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Predictors of Willingness to Enroll in Hypothetical Alzheimer Disease Biomarker Studies that Disclose Personal Results

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Introduction: We examined factors related to willingness to enroll in hypothetical Alzheimer disease (AD) biomarker studies.

Methods: Using linear regression, we assessed the relationship among enrollment willingness and demographics, family dementia history, research attitudes, concern about AD, experiences of discrimination, and belief in AD risk modifiability. Inductive coding was used to assess qualitative data.

Results: In middle-aged and older adult AD research participants (n = 334), willingness to enroll in biomarker studies was driven by biomarker collection method, research attitudes, and disclosure of personal results. Predictors of willingness were similar for Black and White participants. Themes associated with increased willingness included a desire to learn biomarker results and support research.

Discussion: Research attitudes were an important predictor of biomarker study willingness regardless of race. As seen elsewhere, Black participants were more hesitant to participate in biomarker research. Disclosure of biomarker results/risk can bolster willingness to enroll in biomarker studies, particularly for Black participants.

Key Words: Alzheimer disease, biomarkers, recruitment, return of research results, risk communication, research attitudes, mixed-method approach

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Alzheimer disease (AD) research faces challenges in recruitment and retention of study participants.[1] Lengthy study duration and burdensome or potentially risky procedures can hinder participant enrollment and retention.[1,2] Contrarily, facilitators include understandable study information[2] and positive researcher-participant relationships.[3]

It is particularly important to address enrollment of minoritized peoples in AD research. Despite incidence and prevalence of AD being higher in Black Americans than Whites, AD biomarker research samples are largely made up of White[4] participants, meaning findings may not be generalizable to other communities. Historical and contemporary conditions of structural and interpersonal racism shape access to and benefits of research participation for Black older adults.[5] Racialized determinants of health like transportation access, time constraints, and experiences of discrimination (EOD) in health care may influence racialized individual's decisions to participate in biomedical research. Prior studies assessing Black individuals' participation in AD research highlights the critical role community-based events and long-standing relationships play in bolstering recruitment and retention of Black individuals.[3,6,7] Qualitative study results suggest study participation may result from researcher-community relationships that extend beyond immediate research interests, include community dissemination of findings, and emphasize study relevance to Black adults.[8] This prior body of work demonstrates perceived benefit, minimal risk,[9] trust, transparency, and reduced fear may be associated with increased likelihood to participate in AD prevention trials.

Most prior studies focus on barriers/facilitators to participation in AD clinical trials rather than biomarker studies. Further, most studies do not assess details on specific factors shaped by race and racism (eg, access to services, socioeconomic barriers, trust in medical research, knowledge/concern about AD, social norms) that likely contribute to results. Identifying community-specific factors associated with willingness to enroll in AD biomarker research is needed to support study enrollment for historically excluded groups and reduce racial disparities in AD-biomarker research. Here we present findings from the Alzheimer's Biomarker Survey, a telephone survey that collected quantitative and qualitative information about likelihood to enroll in biomarker studies that disclose results. We utilize this novel mixed-method approach to preliminarily address gaps identified above and begin a more nuanced discussion of biomarker research enrollment decisions in underrepresented participant populations. We examined (1) how willingness to enroll in biomarker studies varied by biomarker collection method, (2) what individual factors predicted

enrollment willingness for Black and White participants, and (3) the influence of biomarker test result disclosure on willingness to participate in biomarker studies.

METHODS

Participants

Participants enrolled in the Wisconsin Registry for Alzheimer's Prevention[10] (WRAP) or Wisconsin Alzheimer's Disease Research Center Clinical Core (WADRC) were recruited into the survey. WRAP is a longitudinal observational study enriched for parental dementia history. Participants were middle-aged and cognitively unimpaired upon enrollment in WRAP. The WADRC includes middle-older-aged adults with unimpaired cognition, mild cognitive impairment, or dementia. Both studies include annual or biennial cognitive testing, physical exams, and questionnaires. A subset of both studies offer biomarker testing [eg, cerebrospinal fluid (CSF), magnetic resonance imaging, positron emission tomography (PET)]. Biomarker results were not disclosed to WRAP or WADRC participants before survey enrollment.

