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Reasons for Seeking Genetic Susceptibility Testing Among First-Degree Relatives of People With Alzheimer Disease

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Summary: Advances in genetic research have provided a basis for susceptibility testing for Alzheimer disease (AD). Prior surveys have examined attitudes toward genetic testing for AD in hypothetical scenarios, but it is unclear what reasons would motivate people to seek testing in real-life situations. This study presents data from the first randomized trial to evaluate genetic susceptibility testing for asymptomatic adult children of people with AD. We examined (1) reasons endorsed as motivations for seeking testing, (2) demographic characteristics associated with these reasons, and (3) how these reasons related to the eventual decision to pursue testing. Eligible participants were 206 adult children of people with AD (mean age 53 years; 72% female; 93% white), 77.7% of whom ($n = 160$) went on to seek testing. Participants endorsed numerous reasons for seeking susceptibility testing (mean 7.2), encompassing a range of motivations. The most commonly endorsed reasons were as follows: (1) to contribute to research (93.9%), (2) to arrange personal affairs (87.4%), and (3) the hope that effective treatment will be developed (86.8%). Women strongly endorsed more reasons for seeking testing than men ($p < 0.05$). The best predictor of actual pursuit of testing was strong endorsement of the need to prepare family members for AD (odds ratio $= 3.3$, $p < 0.01$). Findings suggest that genetic susceptibility testing is of interest to individuals at risk for AD for a variety of reasons, even in the relative absence of available treatments. **Key Words:** Genetic testing—Susceptibility testing.

Recent advances in genetic research on Alzheimer disease (AD) have brought about the possibility of genetic susceptibility testing for asymptomatic individuals (Masters and Beyreuther, 1998; Roses, 1997). The apolipoprotein E (APOE) ε-4 allele on chromosome 19 is the only susceptibility gene for AD widely confirmed to date, although several others are under investigation (Blacker and Tanzi, 1998; St. George-Hyslop et al., 2000). Susceptibility genes are distinct from deterministic mutations in that they alter one's risk of developing a given disease, rather than inevitably causing it. Thus, susceptibility testing for AD differs in important ways from predictive testing for rare forms of the disease caused by deterministic genes (Green, 2002; Karlinsky, 1998). Given the greater prevalence of the identified susceptibility gene vis-a-vis the rare disease-causing muta-

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tions, susceptibility testing is relevant to a much larger at-risk population. Yet even as additional genetic markers and environmental factors are identified, susceptibility testing will likely not approach the near 100% certainty of predictive testing for AD. This limitation, coupled with a general lack of treatment options for AD, has prompted several consensus statements cautioning against the premature introduction of susceptibility testing (Brodaty et al., 1995; Farrer et al., 1995; Post et al., 1997; Relkin et al., 1996). However, given that treatment advances and patient demand could make genetic susceptibility testing for AD an increasingly relevant health care issue, leaders in the field have called for research on the process and impact of genetic testing (McConnell et al., 1998). To anticipate response to a health care option that might become available to millions who are at risk for AD, it will be necessary to understand more about what reasons might motivate consideration of susceptibility testing and how these perceived test benefits relate to the actual decision whether to seek testing. Research elucidating such issues will be essential in informing the responsible implementation of genetic testing programs for AD (Coon et al., 1999).

To date, empirically based investigations of attitudes toward genetic testing for AD have relied on surveys posing hypothetical scenarios. For example, a survey of a convenience sample of adults in the southeastern United States found that 69% of respondents would be interested in a hypothetical predictive genetic test for AD (Green et al., 1997). Using a general population telephone survey, Neumann et al. (2001) found that 79% of respondents expressed interest in predictive genetic testing for AD, with a vast majority claiming that a "positive" test result would prompt them to take such actions as signing advance directives (84%), spending more time with family (80%), addressing financial issues (74%), and purchasing long-term care insurance (69%). A survey of first-degree relatives of people with AD in the state of Michigan also found significant interest in genetic testing, with participants rating the following as its most important potential benefits: (1) informing later-life decisions, (2) helping plan future AD care, (3) motivating monitoring of treatment developments, and (4) contributing to AD research (Roberts, 2000). Despite these important findings, it is unclear what reasons would motivate people to pursue genetic susceptibility testing for AD in real life (as opposed to hypothetical) testing situations and how these reasons relate to actual health behaviors.

