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Genetic sample provision among National Alzheimer's Coordinating Center participants

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Abstract

BACKGROUND: Genetic data help detect preclinical Alzheimer's disease and target individuals for clinical trials, making genetic research engagement critical for continued advancement in dementia prevention and treatment.

OBJECTIVE: To understand what individual and institutional factors may relate to provision of genetic samples within the Alzheimer's Disease Centers.

METHODS: Data from the National Alzheimer's Coordinating Center Uniform Data Set (2009–2016) were obtained along with genetic sample availability. Logistic regression was used to assess independent contributions of demographic and clinical characteristics to the probability of sample provision. Sites contributing data completed a brief survey exploring regulatory and scientific issues related to genetic research engagement.

RESULTS: Just over half (52.1%) of the 27,519 unique participants had genetic data available. Female sex, white race, non-Hispanic ethnicity, normal cognition, and greater than 5-years of follow-up were associated with greater probability of availability. Sites identified refusals as the most frequent barrier to sample provision, followed by staff availability.

CONCLUSION: These results highlight the importance of strategies to promote minority engagement and encourage earlier genetic research participation.

Keywords

Genetic research; Patient Participation; Surveys and Questionnaires; Alzheimer's Disease

1. Introduction

Genetic research is becoming increasingly important to the advancement of detection, treatment, cures, prevention strategies, and understanding of Alzheimer's disease (AD) and other degenerative dementias [1, 2]. While research participants often express comfort with and willingness to engage in genetic research [3], greater numbers of individuals willing to participate in genetic research are needed. When faced with hypothetical participation, e.g. willingness to engage in a biorepository, some researchers have reported there may be no differences across population groups [4], whereas others have found that African Americans

are less likely to participate or agree to genetic testing than White individuals [5–7]. In one real-world analysis focusing on participants in a North Carolina Colorectal Cancer Study, researchers found African Americans were less likely to give a blood sample than white participants in support of genetic research [8]. While there are racial differences in perspectives on brain donation and brain autopsy [9], little is known about what other individual demographic, clinical (cognitive, behavioral, and psychiatric features), social (economic, educational, geographic), and caregiver (health care surrogate for genetic consent) factors play a role in willingness to engage in genetic research in the area of aging and dementia. While many factors may contribute to a reluctance of African Americans to participate in genetic research, including a history of unethical research contributing to distrust of physicians and scientists, Ighodaro and colleagues [10] caution that racial differences should be explored in the context of these various other socio-environmental factors.

Despite limited published information on engagement in genetic research in the area of aging and dementia from a recruitment perspective, several studies have looked at willingness to pursue genetic testing to determine self-risk. The most widely cited and recognized of these studies is the REVEAL study, a multisite randomized clinical trial. REVEAL examined demographic factors related to engagement in genetic risk testing, as well as the psychological risks and changes in health behavior that result from genetic risk testing and disclosure in 162 community dwelling participants with a mean age of 53 years [11]. Although limited in its generalizability, the REVEAL study provides useful insights into participant characteristics that may influence engagement in genetic research in the area of aging and dementia. The REVEAL data demonstrate that those most likely to engage in genetic risk assessment are more often female, college educated, and younger than age 65 years [11–15]. This study also found that genetic risk disclosure did not adversely affect the psychological well-being of participants [11, 12, 15]. These data suggest that individual-level demographic and social factors are correlated with willingness to undergo genetic testing [11–13]. It is possible that these same factors, and others, may influence potential subject willingness to engage in genetic research that does not include genetic risk disclosure.

Beyond the individual level factors that may impact genetic research engagement, environmental and interpersonal factors may also influence participation. Research suggests that the way in which information is presented may influence intention to participate [16–18]. It may also influence psychological impact of perceived genetic risk, change in health behaviors, decisions regarding long term health insurance, and personal secondary disclosure of genetic risk [12, 19–25]. In addition, the ease of participation and whether additional travel or visits are required may also impact participation [26]. These previous studies highlight the importance of identifying differences in institutional practices in how genetic participation is approached and discussed to better understand patterns of engagement. In addition to institution-specific “best practices”, regulatory practices, issues of data ownership, and local Institutional Review Board practices may also play an important role in genetic research engagement and genetic data sharing practices. Little is known about such barriers to genetic research engagement, but these could prove to be significant obstacles that should be explored. Improved understanding of the individual

participant and institutional practice and regulatory barriers to genetic research engagement may facilitate increased engagement in this vital area.

