

## Genetic Testing and Counseling

## Disclosing genetic risk of Alzheimer's disease to cognitively impaired patients and visit companions: Findings from the REVEAL Study



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## ABSTRACT

**Objective:** To describe the impact of genetic information on Alzheimer's disease (AD) risk communication to patients with mild cognitive impairment (MCI) and their visit companions.

**Methods:** Participants of the fourth REVEAL Study trial were randomized to receive AD risk assessments with or without genotype results. We coded 79 audio recorded risk disclosure sessions with the Roter Interaction Analysis System. Multilevel analyses explored differences in communication when disclosed risks were based on age and MCI diagnosis alone or in addition to APOE genotype status.

**Results:** The addition of genotype results diminished the patient-centered nature of the sessions ( $p < 0.001$ ). When  $\epsilon 4$  positive relative to  $\epsilon 4$  negative results were disclosed, visit companions were more verbally active ( $p < 0.05$ ), disclosed more medical information ( $p < 0.05$ ), were more positive verbally and non-verbally ( $p < 0.05$ ) and were more proactive in setting the visit agenda ( $p < 0.05$ ).

**Conclusions:** Delivery of complex genetic risk information reduces the patient-centeredness of disclosure sessions. Visit companions are more actively engaged in session communication when patients are at increased genetic risk for AD.

**Practice implications:** AD risk discussions can be improved by supporting the positive role of visit companions and addressing the challenges inherent in the delivery of complex genetic information in a patient-centered manner.

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## 1. Introduction

Prevention and early detection of Alzheimer's disease (AD) is a national priority with research initiatives increasingly targeting individuals who have mild cognitive impairment (MCI) [1,2]. Despite this trend, few studies have described how clinicians disclose AD risk to cognitively impaired individuals. Understanding complex and unfamiliar concepts associated with genomic risk

is difficult for many patients, including older, less literate and more medically complex adults and especially patients with cognitive deficits [3–6]. The few studies that have specifically examined the interaction between clinicians and patients with cognitive impairment have found low levels of verbal engagement. One such study analyzed visit recordings in which a dementia diagnosis was delivered to family accompanied patients already suffering from mild dementia. That study found that the disclosure sessions were characterized by frequent checks for understanding and expression of approval and agreement by clinicians, but low levels of emotionally explicit communication directed to patients or their family members [7]. Another study of informed consent encounters for dementia research found that the more cognitively impaired patients asked fewer questions, initiated little discussion,

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and were more likely to express passive agreement with clinician statements than patients with less impairment [8].

The current study was designed to understand how the communication dynamics of AD risk disclosure to patients with MCI and their visit companions changed when *APOE* genotyping results were included. In light of prior studies that have described AD genotype discussions as complex and biomedically and technically focused [9], we hypothesized that the genotype discussions would be less patient-centered and have a more didactic teaching style, characterized by greater provision of basic biomedical information and less psychosocial, emotional and facilitative talk compared to AD risk discussions that omitted genotype discussions. We also hypothesized that the delivery of results indicating an increased risk of AD (i.e., presence of the *APOE*  $\epsilon 4$  allele) would trigger more active engagement by a visit companion, considering the serious implications of positive results for blood relatives in terms of their own AD vulnerability and implications for caretaker responsibilities.

## 2. Methods

### 2.1. Study design, subjects and setting

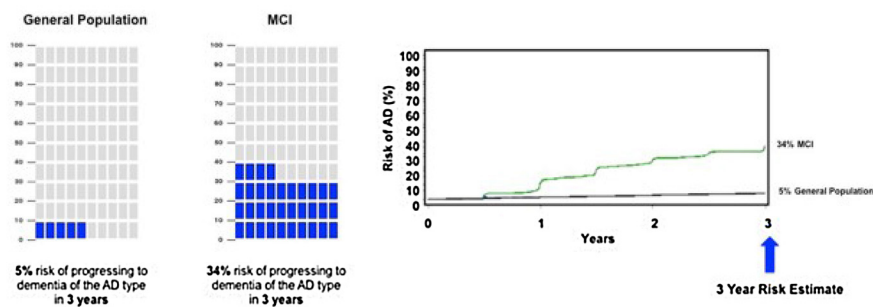
Analyses were based on a sample of audio-recorded AD risk disclosure sessions collected as part of the fourth independent trial of the REVEAL Study, a randomized clinical trial designed to compare the impact of AD risk communication, conveyed with and without genotype results, to patients with MCI diagnoses and their visit companions. The protocol for patient recruitment and risk disclosure were adapted from prior REVEAL Study trials [10–12] to target patients with amnesic diagnoses of MCI and invite them to receive “information about MCI and their chances of progressing to dementia of the AD type in the next three years”. Patients and visit companions, typically a spouse or adult child, were recruited at four REVEAL Study sites (Ann Arbor, Boston, Philadelphia and

Washington, D.C.). Eligible patients were older adults (55–90 years) who did not have dementia, but had clinical diagnoses of MCI from a neurologist or geriatrician and met the following criteria: (1) a memory complaint corroborated by an informant, (2) abnormal memory function per the Wechsler Memory Scale-revised, and (3) minimal impairment in activities of daily living, per interview with participants and informants. Patients were excluded if they had been converted to AD per diagnostic codes in medical records or per the judgment of neurologists or geriatrician providing care to the patients. Patients were also excluded if they could not independently consent to the trial or if they scored in clinically significant ranges on validated measures of cognitive functioning (Mini-Mental State Examination score  $\leq 20$ ), depression (The Geriatric Depression Rating Scale score  $> 12$ ), or anxiety (The State-Trait Anxiety Inventory score  $> 19$ ). As a condition of enrollment, MCI patients also had to have a visit companion for the AD risk disclosure session.