Survey inclusion criteria required participants to be aged 45 to 89, cognitively unimpaired and self-identify as Black/African American or non-Hispanic White. Participants could select multiple racial identities. Participants selecting Black as their sole or partial race were categorized as Black. Participants only selecting White were categorized as White. All participants provided institutionally approved informed consent before participation.

Survey Instrument

The Alzheimer's Biomarker Survey, a telephone survey developed using an iterative process, incorporated existing scales and questions created by the study team. Several drafts were reviewed by our study team, University of Wisconsin Survey Center (UWSC), and external content-expert consultants.

The final instrument included Likert-scale and open-ended questions on participant willingness to enroll in various biomarker studies. The survey included questionnaires on EOD (EOD Day-to-Day Unfair Treatment subscale[11]), research attitudes [Research Attitudes Questionnaire (RAQ-7[12])], and beliefs[13] and concern[14] about AD. The EOD Day-to-Day Unfair Treatment subscale included 9 questions and a 5-point response Likert-scale added together for a cumulative score. The RAQ-7 included 7 questions and a 5-point response Likert-scale added together for a cumulative score. A question adapted from Anderson et al[13] was included, asking "How much do you believe that you can do things to lower your risk of getting Alzheimer's?" on a 5-point Likert-scale. A question from Roberts and Connell[14] was included, asking "How concerned are you that you will develop Alzheimer's?" on a 5-point Likert-scale.

We developed 5 vignettes describing hypothetical AD biomarker studies to assess enrollment willingness (Supplemental Digital Content 1, http://links.lww.com/WAD/A376). The first vignette outlined a general (no collection method described) AD biomarker study with disclosure of results, followed by 2 open-ended questions asking participants to describe why they chose their response and their concerns about the study. The second vignette described the same study as the first but without results disclosure. The third, fourth, and fifth vignettes described a PET, CSF, and blood-based biomarker study with disclosure, respectively. Biomarker collection methods were described in nontechnical terms. Following the vignettes, participants ranked their willingness to enroll in the study on a 5-point Likert-scale.

Data Collection

Data was collected from January 6 through March 16, 2020 using a computer-assisted telephone interviewing (CATI) system. The CATI software employed by the UWSC is CASES 5.6 provided by the Computer-Assisted Survey Methods Program at the University of California-Berkeley.

Quantitative Analysis

Descriptive statistics were used to evaluate demographics and response patterns of willingness by biomarker collection method. We predicted enrollment willingness would be higher for less invasive methods.

Second, we explored factors related to willingness. Using linear regression, we assessed Likert responses (range 1 to 5) for willingness to enroll in the AD biomarker studies by race as well as associations between willingness and age, sex, education, family dementia history, research attitudes (RAQ-7), concern about developing AD, EOD, and belief in ability to modify personal AD risk through self-action. We predicted race, sex, family history, research attitudes, and concern about developing AD would be related to enrollment willingness. As secondary analyses probing further into factors related to willingness, we examined interactions between the variables listed above and race to assess racial differences in predictor-outcome relationships. We centered all covariates and checked for variance inflation. Given that Black and White samples and their decision-making processes likely differed in unmeasured ways, we also conducted stratified regressions using the same covariates as the primary analyses to identify within-group predictors of willingness.[15] Because the willingness outcomes are discrete variables and may not be well-modeled with linear regression, we performed a sensitivity analysis using logistic regression models, dichotomizing the outcome variable as willing or unwilling.

Third, to test the influence of disclosure on enrollment willingness, we used within-subject *t*-tests to compare Likert responses (range 1-5) to the two willingness questions for the general AD biomarker study with results disclosure and without. All analyses were conducted using R i386 3.5.1.[16]

Qualitative Analysis

Data were analyzed using qualitative content analysis.[17] UWSC coders used inductive coding as the initial coding method,[18] using NVivo (version 12). The codes were generated from the responses themselves rather than defined a priori. One UWSC coder initial-coded the responses, and a second UWSC coder reviewed the initial coding. Discrepancies between coders were resolved through discussion. Responses could be coded with multiple themes. The transcripts were then reviewed again to refine coding categories further. Both initial coding categories and further refinements of categories were reviewed with the study team. We took a stepped mixed-method approach to contextualize our quantitative results with qualitative information. Each participant's qualitative response was linked with their willingness Likert responses. The frequencies of each thematic response were then tabulated by Likert response.

