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Factors Affecting Recall of Different Types of Personal Genetic Information about Alzheimer's Disease Risk: The REVEAL Study

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Abstract

Background/Aims—Risk communication and assuring comprehension of risk information are essential components of providing persons with personalized genetic risk information. One measure that is commonly used to assess the efficacy of risk communication is risk recall. Our primary aim was to examine whether particular types of genetic risk information are especially challenging for some people to recall.

Methods—Data were obtained through a multi-site clinical trial in which different types of genetic risk-related information were disclosed to individuals (n=246) seeking a risk assessment for Alzheimer's disease.

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CONFLICTS OF INTEREST

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Results—Six weeks after disclosure, 83% of participants correctly recalled the number of risk-increasing *APOE* alleles they possessed, and 74% correctly recalled their *APOE* genotype. While 84% of participants recalled their lifetime risk estimate to within five percentage points, only 51% correctly recalled their lifetime risk estimate exactly. Correct recall of the number of *APOE* risk-increasing alleles was independently associated with higher education ($p<0.001$), greater numeracy ($p<0.05$) and stronger family history of Alzheimer's disease ($p<0.05$). Before adjustments for confounding, correct recall of *APOE* genotype was also associated with higher education, greater numeracy and stronger family history of Alzheimer's disease, as well as with higher comfort with numbers, and European American ethnicity (all $p<0.05$). Correct recall of the lifetime risk estimate was independently associated only with younger age ($p<0.05$).

Conclusions—Recall of genotype-specific information is high, but recall of exact risk estimates is lower. Incorrect recall of numeric risk may lead to distortions in understanding risk. Further research is needed to determine how best to communicate different types of genetic risk information to patients, particularly those with lower educational levels and lower numeracy. Healthcare professionals should be aware that each type of genetic risk information may be differentially interpreted and retained by patients, and that some patient subgroups may have more problems with recall than others.

Keywords

Risk recall; genetic testing; complex diseases; genetic counseling; risk assessment

INTRODUCTION

Personal genetic and genomic information is increasingly available to individuals and families: patients and their relatives are receiving individual results from clinical genetic testing and genome sequencing for diagnostic purposes [1,2], and healthy individuals are receiving personal genomic results in research studies such as ClinSeq [3], the MedSeq Project [4], and the Personal Genome Project (PGP) [5]. One assumption of personal genomics is that people will retain and act upon the individualized genomic results they receive to reduce their future disease risk. Central to this assumption is that people will recall the genomic information they receive: if they do not recall it, presumably they cannot act upon it. Current theories of health behavior assert that health behavior changes are often driven by changes to perceptions about disease susceptibility [6,7], supporting the potentially important roles of risk recall and risk interpretation in health. Additionally, risk recall is one measure that is commonly used to assess the efficacy of risk communication [8]. Risk communication and assuring comprehension of risk information are essential components of providing persons with personalized genetic risk information. If patients do not accurately recall and interpret genetic risk information they receive, this could influence decision-making: they might engage in inappropriate actions such as pursuing interventions despite low risk on the one hand, or ignoring high risk information on the other hand [9]. Thus, risk recall is an important factor when considering the potential utility of personal genomics. In traditional clinical genetics settings, research has found that individuals often incorrectly recall risk information, even after genetic counseling [10,11]. For example, one

study found that almost 60% of women could not recall their breast cancer risk one month after breast cancer genetic counseling [11].

The REVEAL (Risk Evaluation and Education for Alzheimer's Disease) Study is a series of randomized controlled trials designed to evaluate the impact of providing cognitively normal individuals with a risk assessment for Alzheimer's disease (AD) based on *APOE* genotype (an AD susceptibility variant). Risk recall for *APOE* genotype and AD risk was previously examined in an analysis exploring how well individuals remembered their AD risk assessment results several weeks and months after disclosure [8]. In that study, 41% of subjects could not recall their lifetime risk and 31% could not recall their *APOE* genotype six weeks after they learned of their *APOE* genotype and risk for developing AD. It was proposed that poor recall might have been due to information overload, as subjects were provided with several statistics in addition to complex information about multifactorial inheritance. It is also possible that other characteristics, such as demographic factors, psychological states, and numeracy influenced participants' ability to recall the personal genetic risk information they received.