The REVEAL Study (Risk Evaluation and Education for Alzheimer's Disease) is the first multicenter trial designed to evaluate the impact of genetic susceptibility testing on asymptomatic adult children of people with AD. In this particular analysis, we examined (1) reasons endorsed prior to testing as motivations for seeking risk assessment, (2) demographic characteristics associated with these reasons, and (3) how these reasons related to the eventual decision to seek testing in our study.

METHODS

Participants and Procedures

Recruitment

In the REVEAL study protocol, adult children of patients with AD are offered genetic education, counseling, and risk assessment in a randomized, controlled trial. The study takes place at three university medical centers: Boston University, Case Western Reserve University, and the Weill Medical College of Cornell University. There were two main sources of recruitment in the study. A systematically ascertained group was contacted about REVEAL by virtue of their families' membership in AD research registries at each of the three study sites. Initial contact occurred both via letter and phone and through the affected parent's primary caregiver. For this group, the presence of AD in the affected relative had already been determined by formal clinical evaluation and/or autopsy. A self-referred group volunteered for participation after hearing about REVEAL through memory assessment clinic visits, public presentations, or the media. For most cases in this group, presence of AD in the affected parent was determined by obtaining written documentation of diagnosis via medical records or a letter from the diagnosing physician. Where written documentation was not possible, presence of AD was determined by a detailed interview with the participant about the affected parent's history.

Persons with either a living or deceased affected parent were eligible to enroll in the study. Participation was generally limited to one member per family, although some exceptions were made in cases where more than one member expressed interest in participating. Persons with a family history of AD of average age of onset younger than 60 years (thus suggesting early onset autosomal dominant AD) were excluded from the study, as were persons with two affected parents.

Procedures

Before randomization, potential participants attended an education session, in which a genetic counselor provided information about AD and the study protocol via a scripted slide slow presentation. In this session, the genetic counselor stressed the distinction between susceptibility and deterministic testing for AD and discussed in

a nondirective manner the possible benefits and limitations of susceptibility testing. Benefits included information to guide future planning and increase awareness of candidacy for potential future treatments, while limitations included the imperfect nature of test information and the lack of treatment options to prevent or cure AD. Following the education session, interested participants progressed to the blood draw stage of the study, where APOE genotype was determined for use in the randomized trial. At blood draw, potential participants were also screened with regard to their neuropsychologic functioning and psychiatric status, using the Repeatable Battery for the Assessment of Neuropsychologic Status (Randolph, 1995), Center for Epidemiological Studies-Depression scale (Radloff, 1977), and Beck Anxiety Inventory (Beck and Steer, 1990). Eight individuals with evidence of cognitive impairment and one individual with clinically significant depression and anxiety were excluded from further participation in the protocol (and were not included in data analyses for this study); relevant study personnel (i.e., neuropsychologist or site director) informed these participants of the rationale for exclusion, with follow-up contact from the genetic counselor and referrals for clinical services provided as necessary.

Interested and eligible participants then received risk assessment in the disclosure stage, where they were randomized to either the intervention or control arm of the study. Participants randomized to the intervention arm received genetic counseling and risk assessment based on their sex, family history of AD, and APOE genotype, whereas those randomized to the control group received genetic counseling and risk assessment based only on their sex and family history. Participants in the intervention arm received "lifetime" risk estimates (valid up to the age of 85 years) ranging from 13% to 57%. Participants in the control arm received risk estimates ranging from 18% to 29%. These estimates were derived from a longstanding, multisite program of AD epidemiological research based at Boston University (Farrer et al., 1997; Green et al., 2002). Risk estimates were presented to participants through graphical risk curve representations. Standard error estimates were not provided to participants because of concerns that such information would be more confusing than helpful; however, participants were informed that the risk curves did not represent exact estimates of risk.