The Alzheimer's Disease Centers (ADCs) enable exploration of factors related in genetic research engagement. In 1984, the National Institute on Aging developed the ADCs to create a nationwide program and infrastructure to promote research on cognitive aging, AD, and other dementias [27]. In 2005, the ADCs adopted the Uniform Data Set (UDS), a standardized research protocol including but not limited to demographic variables and neuropsychological testing results [28]. In 1990, the National Cell Repository for Alzheimer's Disease (NCRAD) was established to increase researchers' access to the biological samples and data necessary to identify genes that increase the risk of AD and dementia [29]. In 2009 the Alzheimer's Disease Genetic Consortium (ADGC) was established to conduct genome-wide association studies to identify genes associated with the development of late-onset AD. Currently, ADC participants across sites may be asked to provide genetic samples that their site can submit to NCRAD, which shares data and samples with both NACC and the ADGC, but genetic material is not available for all ADC participants.

The current study seeks to understand what individual and institutional factors may relate to provision of genetic samples within the ADCs. We hypothesize that participants who do and do not have samples available will differ significantly, and that demographic and clinical factors will relate to whether an ADC participant has a genetic sample available at NCRAD.

2. Methods

2.1 Participants

UDS data are aggregated and distributed by the National Alzheimer's Coordinating Center (NACC). UDS data from 2009 to 2016 was obtained in conjunction with status of genetic data or sample availability through ADGC or NCRAD. Data was restricted to this period in order to align with the years the ADGC and NACC have collaborated to collect genetic data on ADC participants. NACC data include participant demographics (i.e., age, education, race/ethnicity, marital status, living situation, and primary language); clinical factors such as cognitive function, including psychiatric illness (i.e., current depression; other psychiatric illness including anxiety, post-traumatic stress disorder, bipolar disorder, and schizophrenia; reported alcohol or substance abuse); and characteristics of the study partner (i.e., relationship to participant).

Local Institutional Review Boards (IRBs) approve ADC research activities, and all ADC participants sign written informed consent. NACC data are de-identified, and research involving the NACC database is approved by the University of Washington IRB.

2.2 Genetic Samples

ADC sites that did not have any genetic data available in NACC (N=4) were excluded from analysis. Genetic data availability was defined as having a genetic sample at NCRAD or data available within any ADGC initiative at any time between 2009 and 2016. However,

participants may still have genetic data at their individual ADC that is not shared with any of these larger genetic initiatives. Those local data were not available for this analysis.

2.3 Statistical Analysis

The demographic and study partner characteristics were fixed at the first UDS visit within the 2009 to 2016 timeframe. Two-group comparisons of participants with and without genetic samples included t tests and chi-square tests. To assess the independent contribution of these factors to provision of samples, the following covariates were entered into a fully adjusted logistic regression model: age in years, sex, race, Hispanic ethnicity, level of education, relationship of study partner to participant, marital status, participant residence type, cognitive status (normal; impaired, not MCI; MCI; dementia), history of drug or alcohol abuse, history of psychiatric disorders other than depression, history of depression (based on participant self-report of physician diagnosis), indicator for at least 5 years of follow-up, and primary spoken language. The 5-year indicator was based on the fact that 5 years represents a full grant cycle for an ADC, along with our hypothesis that longer participation would increase the likelihood of genetic sample provision. The model was reduced by backward selection, and results were checked for robustness against models selected by forward and stepwise selection. To account for potential clustering of participants within ADCs, which each have their own recruitment and bio-specimen practices, we next fit generalized estimating equations (GEE) to the reduced model using a logit link, with ADC as the clustering variable. The GEE model used an exchangeable working correlation structure. All analyses were conducted using SAS version 9.4 (SAS Institute, Inc.; Cary, NC). Statistical significance was set at 0.05.