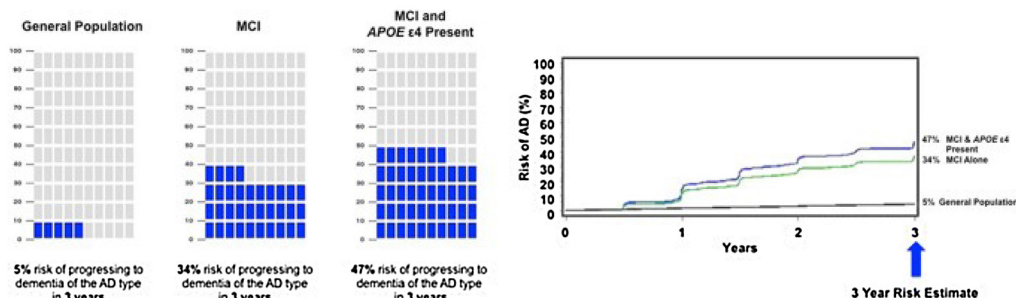
Patients were randomly assigned in a 2:1 ratio to either an *APOE* genotype disclosure group (N=75) or *APOE* genotype nondisclosure group (N=39). Patients assigned to the genotype nondisclosure group received 3-year risk estimates for conversion to AD based on their age and the diagnosis of MCI. Patients in the genotype disclosure group were given risk estimates based on the same factors in conjunction with their *APOE* genotype. Fig. 1 displays sample risk presentations.

The 3-year risk estimate provided to patients was defined as the cumulative risk of progressing to AD over the next three years based on the combination of their MCI diagnoses, their age stratum (55–70, 71–77, or 78+), and when appropriate, their *APOE* genotype ( $\epsilon 4$ -positive versus  $\epsilon 4$ -negative). These risk estimates were calculated from epidemiological data obtained from the Memory Impairment Study, a clinical trial involving 769 amnesic-MCI patients [13]. Patients with one or two  $\epsilon 4$  alleles are at increased risk of developing AD. Although patients with  $\epsilon 4/\epsilon 4$  genotypes were told that their risk for AD may be higher than the risk among

#### A. Genotype nondisclosure group example: Age (71–77)



#### B. Genotype disclosure group example: Age (71–77), *APOE* $\epsilon 4$ positive



**Fig. 1.** Risk of progressing to dementia of the Alzheimer's disease type. (A). Genotype nondisclosure group example: Age (71–77). (B). Genotype disclosure group example: Age (71–77), *APOE*  $\epsilon 4$  positive.

individuals with one copy of the  $\epsilon 4$  allele, they were not provided with a specific risk number stratified by *APOE* genotype because there were not enough  $\epsilon 4/\epsilon 4$  cases in the reference dataset on which to base reliable quantitative risk estimates. Individuals with the  $\epsilon 2/\epsilon 4$ ,  $\epsilon 3/\epsilon 4$  and  $\epsilon 4/\epsilon 4$  genotypes were given the same genotype risk estimates.

Of the 113 patients who received an AD risk assessment, 88 (78%) had their risk disclosure session successfully recorded; the majority of these audio-recorded sessions were led by a board certified genetic counselor (N = 79) and comprise the current study sample; 9 sessions led by a clinical psychology (N = 4), neurologist (N = 3) or general practitioner (N = 2) were excluded from this analysis. Study clinicians reviewed a standard slide presentation with patients during disclosure sessions, but were given latitude to address the specific needs of individual patients.

The current study was reviewed and approved by the Johns Hopkins University Bloomberg School of Public Health Institutional Review Board, as well as institutional review boards at each study site.

## 2.2. Study measures

### 2.2.1. AD risk disclosure communication

Audio recordings of risk disclosure dialogue were coded using the Roter Interaction Analysis System (RIAS), a widely used and well validated system for empirically describing medical visit communication [14]. The unit of analysis is a complete thought communicated as a single word, simple sentence, or a clause in a complex sentence. Statements are coded directly from recordings and assigned to one of thirty-seven mutually exclusive and exhaustive code categories. The code categories address task-focused categories such as questions and information and counseling statements in topical areas related to medical condition, therapeutic regimen, lifestyle and psychosocial information. Also included are socio-emotional categories that capture positive or negative exchange through approvals, compliments, disagreements and criticisms, as well as socio-emotional responses like empathy, concern, reassurance and legitimation. Examples of the RIAS codes are presented in Table 1.