TABLE 1. Alzheimer's Biomarker Survey Participant Characteristics

	Overall	Black Participants	White Participants
Sample size (n)	334	148	186
Age at survey	64.8 ± 7.7	64.9 ± 8.4	64.7 ± 7.0
Sex [female, n (%)]	248 (74.3)	107 (72.3)	141 (75.8)
Education (w/ ≥ Bachelor's, n (%)	195 (58.4)	67 (45.6)	129 (69.4)
Self-identified race, n (%)	148 (44.3) Black 186 (55.7) White	—	—
Family history of dementia (with family history, n (%)	208 (62.3)	76 (51.4)	133 (71.5)
Research Attitudes Questionnaire (range: 7-35)	29.9 ± 3.7	29.6 ± 3.7	30.2 ± 3.3
Concern about developing AD (range: 1-5)	3.0 ± 1.2 (3)	2.9 ± 1.3	3.1 ± 1.1
Experiences of discrimination (range: 9-45)	16.5 ± 6.4	21.0 ± 6.3	12.9 ± 3.6
Belief in personal AD risk modifiability (range: 1-5)	3.7 ± 1.0	3.6 ± 1.0	3.7 ± 1.0

AD indicates Alzheimer disease.

RESULTS

Participant Characteristics

The final sample included 334 participants (mean age = 64.8 ± 7.7, 45% Black, n = 167 from WRAP) (Table 1). The sample was recruited from ongoing Alzheimer's research cohorts and had a median number of 3 study visits before survey participation. About 60% of Black participants were recruited from WADRC. The sample was well-educated (58.4% with a Bachelor's degree), predominantly made up of women (74.3%), and more likely to have a family dementia history (62.3%). Black and White participants differed on years of education, family dementia history, and EOD. Sixty-nine percent of Whites had a Bachelor's degree compared with 46% of Black participants, 72% of Whites had a family dementia history compared with 51% of Black participants. Average EOD scores were significantly higher for Black participants than Whites (21/45 vs. 13/45). Age, sex, research attitudes, concern about developing AD, and belief in personal modifiability of AD risk did not significantly differ between White and Black participants.

Study Enrollment Willingness

In all, 49.7% (n = 166) reported being very or extremely-likely to enroll in the general AD biomarker with disclosure (Table 2). This result varied by biomarker method. About half the sample was very- or extremely-likely to enroll in a PET scan study with disclosure (45.5%, n = 152). A third of the sample was very- or extremely-likely to enroll in a lumbar puncture study with disclosure (32.2%, n = 108), and a majority were very- or extremely-likely to enroll in a blood-based biomarker study with disclosure (86.2%, n = 288).

Factors Related to Study Enrollment Willingness

In the full sample, White participants were more likely than Black participants to express enrollment willingness in all 5 hypothetical AD biomarker studies (Table 3), and more positive research attitudes predicted enrollment willingness. Concern about AD was a significant positive predictor of willingness to enroll in the blood-based and general AD biomarker study with disclosure. For the hypothetical CSF study, older age was significantly related to lower enrollment