2.4 Center Surveys

To examine institutional characteristics that may influence genetic research engagement, we developed a short survey to explore regulatory and scientific issues that could pose barriers to genetic research participation at the ADC site level (Appendix A). Email requests were sent to the Clinical Core leaders at each ADC to complete the survey or requested that they identify another individual at their site to complete the survey. Survey completion was estimated to take between five to ten minutes and no incentive was provided. All survey procedures were approved by the University of Kentucky Institutional Review Board.

Surveys were customized to sites and presented the percentage of their participants with 2016 NACC visits who had genetic samples available. Respondents were asked to identify factors, within a provided list (Appendix A) that they thought may play a role in non-provision of samples. For each item, they were asked to rate how much of a role that factor played. Respondents were then asked a series of questions about their routine practices pertaining to blood sample provision including how frequently participants are asked, who asks, when they are asked; regulatory issues; and whether any educational materials are provided. Options for write-in comments were included throughout. Surveys were administered via REDCap and data were exported to SAS 9.4 for analysis. Results from the survey were summarized to explore differences between ADCs in order to provide additional context to the above individual-level analysis. We explored the extent to which differences in genetic data availability could be attributable to differences in site policies, practices, and

procedures. All procedures related to this survey were approved by the University of Kentucky IRB.

In an exploratory analysis, we investigated whether center-level variables measured on the survey were independently associated with the probability of genetic sample availability given the individual-level predictors. These exploratory analyses were based on the final fitted GEE models. The survey variables were coded as per the survey questions (Appendix A), except the barrier variables. Each barrier were categorized as a binary variable: serves as barrier versus rarely/never serves as a barrier. In addition, we also evaluated the sum of the barriers. Each of the survey variables were added to the GEE model in order to evaluate its effect.

3. Results

3.1 Participant Characteristics

Between 2009 and 2016 there were a total of 119,531 UDS visits, representing 27,519 unique participants (Table 1). These participants had an average age of 74.8 years, 15.8 years of education, and had participated in 3.9 annual visits. Over half (56.9%) were female, 79.8% were White, most were married or partnered (64.5%) and living with a spouse or partner (56.5%), just over half had a spouse or partner as their study partner (52.0%). Participants were mixed in terms of cognitive diagnosis: 39.9% had normal cognition, 16.1% had a diagnosis of MCI, 41.3% had a dementia diagnosis, and 4.5% had an impaired diagnosis but did not meet the criteria for MCI.

3.2 Genetic Data Availability

Of the 27,519 participants seen between 2009 and 2016, just over half (52.1%) had genetic samples available. Sample availability was variable across centers, with median participation of 50.0% (IQR 30.7–65.6%, range 0–95%). Participants without dementia were more likely than those with dementia diagnoses to have genetic data available. Individuals without a depression diagnosis within the last two years were more likely to have genetic samples available than those with such a diagnosis. Participants with genetic data available also had participated in a greater number of UDS visits (mean 4.8) than those without genetic data available (mean 2.9). Accordingly, those with at least 5 years of follow-up were more likely to have a genetic sample available (49.4%) than those with less than 5 years of follow-up (19.1%) (See Table 1).

After removing individuals for whom values were missing on any of the variables 24,957 individuals remained. Older participant age was associated with higher odds of having genetic samples available (Table 2). Female participants were also more likely than male participants to have genetic data available. Individuals with less than a college education were more likely than those with more than a college education to have genetic data available. Non-Hispanic, Caucasian participants were more likely than those with non-White race and with Hispanic ethnicity to have samples available. Primary language, marital status, living situation, and co-participant relationship were not significantly related to sample availability. Those with normal cognition were more likely to have samples available than

individuals with any cognitive impairment (impaired, MCI, or dementia). Individuals with five or more years of follow-up were more likely to have samples available (See Table 2).