**Table 1**  
RIAS composite codes and coding examples.

RIAS Code	Definition	Coding Examples: Genetic Counselor	Coding Examples: Patient & Companion
Information giving (Biomedical)	Information regarding medical condition, symptoms, diagnosis, prognosis, test results, personal and family medical histories, future treatments or tests to be performed.	–Based on these factors, we would say your risk to develop dementia, the AD type, is estimated to be 8% in the next three years.	–That must mean that my parents somewhere along the line were carrying that, but I know of no Alzheimer's on either side of the family.
Information giving (Psychosocial/Lifestyle)	Discussion of emotional reactions, and the impact on family and social relationships relevant to genetic test result and decision making, information on self-care and preventive health habits, implication for work, insurance and finances.	–Other things you can do is maintaining physical, social and mental activity, and limiting alcohol use.	–I tend to be a dark side person. –Maybe that little Lord is telling me “I want to test how strong you are”.
Question asking (Biomedical)	Questions related to medical condition, symptoms, diagnosis, prognosis, test results, personal and family medical histories, future treatments or tests to be performed.	–What do you recall in terms of being told about MCI? –So what can you do to cope with MCI?	–What does APOE stand for? –Whether it's paired with two or three, doesn't seem to make any difference? –Is there medication for people who cannot function?
Question asking (Psychosocial/Lifestyle)	Questions regarding feelings, general state of mind, values and beliefs, lifestyle, family and home situations, work or employment, health habits and self-care issues.	–Do you feel that the knowing that you have one copy of $\epsilon 4$ , does that change at all how you're feeling about this, your personal inner thoughts?	–Wouldn't you want to know whether you've got it or not? –Do I have to tell my insurance company about all this?
Facilitative statements	Asking for opinion, permission and reassurance, checking for understanding, cueing interest for further elaboration, and paraphrasing.	–Does that definition help at all? –Does that make sense? –Were you expecting that? –So when you say that, you mean if you're taking life insurance, there's a two-year suicide clause?	–When you say your doctor, you are talking about family doctor at home?
Positive statements	Laughs, compliments, agreements and approval.	–Sounds like you're in good shape on that one.	–You explained it very well.
Negative statements	Criticism and disapproval.	–That's not what I meant.	–I hoped you can come up some ideas I don't know.
Emotion Statements	Statements of partnership or alliance, expressions of reassurance, concern, empathy and legitimation.	–It's hard to lose people you care about. –I'm not quite sure about the exact number. –What you're talking about is very common in people who are in a similar situation. –If you think of any questions, feel free to ask.	–This makes me happy not only for myself, probably more for my family. –I get frustrate when I can't remember something that I know I should. –Not to be able to live with XXX as a phenomenal relationship, it's a very depressing thought.
Orientation Statements	Gives orientation, instructions, setting visit goals and agenda.	–The purpose of today's visit is to talk about your estimated risk of progressing to Alzheimer's disease in the next three years. –Tell me more what you want to know more about.	–Let me ask you a question. –Go back to that slide.

Four broad measures of communication process were also examined: (1) session length in minutes; (2) the sum of statement by each speaker (genetic counselor, patient and visit companion) as an indication of their contribution to the total session dialogue; (3) speaker verbal dominance constructed as the ratio of genetic counselor to patient and companion statements; and (4) a summary measure of patient-centered communication. The numerator of the measure consists of patient and companion psychosocial and lifestyle disclosure, all patient and companion questions and emotional statements and genetic counselor psychosocial and lifestyle information, questions and facilitative statements. The denominator consists of the sum of genetic counselors' medical questions and orientations, as well as patient, companion, and genetic counselors' statements relating to medical information. The measure has been used in a number of studies and shows predictive and concurrent validity to a variety of patient outcomes including satisfaction, adherence and continuance in care [15,16].

In addition to the verbal categories of exchange, RIAS coders rate each speaker on a 6-point scale (low to high) reflecting both positive (interest, warmth, engagement, empathy, respectfulness and interaction) and negative (dominance and hurried for the genetic counselor, anxiety and distress for the patient and companion) affect. These ratings have been found to reflect emotional tone that is largely independent of literal verbal content [17].

A random 10% sample of audiotapes ( $n=8$ ) was selected for double coding to establish inter-coder reliability. Pearson correlation coefficients averaged 0.83 across clinician categories and 0.93 for patient categories. Reliability for the ratings of emotional tone was calculated as agreement within 1 scale point and these averaged 99% (range 89–100%) for all three speakers.

#### 2.2.2. Participant measures

Patient and companion characteristics, including age, gender, race, level of education, numeracy, dyad relationship and family history of AD/dementia were assessed by self-report questionnaire items. For the purposes of this study, a family history of AD/dementia was defined as self-report of the number of relatives diagnosed with AD or dementia.

Objective numeracy skills were assessed using a validated eight-item scale developed by Lipkus and colleagues [18]. Scores less than or equal to one standard deviation below the mean were used to indicate lower numeracy and one standard deviation above the mean, were interpreted as higher numeracy; intermediate scores were considered to represent average numeracy.

General cognitive function of the patient was assessed by the Mini-Mental State Examination (MMSE) using previously established cut-points [19]. Scores range from 0 to 30. A score greater than or equal to 24 indicates normal general cognitive function, 20 to 24 suggests mild memory problems.

*APOE* genotype was dichotomized depending on carrier status of at least one copy of the *APOE*  $\epsilon 4$  allele, as patients with one or two  $\epsilon 4$  alleles are at increased risk of developing AD compared to patients without a copy of the *APOE*  $\epsilon 4$  allele.

