P*<.001), having a first degree relative with dementia (O.R. 1.49, 95% C.I. 1.16–1.93, *P*=.002), and a greater number of relatives with dementia (O.R. 1.11 per relative, 95% C.I. 1.03–1.19, *P*=.009) all correlated with a willingness to pay out of pocket for genetic testing. 80.2% indicated they would want biomarker testing (especially PET scans). Male gender (O.R. 1.97, 95% C.I. 1.33–2.92, *P*<.001), education (O.R. 0.96 per year of education, 95% C.I. 0.93–1.00, *P*=.04), and number of relatives with dementia (O.R. 1.18 per relative, 95% C.I. 1.07–1.32, *P*=.002) correlated with desire for biomarker testing.

As for how respondents felt they would react to obtaining genetic or biomarker results, 98.5% of respondents indicated they would communicate their APOE results to someone, including a family member (spouse 92.3%, siblings 84.6%, children 81.7%) or friend (53%), and the results were very similar for communicating biomarker results. If found to be at genetically high risk for AD 90.5% responded they would pursue a healthier lifestyle, 76.3% would obtain long term care insurance (if they did not already have it), 18.4% would spend all their money enjoying their remaining life, and 11.6% would “seriously consider suicide.” Responses were similar if instead respondents were found to have biomarker evidence of AD. In multivariate analyses, the decision to lead a healthier lifestyle correlated with education (O.R. 0.91, 95% C.I. 0.87–0.96, *P*<.001); the decision to obtain long term care insurance correlated with age (O.R. 0.95, 95% C.I. 0.94–.96, *P*<.001) and sex (male O.R. 0.73, 95% C.I. 0.55–0.99, *P*=.04); the decision to spend all of one’s money correlated with race/ethnicity (white, non-Hispanic O.R. 0.47, 95% C.I. 0.32–0.69, *P*<.001); consideration of suicide in response to genetic testing correlated with age (O.R. 1.02, 95% C.I. 1.01–1.04, *P*=.008); and consideration of suicide in response to biomarker testing correlated with education (O.R. 1.06, 95% C.I. 1.01–1.11, *P*=.03).

Finally, 86.9% of respondents were able to correctly recognize that the implication of APOE e4 carrier status in a clinically asymptomatic adult indicated increased risk for AD and did not indicate the presence or absence of AD currently. In multivariate analyses, age (O.R. 1.02, 95% C.I. 1.002–1.03, *P*=.02), education (O.R. 0.95, 95% C.I. 0.92–0.98, *P*=.004), and racial background (white, non-Hispanic O.R. 1.05, 95% C.I. 1.06–2.57, *P*=.03) correlated with correctly recognizing APOE e4 carrier implications. In contrast, despite being given information that a positive biomarker test indicated the presence of AD pathology, 32.6% of respondents failed to indicate that positive biomarker tests (amyloid PET and CSF biomarkers) in a patient with mild memory loss reflected either increased risk for or the

presence of AD. There were no univariate or multivariate variables that were significantly correlated with recognizing the significance of positive biomarkers.

Discussion

There is ongoing debate among professionals regarding the proper management of presymptomatic testing and disclosure of results (1,7). The intent of this study was to extend the findings of REVEAL in the contextual absence of a structured clinical or research program to a cohort comprised of individuals who were specifically concerned about AD and forthcoming AD prevention trials, and not surprisingly, the proportion expressing a willingness to undergo presymptomatic testing was high and similar to that previously reported for AD (8), Huntington's disease (9) and in a health economics analysis (10). While they do not represent a random cross section of the population (82.1% of respondents were women, the mean educational level was college graduate, and 91.2% were white, non-Hispanic), they probably do represent those unscreened individuals who are most likely to actively seek presymptomatic testing for AD.

Concordant with the REVEAL experience (11), we too found that family history had the strongest effect on perceptions of risk and fear of AD. Additionally, we found that geographic residence away from where one was raised, and therefore presumably further from one's family and childhood friends (sources of emotional support for many) also correlated with fear of AD. Most of the respondents in this study felt presymptomatic testing, whether genetic or biomarker, was important, and the less costly it would be to obtain, the more likely would they be to obtain it. Past experience with presymptomatic testing for Huntington's disease, however, has shown that not all of those deemed eligible for enrollment in presymptomatic testing programs choose to participate and among those who do enter such programs, 13–40% withdraw during the initial counseling stage (9,12,13). Cost may be a factor for some. The relative decline in willingness to undergo genetic testing based on out of pocket expense among the participants in our study was similar to the findings of the REVEAL study (8), though more than half endorsed continued willingness to do so. Sex had a strong influence on the desire for genetic as well as biomarker testing (men in this survey were more likely to opt for testing than women even though they comprised a much smaller percentage of respondents).