Personal genetic information can be provided to individuals in a number of different ways. As described elsewhere [12-14], individuals receiving personal genetic information about their AD risk in the REVEAL Study received different types of AD risk-related information. First, they were given their specific *APOE* genotype (e.g. ε3/ε4). Second, they were informed how many risk-increasing alleles they have. Because it is the ε4 allele that is the risk-conferring allele, individuals with one ε4 allele were told they had one risk-increasing allele, and individuals with the ε4/ε4 genotype were told they had two risk-increasing alleles. Third, an overall lifetime risk estimate was calculated for them based on a number of factors including their *APOE* genotype, and they were given this risk estimate (e.g. "your lifetime risk of developing Alzheimer's disease is 70%").

Recalling each of these different types of genetic risk information may make different cognitive demands on the recipients of the information, and may be influenced to varying degrees by factors such as numeracy and emotional factors. This is important to examine given that personalized genomic information such as that obtained through panels of genetic tests or eventually through genome sequencing will increasingly require people to handle multiple pieces of genomic information at once. The REVEAL Study provides a useful model for exploring how people differentially recall differing types of genetic risk information arising from a single test. The purpose of this analysis was to investigate the components that may be associated with an individual's ability to recall information related to his or her previously disclosed *APOE* genotype, the number of risk-increasing alleles that he or she was found to possess by genetic testing, and lifetime risk estimate for AD. The study builds on previous research by Eckert et al [8] by examining recall of *APOE* genotype and lifetime risk for AD in two key ways: (1) we use data from an entirely separate REVEAL Study trial; and (2) we examine whether numeracy, self-reported comfort with numbers, and emotional factors influence recall in addition to other socio-demographic factors.

MATERIALS AND METHODS

Study design

This was a randomized controlled trial in which study participants received personal genetic information about their risk of developing AD. Data for this study were collected as part of the third clinical trial conducted in the REVEAL Study. The REVEAL Study is an ongoing series of multi-site randomized controlled trials designed to evaluate the psychological and behavioral impact of a genetic risk assessment for AD. In the study, individuals without cognitive impairment are informed of whether they have one or two copies of a common variant, the *APOE* ε4 allele, which is a genetic risk marker for AD.

Participants

Participants for this REVEAL Study trial were cognitively normal adults recruited through a combination of active strategies (e.g. mailings to research registries, referrals from physicians and other studies) and passive approaches (e.g. newspaper article or advertisements, website postings). Some strategies targeted AD-specific audiences, such as family members in memory clinic waiting rooms, while others targeted the general population, such as community newspapers. To achieve greater diversity of age and sex, the study team established goals to enroll equal numbers of adults over and under the age of 60, to enroll equal numbers of men and women, and to enroll 75% of subjects having a single affected first degree relative (FDR), while 25% had no family history. Individuals were not eligible to participate if they: were less than 18 years of age; had untreated moderate-to-severe anxiety or depression; had possible signs of early dementia on standard psychological screening; had relatives with AD where the age of onset was less than 60 years; or had a family member in the study. Data were collected at Boston University, University of Michigan, Howard University and Case Western Reserve University.

Procedure

Potential participants were initially contacted via telephone to determine eligibility, as well as to obtain verbal informed consent and demographic information. Eligible participants were then mailed an educational brochure, which included information about AD, the *APOE* gene and genotypes, and other risk factors associated with AD, as well as information about the study. An in-person visit was subsequently scheduled and conducted, during which participants had the opportunity to ask a genetic counselor questions about the educational brochure, written informed consent was obtained, and baseline measures were administered. A blood draw for genetic testing was done, and samples were sent to Athena Diagnostics, Inc. for genotyping. Disclosure of the *APOE* test results was performed by a genetic counselor during either a second in-person appointment or a telephone call. During disclosure, in sessions that lasted 16 minutes on average, genetic counselors verbally disclosed participants' results using a scripted template, emphasizing participants' genotypes, number of risk-increasing alleles, and numerical lifetime risk estimates expressed as percentages as described in prior reports [12-15]. Participants were also given written materials that included a risk curve depicting their lifetime risk for AD and a summary statement containing their *APOE* genotype, their estimated lifetime risk of AD, and the factors used to calculate their lifetime risk (see Supplementary Materials). One week after

disclosure, the genetic counselor called participants to ensure they were coping adequately with results and to reiterate disclosure information. Near the end of the disclosure session and safety check-in, genetic counselors confirmed the participant's understanding of information by querying them about their genotype and risk estimates and correcting any misunderstandings. In this paper, we present data from the six-week follow-up, in which validated psychological scales and risk recall surveys were administered.

Measures

Demographics

Self-reported gender, age, race and education were elicited during the initial phone interview. Education was reported as the number of years of schooling that the participant had completed.