#### 2.3. Analyses

To compare baseline variables between the genotype nondisclosure group and the  $\epsilon 4$ -negative and  $\epsilon 4$ -positive subgroups, one-way Analysis of Variance (ANOVA) was used for contrasts of continuous variables and Chi-square test for categorical variables. Differences of risk communication dynamics between groups were analyzed using mixed effect models with a random effect to account for clustering by genetic counselor. Covariates in all communication analyses included patient and companion gender,

MMSE score, 3-year AD risk, patient-companion relationship and visit length. The primary analysis compared the two randomized groups (genotype disclosure and nondisclosure groups). A secondary analysis compared the subgroup of patients in the genotype disclosure group who were informed that they carried at least one  $\epsilon 4$  allele (the  $\epsilon 4$  positive subgroup) with the subgroup of patients who were informed that they did not carry an  $\epsilon 4$  allele (the  $\epsilon 4$  negative subgroup). Missing values were excluded on a list-wise basis in all analyses. In all analyses, 2-tailed tests and  $p$ -values  $<0.05$  were used to draw conclusions regarding statistical significance. Data were analyzed using STATA Version 12.0 (STATA Corp, College Station, Texas).

### 3. Results

#### 3.1. Sample characteristics

A full description of sample characteristics, stratified by genotype disclosure group, is presented in Table 2. Three genetic counselors participated in this study, representing three study sites (Boston, Philadelphia, and Ann Arbor); all the counselors were female Caucasians aged 26, 34, and 48. The number of patients seen by each genetic counselor was 4, 35, and 40.

The 79 patients comprising our study sample averaged 76 years of age, with the majority of patients being male (56%) and Caucasian (96%). The mean level of education among patients was 16 years. Twenty patients (25%) were classified as having low numeracy skills, 37 patients (47%) were classified as having average skills, and 22 (28%) were classified as highly skilled. The majority of patients (86%) showed adequate cognitive function based on the MMSE (MMSE  $\geq 24$ ) despite entering the study with a clinical diagnosis of MCI. Eleven patients scored in the range of mild cognitive impairment (MMSE 20–23). The average 3-year risk estimates of progressing to AD provided to all patients was 37%, and ranged from 8% to 57%.

Of the 54 patients in the genotype disclosure group, 57% ( $N=31$ ) carried at least one  $\epsilon 4$  allele; 10 had the  $\epsilon 4/\epsilon 4$  genotype and 21 had the  $\epsilon 3/\epsilon 4$  genotype. Among those who did not have the  $\epsilon 4$  allele (43%,  $N=23$ ), 20 had the  $\epsilon 3/\epsilon 3$  genotype and 3 had the  $\epsilon 2/\epsilon 3$  genotype.

All patients were accompanied to the session by a visit companion who were predominantly spouses (65%) or adult children (24%); a minority of companions were siblings (1%), significant others (2%) and close friends (8%). Visit companions ( $N=79$ ) were on average 68 years of age and were predominantly female (70%). Companions were well-educated with an average 16 years of education and the majority (89%) had average or high numeracy.

Patients who were  $\epsilon 4$  positive were more likely to report a positive family history of AD or dementia ( $p=0.02$ ) than those who received an  $\epsilon 4$  negative result or patients who did not receive *APOE* disclosure. No other patient or companion baseline attributes differed significantly across the three study groups.

#### 3.2. Verbal activity

The duration of the risk discussions ranged from 9.7 to 63.5 min with a mean of 27.0 min ( $SD=9.7$ ). The sessions averaged 556 statements; the genetic counselor contributed 351 (63%) of statements while patients and companions contributed 19% and 18%, respectively, to session dialogue. The genetic counselor averaged 6 statements for each patient statement (range: 1–69) and contributed 9 times more statements than visit companions (range: 2–97). The relationship between patient and companion statements was less extreme with an average of 2.5 patient statements for each companion statement (range: 0.2–17.3).



**Table 2**  
Sample characteristics of patients and companions.

	All	Genotype nondisclosure	Genotype disclosure	
			ε4 negative	ε4 positive
Sample, N	79	25	23	31
<b>Patient</b>				
Age, mean (SD)	75.7 (7.4)	77.7 (8.0)	75.7 (6.5)	74.0 (7.5)
Female, %	35 (44.3)	9 (36.0)	13 (56.5)	13 (42.0)
Race, %				
African American	3 (3.8)	2 (8.0)	1 (4.3)	0
White	76 (96.2)	23 (92.0)	22 (95.7)	31 (100)
Education years, mean (SD)	16.2 (2.9)	16.0 (2.9)	16.1 (2.9)	16.5 (2.9)
Numeracy, mean (SD)	5.9 (2.1)	5.7 (2.1)	5.8 (2.2)	6.1 (2.1)
MMSE, mean (SD)	26.9 (2.1)	26.5 (2.6)	27.0 (1.9)	27.1 (1.8)
Family history of AD/dementia, %	49 (62.0)	13 (52.0)	11 (47.8)	25 (80.6)*
3-year risk, mean (SD)	37.3 (13.7)	37.0 (8.0)	23.0 (9.2)	48.1 (9.8)**
<b>Visit Companion</b>				
Age, mean (SD)	68.0 (13.3)	64.7 (12.9)	69.0 (13.9)	70.0 (13.2)
Female, %	56 (70.5)	20 (78.6)	16 (65.3)	20 (67.6)
Race, %				
African American	3 (3.8)	2 (8.0)	1 (4.3)	0
White	76 (96.2)	23 (92.0)	22 (95.7)	31 (100)
Education years, mean (SD)	16.2 (2.6)	15.3 (2.3)	16.7 (2.8)	16.5 (2.6)
Numeracy, mean (SD)	6.8 (1.8)	6.8 (1.8)	6.5 (2.0)	6.9 (1.5)
Relationship to participant, %				
Spouse	51 (64.6)	12 (48.0)	14 (60.9)	25 (80.6)
Child	19 (24.1)	10 (40.0)	6 (26.1)	3 (9.7)
Other (other relative or friend)	9 (11.3)	3 (2.0)	3 (13.0)	3 (9.7)