TABLE 2. Willingness to Enroll in AD Biomarker Studies

	Extremely	Very	Somewhat	A Little	Not at All
Willingness to enroll in general AD biomarker study, n (%)					
Overall	62 (18.6)	104 (31.1)	115 (34.4)	30 (9.0)	19 (5.7)
Black participants	15.5 (23)	26.4 (39)	39.9 (59)	9.5 (14)	10 (6.8)
White participants	39 (21.0)	65 (34.9)	56 (30.1)	16 (8.6)	9 (4.8)
Willingness to enroll in general AD biomarker study without disclosure, n (%)					
Overall	47 (14.1)	114 (34.1)	103 (30.9)	37 (11.1)	32 (9.6)
Black participants	14 (9.5)	33 (22.3)	51 (34.5)	23 (15.5)	26 (17.6)
White participants	33 (17.7)	81 (43.5)	52 (35.1)	14 (7.5)	6 (3.2)
Willingness to enroll in PET scan study, n (%)					
Overall	59 (17.7)	93 (27.8)	99 (29.6)	29 (8.7)	53 (15.9)
Black participants	19 (12.8)	32 (21.6)	38 (25.7)	17 (11.5)	42 (28.4)
White participants	40 (21.5)	61 (32.8)	61 (32.8)	12 (6.5)	11 (5.9)
Willingness to enroll in lumbar puncture study, n (%)					
Overall	51 (15.3)	57 (17.1)	56 (16.8)	36 (10.8)	132 (39.5)
Black participants	18 (12.2)	22 (14.9)	22 (14.9)	15 (10.1)	70 (47.3)
White participants	33 (17.7)	35 (18.8)	34 (18.3)	21 (11.3)	62 (33.3)
Willingness to enroll in blood draw study, n (%)					
Overall	141 (42.2)	147 (44.0)	34 (10.2)	9 (2.7)	3 (0.9)
Black participants	47 (31.8)	68 (45.9)	23 (15.5)	7 (4.7)	3 (2.0)
White participants	94 (50.5)	79 (42.5)	11 (5.9)	2 (1.1)	0

AD indicates Alzheimer disease; PET, positron emission tomography.

TABLE 3. Primary Analysis Model Terms

	Beta (SE), *P* for General AD Biomarker Disclosure	Beta (SE), *P* for General AD Biomarker Study Without Disclosure	Beta (SE), *P* for AD PET Disclosure	Beta (SE), *P* for AD CSF Disclosure	Beta (SE), *P* for AD Blood-based Disclosure
Age	−0.011 (0.008), 0.168	−0.002 (0.008), 0.831	−0.007 (0.009), 0.394	−0.033 (0.010), 0.002**	−0.007 (0.005), 0.206
Gender	−0.095 (0.130), 0.463	−0.135 (0.129), 0.296	−0.268 (0.148), 0.072	−0.132 (0.181), 0.467	0.135 (0.094), 0.152
Education	−0.089 (0.120), 0.459	0.000004 (0.119), 1.00	0.008 (0.136), 0.954	−0.116 (0.166), 0.485	0.096 (0.086), 0.269
Family Dementia History	−0.137 (0.128), 0.286	−0.0017 (0.127), 0.895	0.102 (0.146), 0.483	−0.094 (0.1778), 0.600	−0.017 (0.092), 0.855
Research Attitudes	0.097 (0.016), <0.0001***	0.117 (0.016), <0.0001***	0.105 (0.019), <0.0001***	0.141 (0.023), <0.0001***	0.073 (0.012), <0.0001***
Concern about Developing AD	0.112 (0.051), 0.029*	0.022 (0.051), 0.667	0.062 (0.058), 0.290	0.029 (0.071), 0.686	0.106 (0.037), 0.004**
Experiences of Discrimination	0.011 (0.012), 0.342	0.009 (0.002), 0.420	0.008 (0.013), 0.547	0.020 (0.016), 0.223	0.004 (0.008), 0.605
Self-Identified Race	−0.306 (0.154), 0.048*	−0.766 (0.153), <0.0001***	−0.771 (0.175), <0.001***	−0.543 (0.212), 0.011*	−0.362 (0.111), 0.001**
Belief about personal Alzheimer's risk modifiability	0.039 (0.058), 0.508	0.073 (0.058), 0.202	0.105 (0.066), 0.115	0.083 (0.081), 0.301	0.025 (0.042), 0.549

*$P < 0.05$.
**$P < 0.01$.
***$P < 0.001$.
AD indicates Alzheimer disease; PET, positron emission tomography.

willingness. The other variables of interest, sex, education, family dementia history, EOD, and belief in AD risk modifiability, were not significant predictors of enrollment willingness in the full sample. The strength and direction of the relationships modeled in the logistic regression sensitivity analyses were like the linear regression results.