Model selection procedures identified nearly identical models, with the only difference being that the stepwise model retained ‘other psychiatric illness’ while the backward and forward selected models did not. We decided to exclude this variable from the final reduced model, which included age, sex, education, race, Hispanic ethnicity, marital status, cognitive diagnosis, and the indicator for five years of follow-up. Because of the reduced number of variables included, the available sample size for the reduced adjusted logistic regression analysis was 26,647 (See Table 3).

Since logistic regression assumes all observations in the data are independent, we assessed the robustness of our reduced model results by taking into account possible within-ADC correlations. With within-center correlation taken into account, some of the previously identified factors were no longer significant (Table 4). The direction of the associations, however, remained consistent. In this model we found that female participants were still significantly more likely to have genetic samples than male participants, and white participants were still more likely to have samples available than Black/African American participants. In addition, non-Hispanic participants were still more likely than Hispanic participants to have samples available. While all impaired groups still trended in the direction of being less likely to have samples available, individuals with MCI were the only group that still was significantly less likely to have samples available than normal participants. Having five or more years of follow-up was still associated with a greater odds of genetic sample availability (Table 4).

3.3 Survey Results

Of the 30 eligible ADCs, 29 responded to the survey. All responding sites indicated that they obtain blood or other specimens from participants, but there was some variation across sites regarding whether genetic samples are expected from all participants, how frequently participants are asked, by whom, and when they are asked, when sample provision occurs, whether there are any supporting educational materials, and whether certain groups are less likely to provide samples (Table 5). Only six sites (20.7%) used any supporting educational materials. None of these of process variables were independently related to the probability of sample availability after accounting for individual-level characteristics.

Nine respondents indicated certain groups are less likely to agree to provide samples. Of these nine, eight expanded on their responses. Responses were: African Americans, Chinese, Native American, minorities (mentioned by three respondents), various, and cranky people. These responses are consistent with the findings that non-white racial groups are less likely to have samples available than white participants. The response of “cranky” people helps demonstrate that there are also individual characteristics that do not typically appear in databases that may relate to sample availability.

Sites identified various barriers to blood sample provision, indicating that participant and legally-authorized representative (LAR) refusals were the most frequent barriers. Other barriers, such as staff and supply availability were also identified as occurring at least in

some instances (Table 6). Neither any of the barriers nor their sum were significantly associated with sample availability after accounting for individual-level characteristics.

4. Discussion

4.1. General Discussion

The findings from this study suggest that various factors may contribute to the likelihood of genetic data availability. Female sex, white race, non-Hispanic ethnicity, normal cognition, and greater than 5-years of follow-up were all factors associated with a greater likelihood of genetic data availability. The findings highlight groups that could potentially be targeted for interventions to increase genetic research engagement. While research has explored strategies for recruiting racial and ethnic minorities as well as other underrepresented groups to participate in research, ongoing efforts may also be needed to increase genetic participation [30, 31]. In addition, the finding that those with longer follow-up were more likely to have samples available may indicate the need to address genetic research engagement earlier in a participant's course of research participation. Alternatively, longer follow-up represents more opportunities for the participant to be invited to provide a genetic sample. Thus, this finding may also highlight the importance of longitudinal follow-up. In addition to having more opportunities for sample provision by being engaged over a longer period of time, it is possible engagement increases as trusting relationships develop, enabling participants to feel comfortable asking questions and having their concerns alleviated, ultimately resulting in greater willingness to provide samples [32].

The finding that individuals who are not cognitively normal were less likely to have samples available could reflect true differences in preferences for providing samples, more confusion over the value of sample provision, greater hesitancy on the part of staff members to make the request for samples, more competing demands at visits, more home visits without a phlebotomist on hand, or LAR over-protectiveness. While this study does not enable determination of the cause of differences in sample availability, it highlights the need to attend to this issue to better understand contributing factors. Solutions will depend on what contributes to this discrepancy – but a first step is just acknowledging the discrepancy exists.