\* p &lt; 0.05.

\*\* p &lt; 0.01.

### 3.3. Communication profile

Table 3 (first column) displays the communication profiles of the genetic counselors, patients and companions. Overall, the risk disclosure sessions can be characterized as patient-centered with somewhat more psychosocial and emotional focus than biomedical (average patient-centered ratio 1.1; SD=0.4). Inspection of individual communication categories show that more than half of all genetic counselor statements (57%) were devoted to psychosocial and emotionally responsive dialogue. The most frequent communication categories were psychosocial and lifestyle information and counseling (20%), positive statements such as approval and compliment (13%), and partnership facilitation strategies (12%) including counselor's asking for opinion, permission and reassurance, checking for understanding, cueing interest for further elaboration and paraphrasing. Genetic counselors' responsiveness to patient emotion (e.g., empathy, concern, reassurance) was relatively infrequent (6%) and they asked few psychosocial questions (0.4%) to either patients or companions. Other categories of counselor exchange were primarily devoted to medical information (41%) and orientation statements (5%).

The most frequent category of interaction for both patients and companions was disclosure of psychosocial information (35% and 34%) followed by biomedical information (17% and 18%). Positive statements accounted for 21% and 18% of patients' and companions' total dialogue, reflecting high levels of expressed assent to what the genetic counselor had just said. Neither patients nor companions asked many questions (5.5% and 6.6%) or explicitly expressed emotion (9.7% and 7.8%).

### 3.4. Risk communication comparison between genotype disclosure and genotype nondisclosure groups

Also displayed in Table 3 are communication profiles of disclosure sessions that did or did not include genotype discussion. Sessions without genotype disclosure were characterized by a more patient-centered communication pattern than those that

included genotype information (patient-centered communication ratio: 1.4 v.s. 1.0; p < 0.001). More specifically, genetic counselors provided more psychosocial and lifestyle information, and used more facilitative statements to clarify information or check for understanding, but gave less biomedical information when genotype was not discussed. No statistically significant differences were evident in the communication categories for patients or companions.

### 3.5. Risk communication comparison between ε4 positive and ε4 negative groups

Contrasts between communication in sessions disclosing ε4 positive (N = 31) and ε4 negative results (N = 23) (Table 4) indicate that companions of high risk patients were significantly more verbally active overall, disclosed more medical information, made more supportive statements and made more orientation statements indicative of agenda setting. There were no significant differences in genetic counselor or patient communication across these disclosure sessions.

Visit companions were also rated by coders as more exhibiting more positive affect during the session (reflecting higher ratings of interest, warmth, engagement, empathy, respectfulness and interaction) when ε4 positive results were returned.

## 4. Discussion and conclusion

### 4.1. Discussion

Our study results are consistent with our two study hypotheses; disclosure discussions that included genotype results were 30% less patient-centered than discussions that did not include genetic information, and visit companions were more verbally active and engaged in session dialogue when patients received ε4 positive test results.

Overall, the psychosocially oriented, patient-centered communication pattern identified in our study is consistent with previous