Envisioned reactions to genetic and biomarker presymptomatic tests were very similar. Communicating the results of presymptomatic testing with health professionals and friends has been shown to correlate with reduced anxiety and depression a year after APOE genetic disclosure (4), and most respondents indicated a willingness to discuss their results with others, particularly family members and physicians though less than half indicated a willingness to discuss the results with friends (and women were more likely to do so than men). Most participants envisioned constructive reactions should they discover themselves to be at high risk for AD endorsing healthier lifestyles and long term care insurance. REVEAL has shown that levels of distress related to disclosure or nondisclosure can be similar, and post-test distress levels correlate strongly with pre-test levels (14). Tangible benefits of disclosure of patients' genotypes included helping low-risk patients to worry less, and high-risk patients to adopt healthier lifestyles that might mitigate their AD risk (15).

However, the disclosure of results conferred greater levels of distress on the higher-risk patients (4,16): 9% of participants with no significant prior psychiatric problem developed one within a year, and of the three APOE e4 homozygotes included, two developed clinically significant psychological distress (though the relationship to genetic disclosure itself was uncertain) (16).

While most respondents endorsed positively adaptive reactions to “bad news”, over 18% endorsed spending all their money, especially those other than white/non-Hispanic, and roughly 11% endorsed consideration of suicide. Because REVEAL screened out people expressing the possibility of suicidal ideation in response to such information, that study did not directly address this issue. Older age significantly influenced consideration of suicide in response to genetic high risk while higher education influenced consideration of suicide in response to biomarker evidence of AD. In studies examining suicide among those at risk for Huntington’s disease, 35% considered, 18% attempted, and 5% committed suicide (9) necessitating explicit precautions to avoid presymptomatic testing among individuals in this population who are at high suicide risk (17) or who have serious active psychopathology (18). Although the risk of suicide in the Huntington’s disease population appears much higher than in the AD population, similar precautions should be taken especially given the much larger number of individuals at increased risk for AD or who will perceive themselves at increased risk for AD who may elect to undergo presymptomatic testing. Of further concern is that over 13% of respondents did not understand the implications of APOE testing, and nearly a third failed to understand that positive biomarkers indicate elevated risk or even the presence of AD. In the REVEAL study, participants were extensively educated as to the significance of genetic testing and possible result implications at entry, yet even among those who then received information about their APOE genotype and its implicit AD risk, 40–50% forgot this information after a year (14) underscoring not only the importance of education around the time of presymptomatic testing, but also the need to continually assess a person’s ongoing understanding well after presymptomatic testing.

Several limitations should be considered in interpreting our findings. First, as previously mentioned, this survey was posted on a website that would attract individuals interested specifically in AD, and so should not be construed as necessarily representative of the general public. Nonetheless, presymptomatic genetic testing is often obtained through internet-based businesses. Interest in AD is widespread and growing thanks to multiple programs designed to increase awareness. Further, the aging of our society results not only in more patients, but in more children of patients who in turn will perceive themselves to be at greater risk for AD. Second, there are limitations imposed by the methodology of a mass survey. The questions must be simple and straightforward enough to maximize the reliability of responses. Some questions or terms may be misunderstood and some responses may simply be inaccurate. Not all respondents answer every question (see supplementary material). When dealing with large numbers of individuals, unique combinations arise but the subtleties in such cases are lost when averaged into larger categorical groups (for example, individuals of various mixed racial/ethnic background were grouped into a single category). Third, it is difficult to know all the factors that may influence responses. Intelligence, psychiatric issues and personality may all factor into an individual’s responses but these factors were not addressed in the current population. However, we are

administering the survey to a research cohort in who we have acquired such information that will allow us to probe this smaller number of respondents in much greater depth.