Measurement of Reasons for Seeking Genetic Susceptibility Testing

Before attending the education session and before deciding whether to seek susceptibility testing, participants were asked to rate the importance of 12 possible reasons why they might seek such risk assessment (Table 1). Reasons offered encompassed personal, family, altruistic, pragmatic, and financial motivations; items were drawn from our prior work on attitudes toward genetic testing for AD (Green et al., 1997; Roberts, 2000). Participants were asked to indicate the extent to which they agreed with each item, using a 5-point Likert type scale (1 = "strongly agree" to 5 = "strongly disagree"). Two methods were used to quantify reasons endorsed for pursuing susceptibility testing. In the first, we summed all items with which participants agreed (i.e., responded "strongly agree" or "somewhat agree"); in the second, we summed all items with which participants strongly agreed.

Data Analysis

Descriptive statistics were used to characterize the sample in terms of its demographic features and responses to survey items. Predictors of number of endorsed reasons were examined through multiple regression analyses, using demographic characteristics as predictors; these variables were age, gender, race (white vs. other), education level (below college graduate vs. college graduate and above), annual income (<$70,000 vs. ≥$70,000), and number of AD-affected relatives (one vs. two and above). Cut points were chosen that represented meaningful group distinctions and, where relevant, approximated median splits. Also examined were associations between individual reasons endorsed and the decision to pursue testing, which was defined as the progression through the study's disclosure stage. Logistic regression analyses were used to determine if strong endorsement of specific reasons for testing predicted progression through disclosure.

TABLE 1. *Survey items assessing possible reasons for seeking genetic testing for Alzheimer disease*

1.	To prepare my spouse or children for my illness
2.	To arrange my personal affairs
3.	To arrange my long-term care
4.	To do things sooner than I had planned to do them in the future
5.	Curiosity
6.	The feeling that I am already showing symptoms of the disease
7.	The relief I would anticipate from learning that my chances are lower than I think
8.	To plan for suicide in case I learn my chances are high
9.	To confirm the feeling that I am going to get the disease
10.	The hope that an effective treatment will be developed
11.	To learn information that may eventually be useful for family planning
12.	To participate and contribute to AD research

RESULTS

Sample Demographics

A total of 206 eligible participants completed the study survey prior to the education session. All of these participants were adult children of people with AD. Demographic information on the sample can be found in Table 2. The sample was predominantly white, female, and of high socioeconomic status. The vast majority of participants (75%) had served as a caregiver for a relative with AD. The vast majority of affected parents (91%) had either a formal clinical or autopsy-confirmed diagnosis of AD; roughly half of these parents were deceased. Most participants came to the study through the self-referral recruitment source; participants were equally distributed across the three study sites.

Of the 206 participants, 160 (77.7%) proceeded through the disclosure stage. Participants who proceeded through disclosure did not differ from those who declined participation in terms of age, gender, race, income, or number of affected relatives. Participants who proceeded through disclosure had a higher mean level of education than those who declined participation (16.7 years vs. 15.8 years, $p < 0.05$).

Reasons for Seeking Genetic Susceptibility Testing

Nine of 12 reasons for seeking testing were endorsed as "strongly agree" as "somewhat agree" by at least 60% of respondents. The most commonly endorsed reasons were (1) to contribute to AD research (93.9%), (2) to arrange personal affairs (87.4%), (3) the hope that effective treatment will be developed (86.8%), (4) to arrange long-term care (81.4%), and (5) to prepare my spouse and children for my illness (77.8%). More than one fifth of participants reported concern over the feeling that they might already be symptomatic for AD (none of whom actually showed cognitive deficits on neuropsychologic screening). Responses were similar across most items, whereas items with high scatter (e.g., those concerning family planning and fears about already being symptomatic) seemed to reflect particular life stage issues and differences in participant circumstances. A small but significant subset of respondents (3.4%) agreed that "to plan for suicide if I'm at high risk" would be a motivation for seeking testing (2.4%, or 5 respondents, strongly agreed with this item). Endorsement of reasons was similar among the subset of participants who progressed through the disclosure stage of the study. Table 3 presents responses to individual items.