Other groups that this study highlighted as being significantly less likely to have samples available include those with recent depression or psychiatric issues, individuals who are not married or living with a partner, and those with higher levels of education. There are many possible factors at play, including: competing demands, staff hesitancy with certain groups, and social support and encouragement (or lack thereof). The educational finding was more surprising; perhaps individuals with higher levels of education have enough information about how genetic material can be used to have more concerns that prevent them from participating. Or perhaps they feel more at ease in a clinical research setting and therefore feel more comfortable declining blood draws. Cognitive status may also mediate the association between education and sample provision. The explanation is not entirely clear, but identifies another area in which to delve deeper to enhance understanding.

From the site perspective, participant and LAR refusals as well as staff and supply availability all, at least on occasion, served as barriers to blood sample provision. It may be

helpful in the future to record reasons for these refusals to identify ways to be more proactive in avoiding such refusals. One possibility would be to explore the use of educational materials further. Currently, only about 20% of sites use any type of educational materials in regards to sample provision; perhaps greater efforts to explain why this engagement is valuable and important and how it contributes to science would help encourage sample provision.

The recognition that site-level factors may also play a role, and the tremendous variability in how and when samples are obtained, suggests possible opportunities to share best-practices across sites to improve upon local strategies and enhance genetic engagement. The fact that staff and supply availability can, even rarely, impact sample provision suggests the potential value of scheduling and resupplying systems that can help increase the likelihood that the right personnel and materials are always on hand. Unfortunately, integration of the survey findings seemed to be unrelated to probability of sample availability given individual-level characteristics. Future refinement of survey questions, alignment of time periods between the survey and the data collection, and observation of site practices may help better tease out how site factors may relate to genetic engagement.

Although we did not see any significant effects of center-level variables, it is important to note that the survey measured center characteristics in 2016, the individual-level data were aggregated over 2009–2016. Thus, the center-level variables from the survey may not accurately reflect center procedures from 2009–2015. Additionally, the survey responses may be heterogeneous. For example, the survey asked whether “education materials” were provided to participants, but not specifically what these educational materials were. While some educational materials may be effective in increasing participation, it does not follow that every instance will be effective.

4.2. Limitations & Implications

This study had several limitations. While the study highlighted characteristics associated with lower likelihood of sample availability, at present it is hard to distinguish between participant preferences, varying participant recruitment approaches, differing site practices regarding blood samples, or NACC requests and practices. Prior research demonstrates how factors such as recruitment source, race, genetics and behavior are interrelated and cannot be fully understand in isolation; yet, information on recruitment in the current dataset is rather limited [33]. The fact that several factors became insignificant once site was taken into account suggests that some differences may be attributable to site populations and practices, rather than individual factors. Accordingly, ongoing attention to on-the ground recruitment and engagement practices is warranted. Despite these limitations, this study provides important insights into factors to target and areas to explore to help address suboptimal participation.

It’s also important to be explicit about priorities. Sometimes, sites adjust expectations for underrepresented groups. While this helps address underrepresentation overall, these different criteria may lead to less information about these groups. These efforts are important, but efforts can’t stop with getting someone in the door. Continual efforts to educate, address concerns and highlight the importance of engagement are needed to help

reduce disparities in genetic engagement between groups. Ultimately, increasing involved participation across groups will help provide the necessary information to explore group differences and tackle some of the racial and other disparities in AD prevalence [34, 35]. Results of the current study may be instrumental in providing an increased understanding of factors to focus on to increase genetic research engagement initiatives not just for NACC and the ADGC, but also for other NIA clinical trial initiatives such as the Generations Study that rely on recruitment success that is fully dependent on genetic research engagement as part of the screening and eligibility process [36].

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Appendix A: ADC Genetic Research Engagement Survey

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Genetic Research Engagement Survey

Thank you for agreeing to participate in this survey. This survey will help us better understand practices at your center so that we can better identify factors that may impact participant engagement in genetic research.