The results of this and other studies have made it clear that people want presymptomatic tests whether or not there is an immediate tangible impact on their health, and this seems true for a variety of conditions including, but not limited to AD (10). There are a variety of reasons why such testing may be deemed valuable by participants including a general dislike for uncertainty, greater insight into one's health risks, non-medical decision making, future planning, and of course perceived actual disease prevention. To what degree responses to surveys will reflect the actual courses of action that will be taken, however, is less clear. For example, parallels between cardiovascular disease and AD have been proposed, and while most responded they would lead a healthier lifestyle if found to be at high risk for AD, the cardiovascular experience in this regard has fallen short of expectations. Despite the much stronger association between cardiovascular risk factors and outcomes such as heart attack and stroke, in a cohort of 11,993 followed for over 11 years, only 0.2% had all 7 ideal metrics for cardiovascular health (smoking, body mass index, physical activity, healthy diet, total cholesterol, blood pressure, fasting plasma glucose); 18.2% met 5 or more of these metrics, 42.7% met 3 or 4, and 39% had 0–2 (19). There seems little reason to believe, therefore, that compliance with healthy lifestyle recommendations will be greatly enhanced by predictive testing for AD.

Conclusion

AD is a major health concern, and there is significant public interest in preclinical testing. Despite efforts to increase public awareness, however, our survey results suggest that greater education is needed, especially targeting those individuals seeking predictive tests or enrollment in prevention trials. We are technologically positioned for presymptomatic testing, but sociologically, and even possibly medically, appear less prepared, especially for biomarker testing. Interested patients should probably undergo psychological screening to identify those at high risk of adverse psychological outcomes, especially in the absence of definitive therapeutic options. Optimizing healthy behavior is the primary rationale for presymptomatic testing, so that tangible action plans such as healthy lifestyle changes, long term care planning, and when available and appropriate, participation in research trials should be anchored to disclosure of presymptomatic test results.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations

AD	Alzheimer's disease
APOE	Apolipoprotein E
OR	Odds ratio
REVEAL	Risk Evaluation and Education for Alzheimer's Disease

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Table 1

Survey Responses

	Responses
Demographics	
N	4036
Age	58.0 (12.2)
Education	16.1 (3.9)
Gender (% women)	82.1%
Racial/ethnic background (%White Non-Hispanic)	91.2%
Caregiver ever	45.3%
First Degree Relative Affected	61.3%
Number of Relatives Affected	1.8 (1.5)
Region residing same as where raised (%)	57.5%
Disease Perception	
Believe you're at higher risk for Alzheimer's disease	78.3%
% who believe their greatest risk is for:	
-Alzheimer's disease	58.4%
-Cancer	18.1%
-Heart Attack	15.4%
-Stroke	8.1%
% whose greatest fear is developing:	
-Alzheimer's disease	82.0%
-Cancer	10.6%
-Heart Attack	2.3%
-Stroke	5.0%
Genetic Testing: Results and Disclosure	
Important to have genetic testing for AD	70.4%
If insurance paid do you want genetic testing	80.8%
If your cost >$100 do you want genetic testing	58.7%
If tested in research would you want the results	88.7%
If gene disclosure required for research would you do it?	94.9%
Genetic Testing: Communication and Reaction	
If you had the APOE e4 gene you would tell:	
-your doctor	79.4%
-your spouse	92.3%
-your siblings	84.6%
-your children	81.7%
-your friends	53.0%
-your lawyer	60.5%
If you were at high risk for AD would you:	
-begin a healthier lifestyle	90.5%
-get long term care insurance	76.3%

	Responses
-spend all your money for pleasure	18.4%
-seriously consider suicide	11.6%
Biomarker Testing: Results and Disclosure	
Want test to reveal AD years before symptoms start	80.2%
If test part of research would you be willing to have a:	
-PET scan only	40.9%
-Spinal tap only	<1%
-Both	53.3%
-Neither	5.5%
Biomarker Testing: Communication and Reaction	
If you had biomarker evidence of AD you would tell:	
-your spouse	92.2%
-your siblings	80.6%
-your children	75.9%
-your friends	46.5%
-your lawyer	53.8%
If you had biomarker evidence of AD you would:	
-begin a healthier lifestyle	91.0%
-get long term care insurance	76.6%
-spend all your money for pleasure	18.7%
-seriously consider suicide	10.2%
Test Question: Implication of APOE e4 gene in an asymptomatic 60 yo man-answer choices:	
-has AD now	2.0%
-does not have AD but is at higher risk	86.9%
-both correct	8.2%
-neither correct	2.9%
Test Question: Implication of positive amyloid PET and CSF biomarkers in a 71 yo woman with mild subjective memory decline:	
-has AD now	12.0%
-does not have AD but is at higher risk	51.0%
-both correct	4.4%
-neither correct	32.6%