To more directly assess racial differences in enrollment willingness, we conducted additional analyses to understand specific predictors among Black participants. First, using independent sample *t* test, we did not find a significant difference in research attitudes between Black and White participants [*t* (*df*) = −1.42 (299.13), $P = 0.140$]. Next, we included covariate×race interactions in each linear regression model to assess racial differences in their effects on willingness. None of these interaction terms significantly predicted enrollment willingness. Last, in acknowledging Black and White participants were recruited into WRAP and WADRC studies using different strategies,[19] and complex racialized experiences with research likely influence willingness, we opted to conduct stratified regression models. Research attitudes remained the only significant predictor of willingness to enroll in each of the described studies for both the Black and White subsamples. For Black participants, belief in modifiability of Alzheimer's risk also significantly predicted enrollment willingness only for the study without results disclosure (*b*: 0.22, $P = 0.034$).

Enrollment Willingness—Qualitative Responses

Themes associated with increased willingness to enroll in an AD biomarker study that disclosed results included a personal interest in learning one's biomarker results and a desire to support research (Table 4). Both were mentioned more frequently as willingness increased, though a desire to support research increased more substantially as willingness increased. Overall, there were no differences in themes mentioned by White and Black participants. However, when describing their motivation to enroll, a small number of Black participants wanted to boost diversity in research (n = 5).

The main themes related to lower enrollment willingness were anxiety about a high-risk result and limited perceived utility of testing (including ambiguous results and no disease treatment). Among those who were "not at all" willing to enroll in an AD biomarker study that disclosed results, 40% expressed anxiety and slightly over half expressed a concern about utility. These latter themes were rarely mentioned by participants who responded "extremely willing" to participate (5% and 0%, respectively). A few participants mentioned the potential stigma of a positive/elevated result (n = 33), and the time/logistical burdens of participation (n = 32). Concern about harms was cited by about one-third of participants, regardless of their willingness to enroll.

Impact of AD Biomarker Results Disclosure on Willingness to Enroll

In the full sample, participants were more willing to enroll in the general AD biomarker study with results disclosure than the same study without disclosure [*t* (*df*) = 2.43 (328), $P = 0.02$] (Table 5). The average response to the disclosure study was 0.16 points higher than the nondisclosure study. In stratified analyses, White participants did not show a difference in participation willingness for the studies with and without disclosure [*t* (*df*) = −0.76 (184), $P = 0.45$]. In the sample of Black participants, responses to the 2 studies differed [*t* (*df*) = 4.63 (143), $P < 0.0001$]. Willingness to participate in the general AD biomarker study with disclosure was on average 0.44 points higher than responses to the same study without disclosure.

TABLE 4. Qualitative Data Themes Related to Willingness Enroll in a General AD Biomarker Study With Disclosure of Results

Willingness to Enroll in Biomarker Study With Disclosure		Not at All	A Little	Somewhat	Very	Extremely
Number of respondents		18	30	117	105	62
Themes related to higher willingness to enroll	Participant quotes			Number (%)		
Interest in knowing: understand current cognitive status, estimate future risk, to plan, or to modify lifestyle, or to share with their family members	Sometimes I seem to forget things that I'm doing. It's good to know at the beginning if you have it. I'd like to know It would be good to know what level risk I am at. The other good thing about having the marker and knowing if there's a risk is planning ahead for the future. Both my grandparents died from Alzheimer's; they didn't know it was coming on. If you know, you can plan your life accordingly Because I would want to know any future information that could help me plan now I just think that having all the facts is important and knowing that I am more predisposed might make me more willing to change my lifestyle I would really want to know that I could prepare my family. So that I can make them aware of what I'm going through	0	9 (30)	43 (37)	46 (43)	31 (50)
Support research: Support research in general, to help others or one's family, because of personal experience or family history with AD, or to support diversity	To help find a cure for Alzheimer's I believe strongly in research and I believe we have come as far as we have because of research, I believe in it I believe it's my duty as a human being, to contribute what I have to everyone else. Even if I get nothing. So whenever I do studies, I don't think they'll do much for me, but hopefully it'll add to my community, my world If it's not going to help me it might help my children or grandchildren My father died of Alzheimer's. It's what I can do to honor him I think it's important for more studies to involve people of color, so we can better understand what medicine and care is needed for those underserved populations	1 (6)	8 (27)	34 (28)	73 (70)	42 (68)
Themes related to lower willingness to enroll	Participant quotes			Number (%)		
Anxiety: fear of developing AD, or concerns about untreatable disease	I would not want to know if I had the marker and stress about having the disease The major concern is if you had markers and there's no cure you would be looking at the end of your useful life The worry would be upon receiving a negative result I could potentially fall into a very deep state of sadness or depression, that would be hard, ignorance is bliss or is it?	7 (39)	15 (50)	36 (31)	16 (15)	4 (6)
Limited utility of testing: no disease treatment, or the results are ambiguous	Because once you find out there's nothing you can do about it, you're kind of stuck with that info. The fact that there is no medication or treatment for that marker Well I wouldn't wanna know because if you have the marker you might not get the disease… And I know that even if you do not have the marker you would still possible to get the disease	9 (56)	8 (27)	14 (12)	5 (5)	0