Family history

Participants reported the total number of relatives they had with diagnosed AD or with an undiagnosed progressive dementia syndrome.

Actual lifetime risk estimate

A lifetime risk estimate for AD was calculated based on the individual's *APOE* genotype, age, gender, race and family history of AD. The estimate was calculated using an algorithm developed by the study investigators [12,15], and was expressed as a percentage.

Independent cognitive and psychological variables

Numeracy—Numeracy was measured at baseline using a well-validated 8-item measure [16]. The scale includes items to assess an individual's ability to: discern differences in magnitudes of health risk (e.g. “Which of the following numbers represents the biggest risk of getting a disease? 1 in 1000, 1 in 100 or 1 in 10?”); perform simple mathematical tasks related to risk (e.g. “If Person A's risk of getting a disease is 1% in ten years, and person B's risk is double that of A's, what is B's risk?”; and convert between percentages, proportions and probabilities (e.g. “If the chance of getting a disease is 10%, how many people would be expected to get the disease out of 1000?”) [16]. Each item answered correctly receives a score of 1, giving a total scale score ranging from 0 to 8. Because participants scored very highly and the distribution of scores for this measure was highly skewed, scores were dichotomized into “lower numeracy” (score of 7 or lower) versus “higher numeracy” (score of 8). Cronbach's alpha was 0.82 indicating good reliability.

Self-reported comfort with numbers—Self-reported comfort with numbers was conceptualized in this study as an individual's preferences regarding the presentation of (or their ‘comfort with’) numerical information. This was assessed at baseline with the ‘preferences’ subscale of a validated subjective numeracy scale [17,18]. The 4 items in the subjective numeracy ‘preferences’ subscale that were used in this study are: “When reading the newspaper, how helpful do you find tables and graphs that are parts of a story? (1 = not at all, 6 = extremely)”; “When people tell you the chance of something happening, do you prefer that they use words (‘it rarely happens‘) or numbers (‘there's a 1% chance’)? (1 =

always prefer words, 6 = always prefer numbers)"; "When you hear a weather forecast, do you prefer predictions using percentages (e.g., 'there will be a 20% chance of rain today') or predictions using only words (e.g., 'there is a small chance of rain today')? (1 = always prefer percentages, 6 = always prefer words)"; and "How often do you find numerical information to be useful? (1 = never, 6 = very often)". Item 3 was reverse coded, and the average of the four items was calculated to produce a final score with possible range of 1 to 6, where 1 indicates low comfort with numbers, and 6 indicates high comfort with numbers. Cronbach's alpha was 0.70 indicating good reliability.

Anxiety—Anxiety was measured at the 6-week follow-up using the validated Beck Anxiety Inventory (BAI) [19]. This scale lists 21 common anxiety symptoms, such as lightheadedness, shakiness, and trembling. Each item is measured on a scale of 0-3 of how bothersome the symptom has been in the past month (0 = Not at all, 3 = Severely), for a total score between 0 and 63, with higher scores indicating increased anxiety. Scores above 15 indicate moderate anxiety, and scores above 25 indicate severe anxiety.

Distress—Distress was measured at 6-week follow-up using the validated Impact of Event Scale (IES) [20]. This scale lists 15 statements regarding intrusive thoughts and avoidant behavior surrounding a traumatic event, such as "pictures about it popped into my mind" or "I avoided letting myself get upset when I thought about it or was reminded of it." Each item is scored as 0 = not at all, 1 = rarely, 3 = sometimes, 5 = often; for a total score between 0 and 75, with higher scores indicating increased distress. Scores of 20 or above typically indicate significant distress.

Dependent variables

Recall of APOE genotype—To assess participants' recall of their *APOE* genotype, they were asked the following item at 6-week follow-up: "What were your *APOE* genetic test results?" Response options were: ε2/ε2; ε2/ε3; ε2/ε4; ε3/ε3; ε3/ε4; ε4/ε4; and "don't remember." The responses of participants who recalled the correct genotype were coded as 'correct', while the responses of those who recalled the incorrect genotype, who couldn't remember their genotype, or who didn't answer the question, were coded as 'not correct'.