Table 2

Multivariate Analyses of Public Opinions Regarding Presymptomatic Testing for Alzheimer's Disease (AD)

	Age	Male Sex	Higher Education	White Non-Hispanic	Caregiver experience	FDR with AD	No. of affected relatives	Residence not Raised
Perceived higher AD risk	OR .95 *P*<.001 95% CI .93–.96	OR 2.42 *P*=.007 95% CI 1.27–4.60	OR 1.03 *P*=.37 95% CI .97–1.09	OR .54 *P*=.11 95% CI .26–1.15	OR .81 *P*=.37 95% CI .51–1.29	OR 12.76 *P*<.001 95% CI 7.28–22.36	OR 4.89 *P*<.001 95% CI 3.59–6.67	OR 1.18 *P*=.47 95% CI .75–1.85
Fear AD most	OR 1.002 *P*=.67 95% CI .99–1.01	OR 1.11 *P*=.56 95% CI .77–1.63	OR .98 *P*=.35 95% CI .95–1.02	OR 1.22 *P*=.39 95% CI .77–1.95	OR 1.07 *P*=.66 95% CI .79–1.44	OR 3.52 *P*<.001 95% CI 2.46–5.05	OR 1.37 *P*<.001 95% CI 1.20–1.57	OR 1.41 *P*=.02 95% CI 1.05–1.90
APOE gene testing important	OR .99 *P*=.12 95% CI .98–1.002	OR 1.71 *P*<001 95% CI 1.25–2.34	OR .96 *P*=.004 95% CI .93–.99	OR 1.35 *P*=.15 95% CI .89–2.03	OR .87 *P*=.25 95% CI .69–1.10	OR 1.43 *P*=.01 95% CI 1.09–1.88	OR 1.15 *P*=.002 95% CI 1.05–1.25	OR .97 *P*=.77 95% CI .77–1.21
Want gene test if free	OR 1.01 *P*=.16 95% CI 1.00–1.01	OR 1.79 *P*=.003 95% CI 1.23–2.61	OR .93 *P*<.001 95% CI .90–.96	OR 1.25 *P*=.36 95% CI .78–2.00	OR 1.12 *P*=.43 95% CI .85–1.46	OR .85 *P*=.31 95% CI .62–1.17	OR 1.11 *P*=.04 95% CI 1.01–1.22	OR 1.14 *P*=.34 95% CI .87–1.49
Would pay ≥$100 for gene test	OR .99 *P*=.14 95% CI .99–1.002	OR 1.63 *P*<.001 95% CI 1.23–2.16	OR .99 *P*=.35 95% CI .96–1.01	OR 1.30 *P*=.17 95% CI .89–1.88	OR .95 *P*=.65 95% CI .77–1.18	OR 1.49 *P*=.002 95% CI 1.16–1.93	OR 1.11 *P*=.009 95% CI 1.03–1.19	OR1.17 *P*=.16 95% CI .94–1.44
Want research gene result	OR 1.01 *P*=.10 95% CI 1.00–1.03	OR 1.91 *P*=.02 95% CI 1.13–3.22	OR .93 *P*=.001 95% CI .89–.97	OR 1.22 *P*=.53 95% CI .66–2.28	OR.98 *P*=.90 95% CI .68–1.39	OR.69 *P*=.09 95% CI .45–1.06	OR 1.08 *P*=.23 95% CI .95–1.23	OR 1.22 *P*=.27 95% CI .86–1.74
Want Biomarker test	OR .99 *P*=.18 95% CI .98–1.003	OR 1.97 *P*<.001 95% CI 1.33–2.92	OR .97 *P*=.04 95% CI .93–1.00	OR 1.03 *P*=.90 95% CI .65–1.63	OR .85 *P*=.25 95% CI .65–1.12	OR 1.22 *P*=.23 95% CI .88–1.68	OR 1.18 *P*=.002 95% CI 1.07–1.32	OR 1.17 *P*=.26 95% CI .89–1.53
Tell family gene result	OR 1.025 *P*=.02 95% CI 1.003–1.05	OR .97 *P*=.91 95% CI .53–1.78	OR 1.03 *P*=.004 95% CI .96–1.09	OR 1.19 *P*=.68 95% CI .53–2.67	OR .72 *P*=.19 95% CI .44–1.18	OR.71 P= .26 95% CI .39–1.28	OR 1.26 *P*=.04 95% CI 1.02–1.56	OR 1.05 *P*=.84 95% CI .65–1.70
Tell friends gene result	OR .99 *P*=.05 95% CI .98–1.00	OR .66 *P*=.002 95% CI .50–.86	OR .98 *P*=.12 95% CI .95–1.01	OR .69 *P*=.05 95% CI .48–1.01	OR .90 *P*=.36 95% CI .72–1.13	OR .89 *P*=.40 95% CI .69–1.16	OR 1.04 *P*=.31 95% CI .96–1.12	OR 1.02 *P*=.87 95% CI .82–1.27