TABLE 4. (*continued*)

Willingness to Enroll in Biomarker Study With Disclosure		Not at All	A Little	Somewhat	Very	Extremely
Physical harms of testing: Negative physical effects, or overly invasive procedure	I would be concerned if there is a physical side effect I don't like people poking around in my brain I would want to know what process is used like if you had to drill a hole in my head. and extract a sample of my brain I would not be willing	7 (39)	9 (30)	40 (33)	33 (30)	23 (37)
Burden of testing: time commitment or travel distance	The time it would consume, that's just about it that I can think of Distance, if it was a very difficult distance to travel	1 (6)	1 (3)	10 (9)	11 (10)	9 (15)
Stigma: confidentiality concerns, or discrimination in insurance, employment, etc.	How would it affect my health care? Is it going to be put in chart where health care providers might see it? I am concerned about the confidentiality in regards to health insurance I would be a little worried about the anonymity With my job, they'd be interested in learning about my results. I'd be jeopardized, if results got out to those I work for	2 (11)	2 (7)	14 (12)	13 (12)	2 (3)

DISCUSSION

Participants enrolled in AD research endorse willingness to participate in biomarker studies that disclose test results. We observed about half of participants reported high willingness to enroll in a general AD biomarker study with disclosure. When specific biomarker methods were described, participants reported highest enrollment willingness for the blood-based biomarker study and lowest for the CSF biomarker study. These results suggest as biomarker collection method burden decreases, willingness to participate increases. Our findings coupled with advancements in plasma-based biomarkers over the last few years present an opportunity for the future of biomarker studies.

In testing factors related to enrollment willingness, similar to prior studies,[20–25] we found Black participants expressed less willingness to participate in AD biomarker studies. Research attitudes predicted willingness across all hypothetical study designs. Age, sex, education, family dementia history, concern about developing AD, EOD, and belief in personal AD risk modifiability were not consistent predictors of enrollment willingness across all the described studies.

Race is a social construct representing a combination of ancestry and experience. Racialization shapes interactions with institutions/systems, including those that impact health. Robust evidence supports the health influences of environmental and societal conditions associated with being racialized as Black in the United States. To explore the relationship between self-identified race and enrollment willingness we conducted several secondary analyses. We found no difference between Black and White participants in research attitudes, though, scores were high across both groups (average: about 30/35). We did not find any significant interactions between race and other predictors across the willingness outcomes, suggesting predictor effects did not meaningfully differ by race. In stratified analyses, only research attitudes were a significant predictor across each of the enrollment willingness outcomes for both the White and Black subsample analyses. Our findings differ from prior findings that Whites report more positive research attitudes than Black participants,[20,26,27] and are consistent with findings from Glover et al that older Black and White adults did not differ on research attitudes.[6] Research attitudes incorporate but are not solely made up of trust in medical research. Trust is multifaceted[28] and incorporates experiences and perceptions of medical research, access to health care, and prior negative experiences with the health care system. The RAQ-7 assesses a mix of personal and general views toward research and therefore may not fully capture the nuance of trust. Further, older Black adults[6,20] and individuals who have participated in research before,[28] like our sample, likely have more trust in medical research. WRAP and WADRC participant community-based recruitment/engagement strategies coupled with the experience of participating in research could increase our participants trust and therefore improve their attitudes towards research. Our quantitative findings revealed, as expected, research attitudes were an important predictor of willingness regardless of race, but could not explain why Black participants were less willing to enroll or clearly identify target areas to improve recruitment practices.