TABLE 2. *Sample demographics (*N = *206)*

Characteristic	Value
Mean (SD) age (yr) range	52.8 (9.5); 30–78
Sex (% female)	72.3
Race (% white)	94.7
Mean (SD) years of education	16.5 (2.3)
Median household income ($)	70,000–99,999
Status of affected parent (% living)	52.5
Diagnosis of affected parent (%)	
Autopsy-confirmed AD	16.9
Formal clinical diagnosis of AD	74.0
Suspected AD	9.1
No. of relatives with memory problems (%)	
1	40.8
2	31.6
3	16.5
4 (maximum 7)	11.1
Served as caregiver for relative with AD (% yes)	74.8
Recruitment source (%)	
Self-referred	70.9
Systematically ascertained	29.1
Study site (%)	
Boston	33.5
New York	35.0
Cleveland	31.5

Overall, 92.2% of participants endorsed at least five reasons as motivations to seek susceptibility testing (mean 7.2 reasons; median 7 reasons). Women were more likely than men to strongly endorse the following reasons as motivation to seek testing: (1) to arrange personal affairs (59.1% of women strongly endorsing vs. 31.6% of men, $p < 0.001$); (2) to arrange long-term care (52.0% vs. 33.9%, $p < 0.05$); (3) the feeling that I'm already symptomatic (9.4% vs. 0%, $p < 0.05$); (4) to confirm the feeling that I'm going to get AD (6.7% vs. 0%, $p < 0.05$); and (5) to contribute to AD research (67.0% vs. 48.7%, $p < 0.05$). Responses on individual items did not differ by age group (participants <55 years of age vs. those ≥55 years of age).

Predictors of Total Number of Reasons Endorsed

Participants who proceeded to disclosure endorsed more reasons for seeking testing than participants who declined further participation (7.3 vs. 6.7, $p < 0.05$). No significant demographic predictors were found in a regression analysis of total number of reasons endorsed for seeking testing, but a related analysis found that women strongly endorsed more reasons for pursuing susceptibility testing than men (adjusted mean [female] = 3.9 vs. adjusted mean [male] = 2.8, $p < 0.05$). Table 4 presents results from this analysis.

Strongly Endorsed Reasons Predicting Progression to Disclosure

Preliminary chi square analyses were used to select strongly endorsed reasons for seeking testing that showed an association ($p < 0.05$) with progression

TABLE 3. *Endorsement of reasons for seeking genetic testing for Alzheimer disease*

Reason	% of all respondents endorsing (% of respondents progressing through disclosure)				
	Strong agree	Some agree	Undecided	Some disagree	Strong disagree
To contribute to AD research*	62.1 (67.8)	31.8 (28.7)	5.4 (2.6)	0.0 (0.0)	0.7 (0.9)
To arrange personal affairs*	51.5 (55.6)	35.9 (32.5)	6.3 (5.0)	1.9 (2.5)	4.4 (4.4)
Hope for effective treatment	54.6 (56.6)	32.2 (30.2)	5.9 (5.7)	4.4 (5.0)	2.9 (2.5)
To arrange long-term care*	47.1 (51.6)	34.3 (33.3)	11.8 (8.8)	2.9 (2.5)	3.9 (3.8)
To prepare family for my illness	37.9 (43.3)	39.9 (35.7)	8.4 (7.0)	6.4 (6.4)	7.4 (7.6)
To do things sooner than planned	34.8 (33.1)	40.2 (43.8)	14.7 (11.9)	6.4 (6.2)	3.9 (5.0)
To get information for family planning	37.2 (41.5)	32.4 (31.4)	8.8 (8.2)	6.4 (4.4)	15.2 (14.5)
Relief if I learned I was at lower risk	27.4 (26.6)	42.2 (42.4)	18.6 (20.9)	7.4 (6.3)	4.4 (3.8)
Curiosity	19.5 (20.1)	42.9 (44.0)	14.2 (13.8)	11.7 (11.3)	11.7 (10.7)
Feeling that I'm already symptomatic*	6.8 (6.9)	14.6 (15.6)	25.2 (26.9)	18.9 (18.7)	34.5 (31.9)
To confirm the feeling that I'll get AD*	4.9 (6.2)	15.5 (13.8)	20.9 (23.1)	22.8 (21.9)	35.9 (35.0)
To plan for suicide if high risk	2.4 (2.5)	1.0 (1.3)	8.7 (10.6)	9.2 (10.0)	78.6 (75.6)