In 2016, of the participants you saw, 78% have DNA samples available at the National Cell Repository for Alzheimer's Disease (NCRAD) or have genetic data available through an AD genetics consortium (e.g., ADGC, ADSP). This survey is designed to help explain differences in data availability among ADCs.

Does your Center obtain blood or other specimen samples from participants, for local or other use?

- ☐ Yes
☐ No

If your Center obtains blood or other specimens, is it expected that all participants will provide these specimens?

- ☐ Yes
☐ No

In your center, how frequently are participants asked to provide a blood sample?

- ☐ At least every annual assessment
☐ At the first ADC visit only
☐ On certain assessments only
☐ Never

Are all participants asked to provide a blood sample at least once?

- ☐ Yes
☐ No

If no, please describe.

Are there any participant groups who are less likely to agree to provide a blood sample?

- ☐ Yes
☐ No

If yes, please describe.

In your center, who is responsible for asking a participant if they would consent to provide a blood sample? (Check all that apply)

- ☐ Cognitive tester
☐ Physician
☐ Nurse practitioner
☐ Social Worker
☐ Phlebotomist
☐ Other

Please describe who "other" can include.

In your center, when is a participant asked if they would provide a blood sample?

- ☐ Never
☐ Prior to cognitive testing
☐ During a break in cognitive testing
☐ After cognitive testing
☐ Variable, no set time

Please share any comments regarding when participants are asked to provide blood samples.

In your center, when does a participant who has agreed to provide a blood sample do so?

- ☐ Prior to cognitive testing
☐ During a break in cognitive testing
☐ After cognitive testing
☐ Variable, no set time

Please share any comments regarding when participants provide blood samples.

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Does your center provide participants with any educational materials about providing a blood sample?

☐ Yes
☐ No

If yes, please describe the educational materials that are used at your site that pertain to the provision of a blood sample.

The following questions are about barriers to providing participant biospecimens to NCRAD or genetics consortia. For the individuals who do not have any DNA or genetic data available through these channels, please indicate how frequently each of the following factors serves as a barrier:

	Very Frequently serves as a barrier	Frequently serves as a barrier	Occasionally serves as a barrier	Rarely serves as a barrier	Very Rarely serves as a barrier	Never serves as a barrier
Participant is not asked to provide samples	☐	☐	☐	☐	☐	☐
Participant is asked to provide samples, but refuses	☐	☐	☐	☐	☐	☐
Impaired participant's legally authorized representative refuses	☐	☐	☐	☐	☐	☐
No or limited staff available to obtain sample	☐	☐	☐	☐	☐	☐
Lab supplies not available	☐	☐	☐	☐	☐	☐
Funds not available	☐	☐	☐	☐	☐	☐
Participant samples are not requested by NCRAD, etc.	☐	☐	☐	☐	☐	☐
Regulatory issues prevent obtaining and sharing samples	☐	☐	☐	☐	☐	☐
Other	☐	☐	☐	☐	☐	☐

Please describe other responses.

How satisfied are you with the current level of genetic research engagement at your center?

☐ Not at all
☐ A little
☐ Somewhat
☐ Very
☐ Extremely

What is your role within the center?

Do you have anything additional to share regarding the genetic research engagement of participants at your center?

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Table 1.

Participant Characteristics by Availability of Genetic Sample, National Alzheimer's Coordinating Center (2009–2016)