Examination of qualitative themes contextualized by quantitative willingness demonstrated that some themes varied by willingness to enroll. For example, the main concerns among those with lower willingness to participate in biomarker studies were psychological consequences and limited testing utility. While themes of trust were not explicit, these qualitative data suggest increased clarity around the utility or benefits of early detection, coupled with reliable access to emotional supports, may increase willingness among hesitant participants. In contrast, among those with higher willingness, psychological consequences and limited testing utility were rarely mentioned. Instead, common themes of responses included a strong interest in supporting research and knowing results to understand personal dementia risk and plan.

Concerns about harms related to biomarker testing were expressed similarly across willingness responses. A possible explanation is that among individuals already participating in

TABLE 5. Willingness to Participate in Study that Measures and Discloses AD Biomarkers Versus Study that Does Not Disclose Personal Result

	Overall (n = 329)	Black or African American (n = 144)	Non-Hispanic White (n = 185)
Willing to participate in study that measured and *disclosed* result?	Very-extremely: 166 (50%) Somewhat: 115 (34%) Not at all-a little: 49 (15%)	Very-extremely: 62 (43%) Somewhat: 59 (40%) Not at all-a little: 24 (17%)	Very-extremely: 104 (56%) Somewhat: 56 (30%) Not at all-a little: 25 (14%)
Willing to participate in study that measured and *did not disclose* result?	Very-extremely: 161 (48%) Somewhat: 103 (30%) Not at all-a little: 69 (21%)	Very-extremely: 47 (32%) Somewhat: 51 (34%) Not at all-a little: 59 (40%)	Very-extremely: 114 (61%) Somewhat: 52 (28%) Not at all-a little: 20 (11%)
Within-subject (paired) *t* test	$t_{(328)} = 2.43$, $P = 0.016$ Mean difference = 0.16	$t_{(143)} = 4.63$, $P < 0.0001$ Mean difference = 0.44	$t_{(184)} = -0.76$, $P = 0.45$ Mean difference = −0.06

research and familiar with risk of harms, additional potential harms may not substantially change their willingness. This is consistent with the observation that across all response options, few participants reported concerns about burdens of testing (n = 32/334), possibly reflecting testing burdens are not a primary consideration for enrollment, either in decreasing or increasing willingness. An alternative explanation is there may be a subgroup of individuals for whom harms are a primary driver of their participation willingness. For those expressing lower participation willingness, potential harms outweigh benefits. In contrast, perceived benefits of research outweigh the concerns for those expressing high willingness. This may be reflected in the relationship between willingness and biomarker collection method noted in the quantitative analysis. More research into the specific reasons for participation in biomarker research is necessary. This could then inform the development of recruitment and educational materials to more fully address physical risks of study involvement and utility of testing (if results disclosed), which may boost enrollment.

In assessing if disclosure affects enrollment willingness, we first saw apparent indifference toward the inclusion of study results disclosure. After disaggregating by racial group, an effect emerged. Within the Black subgroup, 43% responded very willing or extremely willing to enroll in the study with results disclosure, as opposed to 32% in the study without disclosure. For White participants, there was no statistically significant difference in willingness to enroll in studies with and without results disclosure (56% vs. 61% very or extremely willing, respectively). These results suggest willingness in Black participants was influenced by opportunities to learn their results.

Within-group heterogeneity was clear in our subgroup analyses. For Black participants stronger belief in modifiability of Alzheimer risk was related to higher willingness to enroll in a study without disclosure, such that moving from the lowest belief response to the highest was correlated with a 1-point increase in willingness. There was not a group difference between Black and White participants in belief in AD risk modifiability. These results support that between-group differences are not always as meaningful as within-group differences.