*Women were more likely than men to strongly agree ($p < 0.05$).

through disclosure. These reasons were as follows: (1) to prepare my spouse or children for my illness (88.3% of participants who strongly endorsed this item progressed to disclosure vs. 70.6% of those who did not strongly endorse this item, $p < 0.01$), (2) to contribute to AD research (84.8% vs. 66.1%, $p < 0.01$), (3) to learn information that might be useful for family planning (86.8% vs. 72.7%, $p < 0.05$), (4) to arrange long-term care (85.4% vs. 71.3%, $p < 0.05$), and (5) to arrange personal affairs (84.0% vs. 71.0%, $p < 0.05$). Each of these reasons was assessed in logistic regression models as a predictor of progression through disclosure, controlling for age, gender, race, education, income, and number of affected relatives. Given that we found collinearity among reasons for pursuing testing, they were not included as predictors in the same model but rather assessed in separate analyses. As seen in Table 5, strong endorsement of the need to prepare one's family for AD was the best predictor of progression through disclosure (odds ratio = 3.3, $p < 0.01$).

TABLE 4. *Multiple linear regression predicting number of strongly endorsed reasons for seeking testing*

Demographic predictor (reference group)	β*	*p*
Age	0.01	0.57
Gender (female)	1.07	0.01
Race (white)	–0.15	0.86
Education (college graduate)	0.39	0.36
Income (<$70,000)	0.07	0.86
No. of affected relatives (2+)	0.19	0.63

*β values represent the average difference between the two demographic groups in number of strongly endorsed reasons for pursuing testing.

DISCUSSION

This is the first study to examine reasons for pursuing susceptibility testing for AD in a sample that is presented with the opportunity for actual genetic risk assessment. Participants were assessed prior to an education session on susceptibility testing for AD and before they made the decision whether to seek testing, allowing us to evaluate potential differences between those who sought testing and those who did not. The importance of conducting such research in real life (as opposed to hypothetical) testing situations is underscored by findings from the Huntington's disease literature, in which many more at-risk individuals said they would pursue genetic testing than actually ended up doing so (Quaid and Morris, 1993).

Our results suggest that people at risk for AD pursue susceptibility testing for family, financial, pragmatic, emotional, and altruistic reasons. Most participants endorsed numerous reasons for seeking testing, many of these unrelated to medical care issues. Women in particular were likely to strongly endorse certain reasons for seeking testing, including arrangement of personal affairs and long-term care. Several pretest motivations pre-

TABLE 5. *Strongly endorsed reasons as predictors of progression through disclosure*

Strongly endorsed reason	Odds ratio (95% CI)	*p*
To prepare my spouse or children for AD	3.33 (1.43, 7.77)	0.005
To contribute to AD research	2.75 (1.15, 6.59)	0.024
To arrange personal affairs	2.62 (1.25, 5.29)	0.011
To arrange long-term care	2.52 (1.19, 5.32)	0.015
To learn information for family planning	2.25 (1.02, 4.96)	0.046

dicted the actual pursuit of testing in the study protocol. In particular, strong endorsement of the motivation to prepare one's family for the possibility of AD was the best predictor of test seeking in this study.