Characteristic	Genetic Sample (N=14,333)	No Genetic Sample (N=13,186)
Age, y	71.7±10.2	71.0±10.4
Female sex	8,332 (58.1)	7,315 (55.5)
High Education (≥ 16 y)	8,186 (57.1)	7,253 (55.0)
Race		
White	11,725 (81.8)	10,239 (77.7)
Black	1,719 (12.0)	1,723 (13.1)
Other	711 (5.0)	974 (7.4)
Unknown	178 (1.2)	250 (1.9)
Ethnicity		
Non-Hispanic	13,473 (94.0)	11,921 (90.4)
Hispanic	821 (5.7)	1,207 (9.2)
Unknown	39 (0.3)	58 (0.4)
Primary language		
English	13,522 (94.3)	12,268 (93.0)
Not English	497 (3.5)	788 (6.0)
Unknown	314 (2.2)	130 (1.0)
Marital Status		
Married/Living as Married	9,391 (65.5)	8,458 (64.1)
Not Married	4,817 (33.6)	4,644 (35.2)
Other/Unknown	125 (0.9)	84 (0.6)
Living Situation		
Lives with spouse/partner	3,539 (24.7)	3,112 (23.6)
Lives with someone else	9,142 (63.8)	8,194 (62.1)
Lives alone	1,612 (11.3)	1,861 (14.1)
Other/unknown	40 (0.3)	19 (0.1)
Co-participant relationship		
Spouse/partner	7,834 (54.7)	7,124 (54.0)
Child	3,193 (22.3)	2,915 (22.1)
Sibling/other relative	1,038 (7.2)	1,039 (7.9)
Friend	1,369 (9.6)	1,064 (8.1)
Caregiver/other	281 (2.0)	287 (2.2)
Unknown	618 (4.3)	757 (5.7)
Cognitive diagnosis		
Normal	6,901 (48.2)	4,598 (34.9)
Impaired, not MCI	647 (4.5)	681 (5.2)

Characteristic	Genetic Sample (N=14,333)	No Genetic Sample (N=13,186)
MCI	3,210 (24.3)	2,630 (18.4)
Dementia	4,155 (29.0)	4,697 (35.6)
Depression, last 2 yrs	3,998 (27.9)	4,164 (31.6)
Other psychiatric illness	722 (5.0)	870 (6.6)
Alcohol/Substance abuse	837 (5.8)	876 (6.6)
APOE genotype available	14,028 (97.9)	8,034 (60.9)
APOE genotype		
3/3	7,047 (49.2)	4,044 (30.7)
3/4	4,322 (30.2)	2,463 (18.7)
3/2	1,309 (9.1)	725 (5.7)
4/4	900 (6.3)	543 (4.1)
4/2	387 (2.7)	192 (1.5)
2/2	63 (0.4)	40 (0.3)
Annual visits	4.8±2.7	2.9±2.2
At least 5 years of follow-up	7,085 (49.4)	2,516 (19.1)

Table 2.

Fully adjusted logistic regression model results (N=24,597). Bolded results are significant at 0.05.

Comparison	Adjusted Odds Ratio	95% CI
Age, 1-year	1.01	1.00 – 1.01
Sex, Female vs Male	1.10	1.04 – 1.17
High Education (16+ yrs), yes vs. no	0.93	0.88 – 0.99
Race		
Black vs. White	0.90	0.83 – 0.92
Other vs. White	0.72	0.64 – 0.81
Ethnicity, Hispanic vs. non-Hispanic	0.61	0.52 – 0.71
Primary language, English vs. Other	1.06	0.88 – 1.27
Unmarried vs. Married/Living as married	0.90	0.77 – 1.05
Living Situation		
Spouse/partner vs. alone	1.08	0.93 – 1.27
With other adult vs. alone	1.00	0.90 – 1.10
Co-participant relationship		
Child vs. spouse/partner	1.08	0.98 – 1.16
Sibling vs. spouse/partner	1.03	0.90 – 1.16
Friend vs. spouse/partner	1.12	0.99 – 1.27
Caregiver/other vs. spouse/partner	0.92	0.75 – 1.14
Cognitive diagnosis		
Impaired, not MCI vs. normal	0.62	0.54 – 0.71
MCI vs. normal	0.55	0.51 – 0.59
Dementia vs. normal	0.70	0.65 – 0.75
Depression, yes vs. no	1.02	0.96 – 1.08
Other psychiatric illness, yes vs. no	0.84	0.75 – 0.94
Alcohol/substance abuse, yes vs. no	1.09	0.98 – 1.22
At least 5 years of follow-up, yes vs. no	4.21	3.97 – 4.47

Table 3.