Recall of number of APOE risk-increasing alleles—To assess whether participants recalled the number of *APOE* risk-increasing alleles they had, they were asked the following item at 6-week follow-up: "Do you have the form (allele) of *APOE* that increases risk for Alzheimer's disease?" There were four responses options: "Yes, I have one copy of the risk increasing form of *APOE*"; "yes, I have two copies of the risk increasing form of *APOE*"; "no"; and "I don't remember". Responses were coded as either 'correct' (i.e. the response matched the actual number of ε4 risk alleles the participant had) or 'not correct' (i.e. the response did not match the number of ε4 risk alleles the participant had, the participant could not remember how many ε4 risk alleles they had, or the participant did not answer the question).

Recall of lifetime risk estimate—To assess recall of the lifetime risk estimate based on genetic and non-genetic risk factors, the following item was used at 6-week follow-up:

"Please write in (or approximate if you can't remember the exact number) the percentage you were given as your lifetime risk of developing Alzheimer's disease." Participants were also reminded that in this study lifetime risk referred to the risk of developing the disease between birth and the age of 85 years. We analyzed recall of lifetime risk estimate in two ways. First, participants who correctly recalled the lifetime risk value they had received to within five percentage points were coded as having 'correct' responses, while those who recalled a different value to that which they had been given, or who did not answer the question, were coded as having 'not correct' responses to this question. Second, only those participants who correctly recalled the *exact* AD lifetime risk value they had received within the study were coded as having 'correct' responses. We also report the proportion of participants whose responses fell within 10% of the exact lifetime risk estimate value they had been given.

Statistical analyses

Descriptive statistics were generated to characterize the demographics of the sample and outcome measures. Univariate analyses included ANOVA and chi-square tests to compare each continuous and categorical predictor, respectively, for correct versus not correct recall groups for each recall measure. Fisher's exact tests were used for race given the small numbers of participants in one of the response categories. Logistic regression analyses were conducted to calculate the independent associations between variables and recall of each of the three types of genetic risk information. Variables to be included in the multivariate models were selected prior to analysis. All tests of significance were 2-sided. Data was analyzed using SAS 9.3.

RESULTS

Socio-demographic and baseline characteristics

Of 380 individuals who entered the study, 13 were screened out because they had two or more AD-affected FDRs, two could not meet appointment demands, one scored too low on neuropsychological testing, one scored too high on both baseline depression and anxiety measures, and one because she was simultaneously enrolled in a similar study. An additional 106 enrollees withdrew or were lost to follow-up, and 10 were excluded because they inadvertently received miscalculated risk information and these were corrected after the initial risk disclosure. This gave a final sample of 246 participants who were included in the present analyses (65% of initial enrollees). The ages of these participants ranged from 21 to 83 years, with a mean of 58.4 years (SD = 13.1). There were slightly more women than men, with 53% of the sample being female. The majority (84%) were European-American, while 15% were African-American, and 1.6% were classified as "Other". Two percent reported Hispanic ethnicity. The mean years of schooling completed was 16.8 years (SD = 2.3 years; range 10-20 years). On average, participants reported having two relatives with AD or progressive dementia, ranging from a minimum of 0 up to a maximum of 11 relatives. The participants' calculated lifetime risk estimates for AD ranged from 6% to 70%, with a mean of 29% (SD = 15%). The mean numeracy score was 7.2 (SD = 1.35, range 1 to 8 on a scale of 0 to 8). When dichotomized into lower (score=1-7) versus higher (score=8) numeracy, 150 participants were classified as having higher numeracy and 93 participants were

classified as having lower numeracy. The mean self-reported comfort with numbers score was 4.6 (SD = 1.0, range = 1.5 to 6.0) on a scale where 1 = low comfort and 6 = high comfort. See Table 1 for full descriptive statistics of the participants at baseline.

Anxiety and distress at follow-up

At six weeks after disclosure, the mean anxiety score was 3.39 (SD=4.27, range=0 to 26) and the mean distress score was 3.90 (SD=7.20, range=0 to 45). Both means were well below predefined cutoffs for clinical concern.

Recall of APOE genotype

Absolute level of risk recall at follow-up—Three participants did not answer the question regarding which *APOE* genotype they had (including response option, 'I don't remember'), and so were coded as having a "not correct" response. Overall, 182 (74.0%) participants were coded as having correctly recalled their *APOE* genotype.

Factors associated with risk recall: univariate analyses—In univariate analyses, participants who were more likely to correctly recall their *APOE* genotype were of European-American (p=0.03), had a stronger family history of AD (p=0.025), had more years of education (p=0.01), had higher numeracy (p=0.010), and had higher self-reported comfort with numbers (p=0.002) (Table 2).