Participants' reasons for pursuing testing reflect what has been described in the health psychologic literature as problem-focused and emotion-focused coping (Lazarus and Folkman, 1984). That is, people may wish to pursue susceptibility testing not only to inform how they will resolve pragmatic concerns of later life (e.g., arranging for health care) but also to help address the anxiety of being at risk for a severe, progressive, and incurable neurologic disorder. Our findings also support and extend prior research demonstrating that participants frequently endorse altruistic motivations both for participation in clinical research in general (Cassileth et al., 1982; Madsen et al., 2002) and genetic testing research in particular (Geller et al., 1999). Social scientists have typically defined altruism as a form of helping behavior that provides no anticipated material benefits to the agent and may incur some loss. In our study, the desire to contribute to research was the most commonly endorsed reason for participation. Thus, altruistic motivations are clearly important in individuals' consideration of susceptibility testing for AD. The fact that all individuals were contemplating participation in a research protocol at the time of assessment may help explain why this altruistic reason was so frequently endorsed. Because such unselfish motivations are not always relevant in a clinical setting, other more self-focused motives may be responsible for individuals' desire to seek testing in actual clinical practice. Here, what evolutionary psychologists might call kin altruism, or the motivation to increase the welfare of immediate family members, might be more relevant (Batson, 1991).

Our findings reflect similar motivations for seeking testing as endorsed in prior hypothetical scenario-based surveys on genetic testing for AD (Green et al., 1997; Roberts, 2000). Thus, whereas assessment of reasons for seeking genetic testing for AD is ideally done in real-life testing situations, our results suggest that surveys using hypothetical scenarios may be a reasonable alternative in determining the issues of greatest importance to individuals at risk. Our findings were also consistent with research on real-life deterministic DNA testing for early-onset familial AD and frontotemporal dementia (Steinbart et al., 2001), where the most commonly cited reasons for seeking testing were for assistance with family and financial planning and to gain relief from anxiety. These findings underscore the notion that individuals at risk for AD may pursue genetic testing for reasons that are not directly related to their medical care.

Our results further suggest that people pursue genetic testing for AD for many of the same reasons that they seek testing for other disorders, such as Huntington's disease and breast cancer (Croyle and Lerman, 1995; Lerman et al., 1996; Marteau and Croyle, 1998). Similar themes across these testing situations are the desires to inform future planning (e.g., arranging health care and finances) and to help prepare family members for one's potential illness. Notable exceptions seem related to the differing ages of onset of the disorders. For example, reproductive decision-making concerns, although not irrelevant in the case of AD, are more urgent for those considering testing for breast cancer and earlier onset neurologic disorders. However, planning for long-term care is a more salient issue for those at risk for AD. Another reason particular to testing for AD involves what has been described as "anticipatory dementia," or anxiety among asymptomatic first-degree relatives about developing the disorder (Cutler and Hodgson, 1996). For example, more than 20% of our respondents said that they were motivated to pursue testing because of the feeling that they might already be showing symptoms of the disorder (even though none of these participants was found to show significant cognitive deficits on the study's pretest screening measures). This finding suggests that genetic susceptibility testing programs will need to develop methods to address participants' understandable, yet often unfounded, anxieties about perceived current cognitive deficits.

A small but notable subset of participants indicated that they might use genetic testing results to plan for suicide. However, follow-up interviews with participants endorsing this item suggested that they thought they would consider this option only if and when they became symptomatic for AD and not in reaction to test results per se. Fortunately, no participants to date have expressed suicidal ideation in response to risk assessment in REVEAL. Nevertheless, managing the risk of suicide in reaction to test results has been an important issue in the development of genetic testing programs for Huntington's disease (Almqvist et al., 1999; Farrer, 1986) as well as in clinical research studies with early-stage AD patients with preserved insight (Ferris et al., 1999). The importance of risk management is further underscored by the anecdotal report of a Swedish individual who developed suicidal ideation after receiving a positive test result for a genetic mutation that causes an autosomal dominant form of AD (Lannfelt et al., 1995). While the relatively ambiguous risk information from susceptibility testing may be less likely than deterministic predictive test results to prompt such reactions, the REVEAL Study included safety measures to guard against adverse

events, with extended genetic counseling support and referral for mental health services available if participants experienced significant emotional distress following risk disclosure.