Reduced adjusted logistic regression model results (N=26,647). All variables retained were significant at 0.05.

Comparison	Adjusted Odds Ratio	95% CI
Age, 1-year	1.01	1.00 – 1.01
Sex, F vs M	1.09	1.04 – 1.16
High Education, yes vs. no	0.93	0.88 – 0.98
Race		
Black vs. White	0.88	0.81 – 0.95
Other vs. White	0.71	0.64 – 0.79
Ethnicity, Hispanic vs. non-Hispanic	0.61	0.54 – 0.68
Unmarried vs. Married/Living as married	0.88	0.83 – 0.94
Cognitive diagnosis		
Impaired, not MCI vs. normal	0.65	0.58 – 0.74
MCI vs. normal	0.61	0.57 – 0.65
Dementia vs. normal	0.76	0.71 – 0.80
At least 5 years of follow-up, yes vs. no	3.90	3.69 – 4.13

Table 4.

Reduced adjusted logistic regression model results based on generalized estimating equations (N=26,647).
 Bolded results are significant at 0.05.

Comparison	Adjusted Odds Ratio	95% CI
Age, 1-year	1.01	1.00 – 1.01
Sex, F vs M	1.11	1.04 – 1.19
High Education, yes vs. no	0.96	0.89 – 1.03
Race		
Black vs. White	0.67	0.52 – 0.87
Other vs. White	0.75	0.54 – 1.04
Ethnicity, Hispanic vs. non-Hispanic	0.78	0.62 – 0.99
Unmarried vs. Married/Living as married	0.93	0.86 – 1.00
Cognitive diagnosis		
Impaired, not MCI vs. normal	0.81	0.57 – 1.16
MCI vs. normal	0.73	0.59 – 0.90
Dementia vs. normal	0.93	0.75 – 1.14
At least 5 years of follow-up, yes vs. no	3.55	2.87 – 4.40

Table 5.

Site Practices and Satisfaction

Variable	N (%)
<i>Blood or other specimens expected from all participants</i>	
Yes	26 (89.7)
No	3 (10.3)
<i>Frequently that participants are asked to provide a blood sample</i>	
At the first ADC visit only	5 (17.9)
On certain assessments only	4 (14.3)
At least every annual assessment	19 (67.9)
<i>Participants groups who are less likely to agree to blood sample provision</i>	
Yes	9 (31.0)
No	20 (69.0)
<i>Who asks if participant will consent to blood sample</i>	
Cognitive tester	11 (37.9)
Physician	8 (27.6)
Nurse practitioner	7 (24.1)
Social worker	5 (17.2)
Phlebotomist	1 (3.4)
Others	17 (58.6)
<i>When participants are asked to provide a blood sample</i>	
Prior to cognitive testing	22 (75.9)
During a break in cognitive testing	1 (3.4)
After cognitive testing	1 (3.4)
Variable, no set time	5 (17.2)
<i>When participants provide blood samples</i>	
Prior to cognitive testing	8 (27.6)
After cognitive testing	7 (24.1)
Variable, no set time	14 (48.3)
<i>Center provides educational materials about blood sample provision</i>	
Yes	6 (20.7)
No	23 (79.3)
<i>Satisfaction with genetic engagement</i>	
Not at all	2 (7.1)
A little	1 (3.6)
Somewhat	7 (25.0)
Very	9 (32.1)
Extremely	9 (32.1)

Table 6.

Site Identified Barriers to Blood Sample Provision

Potential Barrier	Ever endorsed	Mean (SD)
Not asked	11	1.61 (1.07)
Refused	28	2.64 (1.06)
LAR Refused	23	2.48 (1.16)
Staff unavailable	19	2.29 (1.33)
Supplies unavailable	11	1.71 (1.18)
Funds unavailable	10	1.79 (1.32)
Not requested by NCRAD	7	1.48 (1.01)
Regulatory issues	10	1.82 (1.42)
Other	5	1.67 (1.23)

Note: Responses were reverse scored such that higher numbers indicate more frequently endorsed as a barrier.