Factors associated with risk recall: multivariate analysis—In the multivariate analysis, we examined the adjusted odds ratios (ORs) and 95% confidence intervals (95% CIs) for each of the variables and each of the recall outcomes, and compared these to the unadjusted ORs (95% CIs). The point estimates changed (and the confidence intervals widened) considerably for each of the predictor variables, suggesting that there was confounding between them. None of the variables remained significantly associated with recall in the multivariate model (Table 3). In order to check whether there were differences in associations between participants who received their results in-person vs. over the telephone, we ran the analyses again, first among only the in-person group, and second among only the telephone group. As Supplemental Table 1 shows, there were some differences between the two subgroups. For example, women had better recall than men in the in-person disclosure group, whereas men had better recall than women in the telephone disclosure group.

Recall of number of *APOE* risk-increasing alleles

Absolute level of risk recall at follow-up—One participant did not answer the question regarding recall of *APOE* risk-increasing alleles. Overall, 205 (83.3%) participants correctly recalled their number of *APOE* risk-increasing alleles.

Factors associated with risk recall: univariate analyses—In univariate analyses, participants who were more likely to correctly recall their number of *APOE* risk-increasing alleles were younger (p=0.002), had more years of education (p<0.001), were European-American (p=0.005), had a stronger family history of AD (p=0.006), had higher numeracy (p<0.001), and had higher self-reported comfort with numbers (p<0.001) (Table 2).

Factors associated with risk recall: Multivariate analysis—In multivariate analysis, the point estimates changed for race/ethnicity and self-reported comfort with numbers, and these two variables were no longer associated with correct recall of number of *APOE* risk-increasing alleles, suggesting that there was confounding with the other variables in the model. The point estimates also changed for the education, family history and numeracy ORs, but the 95% CIs for these values did not cross 1.00: these variables remained significantly associated with correct recall, suggesting that they were independently associated with recall (Table 3). There were some differences between the in-person and telephone disclosure subgroups (see Supplemental Table 2).

Recall of Alzheimer's disease lifetime risk estimate

Absolute level of risk recall at follow-up—When asked to recall the AD lifetime risk estimate they had been given, 14 participants did not answer the question. Among the 232 participants who answered the question, the mean lifetime risk value recalled was 27.4% (SD=14.9, range=4% to 70%), which was slightly lower than the lifetime risk values that were provided to participants within the study (mean=28.8%, see Table 1). Overall, 126 (51.2%) were coded as having correctly recalled their exact AD lifetime risk estimate. Participants who did not correctly recall their exact lifetime risk were approximately twice as likely to underestimate (n = 74; 69.8%) as overestimate (n = 32; 30.2%) their lifetime risk of AD. A total of 207 (84.1%) recalled their lifetime risk within 5% of the lifetime risk estimate value they were given. Two hundred and seventeen (88.2%) recalled their lifetime risk within 10%.

Factors associated with risk recall: Univariate analyses—Age, education, race/ethnicity, numeracy and self-reported comfort with numbers were associated with correct recall of lifetime risk estimate to within 5% of the lifetime risk estimate they were given (Table 2). Age was the only characteristic found to be associated with correct recall of *exact* lifetime risk estimate, with younger participants being more likely than older participants to correctly recall their exact lifetime risk estimate (p=0.019) (Table 2).

Factors associated with risk recall: Multivariate analysis—We ran a multivariate model with recall of lifetime risk to within 5% points as the outcome: in this model, the point estimates changed for education, race/ethnicity, numeracy and self-reported comfort with numbers, and these variables were no longer associated with correct recall of number of *APOE* risk-increasing alleles, suggesting that there was confounding with the other variables in the model. For age, the point estimate did not change and the 95% CI did not cross 1.00, suggesting that age was independently associated with correct recall of lifetime risk to within 5 percentage points (Table 3). Although no other variables were associated with recall of *exact* lifetime risk in the unadjusted analyses, for completeness we ran the multivariate model with age and the other potential predictors of exact recall included and the OR for age and recall was unchanged (see Table 3). Because of the larger number of missing responses to this question than to the previous two questions, we re-ran the model with the missing responses excluded (data not shown) and there was no significant difference between the two models. There were few differences between the in-person and telephone disclosure subgroups (see Supplemental Table 3).