**Table 3**  
AD risk communication comparison between disclosure and nondisclosure groups.

Communication Profile	All (N = 79)			Genotype Nondisclosure (N = 25)		Genotype Disclosure (N = 54)		P-value
	mean	%	(95%CI)	adjusted mean	(95%CI)	adjusted mean	(95%CI)	
Ratio of patient-centered communication	1.1	NA	(1.1, 1.2)	1.4	(1.2, 1.5)	1.0	(1.0, 1.1)	<b>&lt;0.001</b>
<b>Genetic Counselor</b>								
All statements	351.1	100	(329.4, 372.8)	343.0	(325.1, 360.7)	352.9	(337.7, 368.1)	0.17
Biomedical information	143.2	40.8	(134.9, 151.6)	127.0	(114.4, 139.6)	152.3	(141.7, 162.9)	<b>&lt;0.001</b>
Psychosocial/Lifestyle information	71.1	20.3	(67.9, 74.3)	74.1	(64.6, 83.6)	65.3	(56.7, 74.0)	<b>0.003</b>
Questions (Biomedical)	5.9	1.7	(5.1, 6.7)	5.9	(3.3, 8.4)	5.3	(2.8, 7.7)	0.26
Questions (Psychosocial/Lifestyle)	1.5	0.4	(1.1, 1.8)	1.4	(0.7, 2.0)	1.5	(1.0, 1.9)	0.79
Facilitative statements	41.8	11.9	(35.2, 48.4)	46.5	(41.7, 51.4)	39.6	(36.4, 42.8)	<b>0.02</b>
Positive statements	47.0	13.4	(41.4, 52.6)	47.8	(41.9, 53.7)	46.6	(42.7, 50.5)	0.74
Negative statements	0.7	0.2	(0.5, 0.9)	0.6	(0.3, 0.9)	0.7	(0.5, 0.9)	0.82
Emotion Statements	22.2	6.3	(20.1, 24.2)	22.4	(20.0, 24.8)	22.0	(20.4, 23.7)	0.81
Orientation Statements	17.7	5.0	(16.2, 19.2)	17.5	(13.2, 21.8)	19.8	(16.0, 23.6)	0.13
Positive affect (nonverbal)	4.1	NA	(4.0, 4.2)	4.1	(4.0, 4.3)	4.1	(4.0, 4.2)	0.95
Negative affect (nonverbal)	3.7	NA	(3.6, 3.9)	3.7	(3.5, 3.9)	3.7	(3.6, 3.9)	0.81
<b>Patient</b>								
All statements	108.1	100	(84.5, 131.7)	110.4	(83.5, 137.2)	107.1	(89.3, 124.9)	0.85
Biomedical information	18.0	16.7	(13.4, 22.6)	19.2	(13.5, 24.9)	17.4	(13.7, 21.2)	0.62
Psychosocial/Lifestyle information	38.1	35.2	(27.1, 49.2)	37.7	(23.3, 52.1)	38.3	(28.8, 47.9)	0.95
Questions (Biomedical)	4.4	4.1	(3.4, 5.4)	4.3	(3.1, 5.5)	4.4	(3.6, 5.2)	0.90
Questions (Psychosocial/Lifestyle)	1.5	1.4	(1.0, 2.1)	2.1	(1.3, 2.9)	1.3	(0.7, 1.8)	0.12
Facilitative statements	8.5	7.9	(6.0, 11.1)	9.5	(6.0, 13.0)	8.1	(5.7, 10.4)	0.53
Positive statements	22.9	21.2	(18.6, 27.1)	23.1	(17.9, 28.3)	22.8	(19.3, 26.2)	0.92
Negative statements	1.3	1.2	(0.8, 1.8)	1.2	(0.5, 2.0)	1.4	(0.8, 1.9)	0.80
Emotion Statements	10.5	9.7	(8.3, 12.6)	10.7	(7.8, 13.6)	10.4	(8.4, 12.3)	0.87
Orientation Statements	2.4	2.2	(1.8, 2.9)	2.2	(1.1, 3.3)	2.5	(1.6, 3.4)	0.57
Positive affect (nonverbal)	4.0	NA	(3.8, 4.1)	3.9	(3.7, 4.2)	4.0	(3.8, 4.1)	0.70
Negative affect (nonverbal)	1.5	NA	(1.4, 1.7)	1.8	(1.3, 2.3)	1.7	(1.2, 2.1)	0.42
<b>Visit Companion</b>								
All statements	75.5	100	(64.3, 86.8)	76.6	(59.3, 93.8)	75.1	(63.6, 86.5)	0.89
Biomedical information	13.4	17.7	(10.3, 16.6)	10.8	(5.8, 15.9)	14.6	(11.2, 18.0)	0.23
Psychosocial/Lifestyle information	25.5	33.8	(20.1, 30.8)	29.4	(20.8, 38.0)	23.7	(18.0, 29.4)	0.29
Questions (Biomedical)	3.8	5.0	(2.8, 4.9)	2.9	(1.3, 4.6)	4.3	(3.2, 5.4)	0.20
Questions (Psychosocial/Lifestyle)	1.2	1.6	(0.8, 1.5)	1.5	(0.9, 2.1)	1.0	(0.7, 1.4)	0.20
Facilitative statements	8.1	10.7	(5.8, 10.4)	6.9	(2.9, 10.9)	8.7	(6.0, 11.3)	0.49
Positive statements	13.3	17.6	(11.2, 15.4)	13.9	(10.5, 17.2)	13.1	(10.8, 15.3)	0.70
Negative statements	1.6	2.1	(1.1, 2.1)	2.2	(1.4, 3.1)	1.3	(0.7, 1.9)	0.10
Emotion statements	5.9	7.8	(4.7, 7.1)	6.1	(3.9, 8.3)	5.8	(4.4, 7.3)	0.84
Orientation statements	2.1	2.8	(1.4, 2.7)	2.1	(0.7, 3.5)	2.0	(0.9, 3.2)	0.92
Positive affect (nonverbal)	4.0	NA	(3.8, 4.1)	3.9	(3.6, 4.1)	4.0	(3.8, 4.2)	0.24
Negative affect (nonverbal)	1.3	NA	(1.2, 1.4)	1.4	(1.1, 1.7)	1.4	(1.1, 1.6)	0.83

Adjusted means derived from mixed effects models that controlled for patient and companion gender, patient-companion relationship, patient MMSE score, 3-year AD risk and visit length.