	Age	Male Sex	Higher Education	White Non-Hispanic	Caregiver experience	FDR with AD	No. of affected relatives	Residence not Raised
Lead healthier lifestyle	OR .98 *P*=.05 95% CI .97–1.00	OR 1.10 *P*=.70 95% CI .68–1.78	OR .91 *P*<.001 95% CI .87–.96	OR 1.37 *P*=.40 95% CI .65–2.89	OR .83 *P*=.35 95% CI .56–1.23	OR 1.09 *P*=.70 95% CI .69–1.74	OR 1.09 *P*=.23 95% CI .95–1.26	OR .97 *P*=.89 95% CI .67–1.42
Get long term care insurance	OR .95 *P*<.001 95% CI .94–.96	OR .73 *P*=.04 95% CI .55–.99	OR 1.003 *P*=.83 95% CI .97–1.04	OR 1.15 *P*=.55 95% CI .73–1.80	OR 1.13 *P*=.37 95% CI .87–1.45	OR 1.14 *P*=.40 95% CI .84–1.55	OR 1.00 *P*=.93 95% CI .91–1.09	OR .99 *P*=.95 95% CI .77–1.27
Spend all money	OR 1.0 *P*=.82 95% CI .99–1.01	OR .78 *P*=.18 95% CI .54–1.12	OR 1.01 *P*=.66 95% CI .98–1.04	OR .47 *P*<.001 95% CI .32–.69	OR .83 *P*=.19 95% CI .63–1.10	OR .94 *P*=.72 95% CI .68–1.31	OR .99 *P*=.81 95% CI .90–1.09	OR 1.02 *P*=.89 95% CI .78–1.34
Consider suicide (APOE)	OR 1.02 *P*=.008 95% CI 1.01–1.04	OR 1.12 *P*=.57 95% CI .75–1.69	OR 1.02 *P*=.37 95% CI .98–1.07	OR .52 *P*=.08 95% CI .25–1.09	OR 1.002 *P*=.99 95% CI .71–1.42	OR 1.10 *P*=.65 95% CI .73–1.66	OR .99 *P*=.92 95% CI .72–1.41	OR 1.01 *P*=.97 95% CI .72–1.41
Consider suicide (biomarker)	OR 1.001 *P*=.85 95% CI .99–1.02	OR 1.16 *P*=.52 95% CI .75–1.79	OR 1.06 *P*=.03 95% CI 1.01–1.11	OR .67 *P*=.26 95% CI .33–1.35	OR .93 *P*=.70 95% CI .64–1.35	OR 1.15 *P*=.54 95% CI .74–1.79	OR .95 *P*=.43 95% CI .84–1.08	OR 1.03 *P*=.87 95% CI .72–1.48
APOE question correct	OR 1.02 *P*=.02 95% CI 1.002–1.03	OR .89 *P*=.55 95% CI .61–1.30	OR .95 P=.004 95% CI .92–.98	OR 1.05 *P*=.03 95% CI 1.06–2.57	OR .85 *P*=.29 95% CI .63–1.15	OR .81 *P*=.24 95% CI .57–1.15	OR 1.004 *P*=.94 95% CI .91–1.11	OR 1.17 *P*=.28 95% CI .88–1.57
Biomarker question correct	OR .99 *P*=.10 95% CI .98–1.002	OR .96 *P*=.80 95% CI .68–1.35	OR 1.0 *P*=.92 95% CI .96–1.03	OR .71 *P*=.12 95% CI .46–1.09	OR 1.02 *P*=.87 95% CI .77–1.36	OR 1.01 *P*=.96 95% CI .72–1.41	OR 1.01 *P*=.90 95% CI .91–1.11	OR 1.06 *P*=.71 95% CI .80–1.40

OR=Odds Ratio; FDR=First Degree Relative; CI=Confidence Interval