DISCUSSION

This study examined factors associated with recall of a disclosed genetic risk assessment for AD, based on a susceptibility variant genotype (*APOE*). We found that 26% of individuals were unable to recall their *APOE* genotype, 17% were unable to recall the number of risk-increasing alleles they were found to have, 16% were unable to recall their lifetime risk estimate to within 5 percentage points, and 49% of individuals were unable to precisely recall their lifetime risk estimate, at six weeks post-disclosure. These results are consistent with previous research regarding risk recall, which has found that a significant number of people are unable to recall their risk assessment after a short time [8,10,11]. Our results build on previous research by suggesting that different types of genetic risk information may have different cognitive demands or be influenced by different factors when recalling the information. Correct recall of *APOE* genotype was not associated with any of the variables examined in adjusted analyses, whereas correct recall of exact lifetime risk was associated with age only, and correct recall of the number of risk-increasing alleles possessed was independently associated with each of these variables: education, numeracy and family history.

This study suggests that numeracy is an important influence on how well people remember the number of risk-increasing alleles they have. These results are supported by several studies in other fields, which have also found low numeracy to have a negative impact on how well patients recall their risk, how well patients recall other types of medical information, and whether they engage in risky health behaviors [21-23].

Higher educational attainment was found to be a significant predictor of correct recall of the number of risk-increasing alleles an individual possessed. Our results also demonstrate that the association between numeracy and risk recall is independent of education, further confirming previous research that has found educational levels and numeracy are distinct determinants of recall [16, 24]. It is possible that recalling the number of risk-increasing alleles possessed is a more complex task for an individual than simply remembering a genotype as positive or negative, since to do this they must have at least a rudimentary understanding of how each individual has two copies of each gene and what an ‘allele’ is – essentially, they need a basic understanding of genetic principles.

One question arising from our study is, what criteria should be used to define people's recall of their lifetime risk estimates as correct or incorrect? In this study, we classified people as having ‘correct’ recall of their lifetime risk estimate in two ways: first, they were classified as ‘correct’ if they recalled their lifetime risk to within 5 percentage points of the value that had been communicated to them, and second, they were classified as ‘correct’ if they recalled the value exactly. The former of these is the approach we employed in our previous publication examining recall [8]. There are advantages to both approaches. On the one hand, it is possible to argue that any cut-off for correct recall is arbitrary, e.g. if within-5 percentage points were used to classify responses as ‘correct’, and the risk estimate presented was 28%, then a response of 23% would be categorized as correct and a response of 22% as incorrect. This could perhaps merely extend the problem and not provide any more meaningful information than using *exact* recall to define ‘correct’ (i.e. only classifying

people who recall 28% as recalling the ‘correct’ lifetime risk estimate). However, on the other hand, it is arguably not clinically relevant to require that people recall an exact lifetime risk. An additional consideration is that participants are being asked to recall lifetime risk numbers that are by definition *estimates* and not true values. Given this, then what we are assessing is people's *recall* of a numeric value that was provided to them, a number that is by definition inexact. This could support the more lenient approach of categorizing the wider range of values as ‘correct’.

Of note, recall rates were higher in this trial than in prior trials [8], likely because the protocol had been changed to have genetic counselors confirm understanding and reiterate results during the 1-week safety check, unlike in prior REVEAL Study trials. Genetic test providers can likely help patients retain important details about their test results by making similar modifications to their own protocols. In addition, participants in this study were more likely to recall the number of risk alleles than their specific genotype, suggesting that these participants were more likely to retain the gist of the information – in this case, whether or not they had a risk-increasing form of APOE - than the descriptive data about their genotype.

There were some limitations to this study. An ascertainment bias probably exists, as people actively interested in receiving a genetic risk assessment may be more likely to recall the information that is presented to them. Therefore, the information gathered from this study may not be relevant to individuals who are less interested in learning about their risk for a particular disease. This study was conducted with a population of highly educated, highly numerate individuals, characteristics that are not representative of the general population, and study participation rates following opportunity to enroll could not be calculated due to the combination of recruitment strategies. It is also important to note that risk recall does not necessarily imply understanding of risk. While a participant may be able to retain risk-specific information, he or she may simply be recalling numbers without processing their meaning. A REVEAL Study publication previously addressed this issue by investigating individuals who were found to accurately recall their risk, and asking whether they truly internalized this communicated risk assessment [25]. That study found that many individuals who accurately recalled their risk nonetheless continued to hold many of their previous contradictory beliefs regarding their risk of developing AD.