\*P < 0.05, \*\*P < 0.01, \*\*\*P < 0.001.

findings of dementia diagnosis disclosure sessions [7]. We found that AD risk disclosure sessions (regardless of genotype inclusion) reflect a largely psychosocial process that includes broad address of anticipatory coping strategies for patients with MCI and their caregivers. In addition to the presentation of risk information, the genetic counselors in this study established emotional rapport and facilitated active patient and companion participation in the dialogue. In these instances, the counselors used patient-centered communication strategies to establish a shared understanding of the risks conveyed and to elicit the both the patient and companion perspectives on the information conveyed.

The findings also indicate that the general approach taken by genetic counselors in this study is somewhat different than that observed in other genetic counseling contexts [20–22]. This is especially evident in contrast to the analysis of *APOE* genotype disclosure to asymptomatic adult children of an AD parent [9] wherein sessions were largely didactic in nature with relatively little emphasis on psychosocial and emotional topics. The patient-centered approach adopted by the genetic counselors in the current study seems to result in greater patient and companion engagement in the dialogue. This is evidenced by more than half of patient and companion statements in categories reflecting the

sharing of both biomedical and psychosocial information, and relatively little passive assent or agreement with counselor statements.

Differences in findings between the current study and others may be attributed at least in part to the patient inclusion criteria of a MCI diagnosis. MCI introduces unique complexities to the communication process and as these patients are likely to have difficulty processing the often abstract and complex information provided to them. As observed by Zaleta and Carpenter during the dementia diagnosis disclosure [7], clinicians are likely to make special efforts to check patient understanding and to facilitate patient engagement by making supportive statements and cueing interest in patient disclosure [8].

An additional goal of the study was to explore visit companions' involvement in AD risk discussions. Companions were present in all of the study sessions, a common feature of medical care for older adults with memory complaints [23,24]. The majority of the visit companions in this study were spouses and adult children. An  $\geq 4$  positive test result may thus have implications for their own increased risk for late-onset AD as well as the prospect of assuming the physical and emotional burden of caregiving for an affected family member. Consequently, we expected that companions

**Table 4**  
AD risk communication comparison between ε4 positive and ε4 negative groups.

Communication Profile	ε4 negative (N=23)		ε4 positive (N=31)		P-value
	adjusted mean	(95%CI)	adjusted mean	(95%CI)	
Ratio of patient-centered communication	1.1	(0.9, 1.3)	1.0	(0.9, 1.2)	0.69
<b>Genetic Counselor</b>					
All statements	378.3	(356.5, 400.0)	356.0	(336.1, 375.9)	0.13
Biomedical information	163.6	(144.2, 182.9)	152.6	(133.9, 171.3)	0.30
Psychosocial/Lifestyle information	66.8	(60.5, 73.0)	72.3	(67.3, 77.3)	0.27
Questions (Biomedical)	6	(3.3, 8.7)	5	(2.3, 7.7)	0.39
Questions (Psychosocial/Lifestyle)	0.8	(0.1, 1.6)	2.0	(1.4, 2.5)	<b>0.06</b>
Facilitative statements	45.6	(38.7, 52.6)	40.3	(34.7, 45.8)	0.34
Positive statements	56.3	(47.0, 65.6)	44.4	(37.0, 51.8)	0.11
Negative statements	1.0	(0.5, 1.6)	0.6	(0.2, 1.0)	0.28
Emotion statements	22.3	(18.9, 25.6)	23.5	(20.9, 26.3)	0.62
Orientation statements	19.9	(15.1, 24.6)	20.6	(16.1, 25.1)	0.81
Positive affect (nonverbal)	4.0	(3.8, 4.2)	4.3	(4.1, 4.4)	0.15
Negative affect (nonverbal)	3.6	(3.3, 4.0)	3.7	(3.5, 3.9)	0.84
<b>Patient</b>					
All statements	129.5	(86.6, 172.4)	103.6	(69.4, 137.8)	0.45
Biomedical information	19.1	(10.8, 27.4)	18.2	(11.6, 24.8)	0.90
Psychosocial/Lifestyle information	55.2	(31.3, 79.0)	31.0	(12.0, 50.0)	0.21
Questions (Biomedical)	4.6	(2.7, 6.6)	4.8	(3.2, 6.3)	0.93
Questions (Psychosocial/Lifestyle)	1.4	(0.3, 2.5)	1.5	(0.7, 2.4)	0.85
Facilitative statements	7.8	(2.9, 12.6)	9.6	(5.7, 13.4)	0.65
Positive statements	24.4	(16.1, 32.8)	23.7	(17.1, 30.4)	0.92
Negative statements	1.5	(0.3, 2.8)	1.4	(0.4, 2.4)	0.88
Emotion statements	13	(8.7, 17.4)	9.6	(6.1, 13.0)	0.32
Orientation statements	2.2	(0.7, 3.7)	2.8	(1.5, 4.2)	0.53
Positive affect (nonverbal)	4.1	(3.7, 4.5)	3.9	(3.6, 4.2)	0.51
Negative affect (nonverbal)	1.5	(0.8, 2.1)	2.0	(1.3, 2.6)	<b>0.07</b>
<b>Visit Companion</b>					
All statements	54.1	(27.7, 80.6)	98.6	(77.6, 119.7)	<b>0.04</b>
Biomedical information	7.7	(−0.5, 15.8)	20.6	(14.1, 27.1)	<b>0.049</b>
Psychosocial/Lifestyle information	16.4	(2.9, 30.0)	32.9	(22.1, 43.7)	0.13
Questions (Biomedical)	2.5	(−0.1, 5.1)	5.9	(3.8, 7.9)	0.10
Questions (Psychosocial/Lifestyle)	1.0	(0, 1.8)	1.3	(0.6, 2.0)	0.60
Facilitative statements	8.0	(1.2, 14.9)	10.2	(4.7, 15.7)	0.70
Positive statements	9.7	(5.7, 13.8)	16.1	(12.9, 19.3)	<b>0.048</b>
Negative statements	1.7	(0.4, 3.1)	1.2	(0.1, 2.3)	0.63
Emotion statements	5.9	(2.7, 9.2)	6.3	(3.7, 8.9)	0.88
Orientation statements	0.8	(−1.0, 2.5)	3.5	(1.9, 5.0)	<b>0.04</b>
Positive affect (nonverbal)	3.7	(3.5, 4.0)	4.3	(4.1, 4.6)	<b>0.006</b>
Negative affect (nonverbal)	1.4	(1.0, 1.8)	1.3	(1.0, 1.7)	0.72