That we found women to strongly endorse more reasons for seeking testing than men seems consistent with related research on genetic testing for other disorders (e.g., cystic fibrosis), where women were more likely to undergo testing (Marteau and Croyle, 1998; Marteau et al., 1997). Our finding may also be related to the fact that women are three times more likely than men to have participated in dementia caregiving (Alzheimer's Association & the Alliance for Caregiving, 1999); they may therefore be more intimately aware of the severe consequences of AD and thus have more motivations to seek testing. However, we found no sex differences in the proportion of eligible participants who actually followed through with testing.

This study was the first to examine the relationship between stated reasons for seeking susceptibility testing for AD and the subsequent decision to pursue testing. Several stated reasons, most of which involved informing future plans, were associated with actual pursuit of testing in our study. The best predictor of test seeking was strong endorsement of the need to prepare one's spouse or children for the possibility of AD. This suggests that concern over "being a burden" to one's family is a prime motivator of pursuit of genetic testing. In this manner, individuals at risk for AD may seek genetic risk assessment with an overarching goal of generativity, or caring for the next generation (McAdams and de St. Aubin, 1992). Generative concerns have also been noted in research on susceptibility testing programs for breast cancer, where learning about children's disease risk was cited as the most important benefit of testing (Lerman et al., 1996). "Contributing to others" has also been identified in other medical research as a means by which individuals confront feelings of mortality (Steinhauser et al., 2000).

There are several limitations that should be taken into account when considering results of the study. For example, our results should be interpreted with caution given the nonrepresentative nature of the sample. Participants were disproportionately female, white, and of high socioeconomic status. Also, we assessed reasons for pursuing testing using a forced-choice answer format. Participants may have had other reasons for pursuing testing that were not included among the 12 reasons listed. In addition, this study addressed only pretest reasons for pursuing genetic susceptibility testing. It remains to be seen how views on the benefits and limitations of susceptibility testing might change once participants have actually completed genetic counseling and risk disclosure. Also, given that assessment took place before the study education session, it is unclear to what extent participants' reasons for pursuing susceptibility testing are grounded in a realistic appreciation of its limitations; it is also not known if and how motivations for seeking testing will translate into specific health behaviors (e.g., changes in lifestyle, health insurance) following risk assessment. Participants in this study were not required to pay for testing, which may be a significant factor in the decision to pursue testing in a clinical context. This study was also carried out with explicit, written guarantees of patient confidentiality, which may not be available to the same extent in actual clinical practice. Further studies of these variables, particularly those that incorporate combined quantitative and qualitative approaches, are clearly warranted. As the REVEAL Study is completed, we hope to be able to examine further these and related issues. For example, we have initiated a series of intensive, open-ended interviews with a subset of participants who have completed the protocol; this qualitative study is designed to help understand in richer detail how participants decided to pursue testing and how risk information has affected them. Also, we plan in future quantitative analyses to examine (1) demographic and attitudinal predictors of who sought risk assessment in REVEAL, (2) the psychologic impact of risk disclosure, and (3) the impact of risk disclosure on participants' health behaviors and insurance/retirement plans.

The "genetic revolution" in modern medicine will increasingly present individuals and families with complex health care dilemmas. To respond to these changes with responsible, effective health policy and services, it will be crucial to examine how people confront, comprehend, and are affected by genetic risk assessment options. This study represents a first step in learning why people at risk for AD might seek out susceptibility testing, despite limited prevention options and the inherent limitations of the available risk estimates.

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