In conclusion, the findings from this study suggest that accurate recall may be lower for exact lifetime risk estimates than for other domains of genetic risk information. Poor recall may indicate lower levels of risk understanding, which could have adverse implications for informed medical decision-making. Further research is needed to determine how best to communicate different types of genetic risk information to patients, particularly those with lower educational levels and lower numeracy. Healthcare professionals should be aware that each type of genetic risk information may be differentially interpreted and retained by patients, and that some patient subgroups may have more problems with recall than others.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1

Sociodemographics and baseline characteristics

N = 246	**Mean±SD**
Age, years	58.4 ± 13.1 years, range 21- 83 years
Gender	
Female, N (%)	130 (52.8%)
Male, N (%)	116 (47.2%)
Education, years of schooling	16.8 ± 2.3 years, range 10 - 20 years
Race	
African-American, N (%)	36 (14.6%)
European-American, N (%)	206 (83.7%)
Other, N (%)	4 (1.6%)
Family history (total number of relatives with Alzheimer's)*	2.0 ± 1.6 relatives, range 0 - 11 relatives
Numeracy**	
Low numeracy (score=1-7)	93 (38.3%)
High numeracy (score=8)	150 (61.7%)
Self-reported comfort with numbers (possible range = 1-6)*	4.6 ± 1.0, range 1.5 - 6.0
Actual lifetime risk (percent risk of AD by 85 years of age)	29% ± 15%, range 6% - 70%

* Data missing for 2 cases

** Data missing for 3 cases

Table 2

Unadjusted associations between participant characteristics and correct recall of APOE genotype, number of risk-increasing alleles and lifetime risk estimate

	APOE genotype			Number of risk-increasing alleles			Lifetime risk estimate (± 5 percentage points)			Lifetime risk estimate (exact)		
Characteristic	**Correct**	**Incorrect**	**Unadj. sig.**	**Correct**	**Incorrect**	**Unadj. sig.**	**Correct**	**Incorrect**	**Unadj. sig.**	**Correct**	**Incorrect**	**Unadj. sig.**
Overall	182 (74.0 %)	64 (26.0%)	N/A	205 (83.3%)	41 (16.7%)	N/A	207 (84.1%)	39 (15.9%)	N/A	126 (51.2%)	120 (48.8%)	N/A
Age												
Mean (SD)	57.91 (13.09)	59.62 (13.00)	p=0.37	57.24 (13.14)	63.95 (11.21)	**p=0.002**	57.43 (13.00)	63.26 (12.62)	**p=0.010**	56.46 (13.13)	60.35 (12.73)	**p=0.019**
Gender												
Female, N (%)	95 (73.1%)	35 (26.9%)	p=0.73	108 (83.1%)	22 (16.9%)	p=0.91	109 (83.8%)	21 (16.2%)	p=0.89	62 (47.7%)	68 (52.3%)	p=0.24
Male, N (%)	87 (75.0%)	29 (25.0%)		97 (83.6%)	19 (16.4%)		98 (84.5%)	18 (15.5%)		64 (55.2%)	52 (44.8%)	
Education, years of schooling												
Mean (SD)	16.97 (2.24)	16.14 (2.51)	**p=0.01**	17.13 (2.15)	14.88 (2.33)	**p<0.001**	16.97 (2.21)	15.62 (2.66)	**p=0.001**	16.78 (2.14)	16.73 (2.53)	p=0.88
Race												
African American, N (%)	21 (58.3%)	15 (41.7%)		23 (63.9%)	13 (36.1%)		25 (69.4%)	11 (30.6%)		19 (52.8%)	17 (47.2%)	
European-American, N (%)	159 (77.2%)	47 (22.8%)	**p=0.03**	178 (86.4%)	28 (13.6%)	**p=0.005**	178 (86.4%)	28 (13.6%)	**p=0.047**	105 (51.0%)	101 (49.0%)	p=0.95
Other, N (%)	2 (50.0%)	2 (50.0%)		4 (100.0%)	0 (0.0%)		4 (100%)	0 (0%)		2 (50.0%)	2 (50.0%)	
Family history (total number of relatives with Alzheimer's)												
Mean (SD)	2.1 (1.9)	1.6 (1.2)	**p=0.025**	2.1 (1.6)	1.4 (1.2)	**p=0.006**	2.0 (1.5)	1.9 (2.0)	p=0.80	2.1 (1.6)	1.9 (1.6)	p=0.37
Numeracy												
High, N (%)	120 (80.0%)	30 (20.0%)	**p=0.012**	136 (90.7%)	14 (9.3%)	**p<0.001**	133 (88.7%)	17 (11.3%)	**p=0.03**	83 (55.3%)	67 (44.7%)	p=0.12
Low, N (%)	61 (65.6%)	32 (34.4%)		66 (71.0%)	27 (29.0%)		73 (78.5%)	20 (21.5%)		42 (45.2%)	51 (54.8%)	
Self-reported comfort with numbers												
Mean (SD)	4.72 (0.92)	4.28 (1.11)	**p=0.002**	4.74 (0.96)	3.96 (0.88)	**p<0.001**	4.66 (0.97)	4.30 (1.07)	**p=0.042**	4.70 (0.98)	4.51 (1.00)	p=0.14
Anxiety												
Mean (SD)	3.18 (4.03)	4.05 (4.92)	p=0.17	3.27 (4.16)	4.08 (4.85)	p=0.28	3.24 (3.87)	4.31 (6.11)	p=0.32	3.11 (3.98)	3.70 (4.56)	p=0.29
Distress												