Adjusted means derived from mixed effects models that controlled for patient and companion gender, patient-companion relationship, patient MMSE score, 3-year AD risk and visit length.

\*P < 0.10, \*\*P < 0.05.

would more actively engage in the disclosure dialogue when patients were at high AD risk and received a ε4 positive result.

This was the case, but we also uncovered more detail regarding how they engaged in the sessions. We found that companions appeared to play a supportive and proactive role in these visits by provided or clarified medical and family history and directed the course of the session by prompting additional discussion or introducing new agenda items. Higher positive communication by companions, both verbally and reflected in the global affect ratings also demonstrate greater positive emotional support for patients when the need for more emotional support was greatest.

Patients receiving ε4 positive results were rated by coders as more nonverbally negative, indicating that they were experiencing and demonstrating overt distress and anxiety in receiving their results. Interestingly, counselors' and companions' communication did not have an impact on patients' verbal engagement in the dialogue. While it may be possible for a skilled counselor to elicit patient and companion psychosocial responses, this was not commonly observed in the study sessions. A challenge in this regard, evident throughout the medical communication literature, is training guidance to clinicians in ways in which they may

effectively facilitate more active patient engagement in the communication process.

The study had several notable limitations. The risk estimates provided to participants did not consider other potential risk factors for the disease, including other genes, environmental exposures and gene-gene or gene-environment interactions. The study sample was relatively homogenous with little variation in patient and genetic counselor race. Participants who were omitted from analyses because of technical problems or because they did not receive results from a genetic counselor were younger, were more likely to be White and female, scored higher on the MMSE and had lower AD risk estimates than individuals who were analyzed, although the association between these characteristics and omission from analyses did not vary by randomization status or APOE status. The participants were self-referred and well-educated which may differentiate them from the broader population of individuals who are at high risk and might seek genetic counseling for AD. Only three genetic counselors were included in these analyses, and findings may not apply to AD risk disclosure sessions conducted in more typical non-research contexts not driven by a research protocol. Although external

validity is limited in this way, the establishment of randomization ensures internal validity in regard to the primary research questions.

#### 4.2. Conclusions

This study is the first randomized trial to describe differences in genetic counselors' communication of AD risk to patients with MCI and their visit companions with and without genotype findings. Our findings contribute to the literature in two ways. First we have found that while important and valued, the delivery of complex genetic risk information to patients reduces the patient-centeredness of disclosure sessions. This includes the type of exchanges that facilitate meaningful integration of the information conveyed within the context of patient and family concerns, values, expectations and preferences for care and treatment decisions.

The second contribution of this study is the detailed description of the active communication role assumed by a visit companion when a patient with MCI received a positive  $\epsilon 4$ -genotype result. Despite little emphasis on the communicative role of visit companions when accompanying a vulnerable patient to disclosure sessions, this study suggests that they may positively contribute to the comprehensiveness of the information made available to the genetic counselor and how the patient might cognitively and emotionally process the genetic risks conveyed.

#### 4.3. Practice implications

Clinicians of all types face significant challenges in effectively communicating with patients who suffer from cognitive deficits and their families. These challenges are anticipated to grow exponentially with the aging population at risk for AD and the likelihood that these patients will seek early diagnosis and guidance from their health care providers that will increasingly include genotype status. Our findings suggest that AD risk discussions can be improved by supporting the positive role of visit companions and by addressing the challenges inherent in the delivery of genetic information in a patient-centered manner.

We recognize and appreciate the importance and value attributed to the genetic risk information conveyed during disclosure sessions and do not at all advocate that clinicians limit the amount information conveyed to patients and their families. However, we believe that the way in which complex and abstract genetic risk information is delivered matters. This can be done in a patient-centered way that includes psychosocial, lifestyle and emotional exchanges that facilitates the meaningful integration of the biomedical and technical information conveyed or the discussion can shift to a focus on technical information that limits the discussion that helps the patient and their family contextualize the information in terms of their concerns, values, expectations and preferences for care and treatment decisions. We believe this is the important finding of the study and the basis for our recommendation that communication skills training for clinicians and patients, including those with MCI, and their family members and friends who routinely accompany them to medical visits, can help improve effective and meaningful disclosure of genetic risks and test results.

#### Conflicts of interest

The authors report no conflicts of interest.

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