Characteristic	APOE genotype			Number of risk-increasing alleles			Lifetime risk estimate (± 5 percentage points)			Lifetime risk estimate (exact)		
	Correct	Incorrect	Unadj. sig.	Correct	Incorrect	Unadj. sig.	Correct	Incorrect	Unadj. sig.	Correct	Incorrect	Unadj. sig.
Mean (SD)	4.21 (7.40)	2.95 (6.51)	p=0.24	3.95 (7.46)	3.65 (5.64)	p=0.82	3.76 (6.57)	4.76 (10.32)	p=0.59	3.83 (7.01)	3.97 (7.43)	p=0.88

Table 3

Unadjusted and adjusted independent associations between participant characteristics and correct risk recall in bivariate and multivariate analyses

	***APOE* genotype**		**Number of *APOE* risk-increasing alleles**		**Alzheimer's disease lifetime risk (± 5 percentage points)**		**Alzheimer's disease lifetime risk (exact)**	
	Unadjusted OR (95% CI)	**Adjusted OR (95% CI)**	**Unadjusted OR (95% CI)**	**Adjusted OR (95% CI)**	**Unadjusted OR (95% CI)**	**Adjusted OR (95% CI)**	**Unadjusted OR (95% CI)**	**Unadjusted OR (95% CI)**
Age	0.99 (0.97-1.01)	0.99 (0.98-1.02)	**0.96 (0.93-0.99)***	0.97 (0.94-1.01)	**0.96 (0.94-0.99)***	**0.96 (0.93-1.00)***	**0.98 (0.96-1.00)***	**0.98 (0.96-1.00)***
Male (ref: female)	1.10 (0.62-1.96)	0.77 (0.40-1.49)	1.04 (0.53-2.04)	0.48 (0.19-1.19)	1.05 (0.53-2.08)	0.76 (0.34-1.68)	1.35 (0.82-2.23)	1.35 (0.82-2.23)
Years of education	**1.16 (1.03-1.31)***	1.03 (0.90-1.19)	**1.53 (1.30-1.80)****	**1.39 (1.16-1.68)****	**1.28 (1.10-1.48)***	1.17 (0.98-1.39)	1.01 (0.91-1.12)	1.01 (0.91-1.12)
African American or other (ref: European-American)	**0.40 (0.20-0.81)***	0.55 (0.25-1.21)	**0.33 (0.15-0.71)***	0.49 (0.18-1.31)	**0.42 (0.19-0.92)***	0.39 (0.15-1.02)	1.06 (0.54-2.09)	1.06 (0.54-2.09)
Family history	**1.29 (1.03-1.61)***	1.23 (0.98-1.54)	**1.52 (1.13-2.04)***	**1.44 (1.04-1.98)***	1.04 (0.82-1.31)	0.94 (0.75-1.18)	1.08 (0.92-1.27)	1.08 (0.92-1.27)
Higher numeracy (ref: lower numeracy)	**2.10 (1.17-3.77)***	1.65 (0.83-3.30)	**3.97 (1.96-8.08)****	**2.79 (1.12-6.93)***	**2.14 (1.06-4.35)***	1.20 (0.50-2.86)	1.50 (0.89-2.53)	1.50 (0.89-2.53)
Self-reported comfort with numbers†	**1.56 (1.16-2.09)***	1.37 (0.98-1.93)	**2.18 (1.53-3.10)****	1.41 (0.92-2.16)	**1.42 (1.01-2.00)***	1.08 (0.72-1.62)	1.22 (0.94-1.57)	1.22 (0.94-1.57)

*p<0.05

**p<0.001

†Per one-unit increase