The study is limited by the research sample. First, the sample was recruited from existing AD research cohorts, meaning these individuals were intimately familiar with AD research. Generalizability to non-research populations is therefore limited. However, this population is relevant as these individuals are likely to be targeted for early-stage clinical trials. Further, studying individuals already engaged in actions nearer to the intended behavior may improve the correlation between reported intention to participate in research and actual study enrollment. Second, recruitment and retention of Black and White participants within the main studies differs[19]; intentional sustained community outreach and engagement strategies are employed to improve representation of diverse Black participants. Racial differences in factors motivating enrollment in the parent studies may lead to different responses in this study. We approached this possibility by conducting our analyses in the full sample and then stratifying by race. Third, we do not account for all factors that may influence enrollment willingness, namely knowledge about AD and research, time scarcity, and current caregiver status. Individuals that are currently caregivers likely have limited flexibility to participate in studies.[29,30] Fourth, the survey itself could be improved. Each vignette did not include an option with/without disclosure, limiting the ability to perform balanced comparisons; we did not collect detailed information about the value of disclosure for each test; we did not follow-up to identify study changes that may increase participants' willingness; and the vignette phrasing could be improved by framing disclosure as a choice rather than a study requirement. Lastly, our power was limited to assess all the interactions included in our secondary models.

As advancements in biomarker collection reduce procedure invasiveness and increase accessibility, understanding participant willingness to enroll in AD biomarker studies will be important for improving participation and informing study development, particularly when considering whether to include result disclosure. For both Black and White participants, we found research attitudes drive willingness to participate in biomarker studies. Although a direct comparison of attitudes in this sample did not reveal differences between White and Black participants, self-identified race was also a factor associated with willingness. We suggest that historical and contemporary conditions of racism in biomedical institutions shape willingness to participate in biomarker research. However, our findings also point to a greater willingness to enroll in studies offering result disclosure compared with studies without disclosure. For biomarker studies without disclosure, providing information on modifiable risk factors for AD dementia may bolster participation in Black persons. Our results and expanded work in future studies may help tailor recruitment and retention efforts of minoritized populations into AD biomarker research. Further research in larger Black samples, recruiting individuals not currently involved in research, within-group studies of other underrepresented groups, and more qualitative data will support this progress.

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REFERENCES

1. Grill JD, Karlawish J. Addressing the challenges to successful recruitment and retention in Alzheimer's disease clinical trials. *Alzheimers Res Ther*. 2010;2:34.
2. Clement C, Selman LE, Kehoe PG, et al. Challenges to and facilitators of recruitment to an Alzheimer's Disease Clinical Trial: a qualitative interview study. *J Alzheimers Dis*. 2019;69:1067–1075.
3. Denny A, Streitz M, Stock K, et al. Perspective on the "African American participation in Alzheimer disease research: Effective strategies" workshop, 2018. *Alzheimers Dement*. 2020;16:1734–1744.
4. Indorewalla KK, O'Connor MK, Budson AE, et al. Modifiable barriers for recruitment and retention of older adults participants from underrepresented minorities in Alzheimer's disease research. *J Alzheimers Dis*. 2021;80:927–940.
5. Clemons AM. New Blacks: language, DNA, and the construction of the African American/Dominican boundary of difference. *Genealogy*. 2021;5:1.
6. Glover CM, Creel-Bulos C, Patel LM, et al. Facilitators of research registry enrollment and potential variation by race and gender. *J Clin Transl Sci*. 2018;2:234–238.
7. Gilmore-Bykovskyi AL, Jin Y, Gleason C, et al. Recruitment and retention of underrepresented populations in Alzheimer's disease research: a systematic review. *Alzheimers Dement Transl Res Clin Interv*. 2019;5:751–770.
8. Williams MM, Scharff DP, Mathews KJ, et al. Barriers and facilitators of African American participation in Alzheimer disease biomarker research. *Alzheimer Dis Assoc Disord*. 2010; 24(suppl):S24–S29.
9. Zhou Y, Elashoff D, Kremen S, et al. African Americans are less likely to enroll in preclinical Alzheimer's disease clinical trials. *Alzheimers Dement Transl Res Clin Interv*. 2016;3:57–64.
10. Johnson SC, Koscik RL, Jonaitis EM, et al. The Wisconsin Registry for Alzheimer's prevention: a review of findings and current directions. *Alzheimers Dement Diagn Assess Dis Monit*. 2017;10:130–142.
11. Krieger N, Smith K, Naishadham D, et al. Experiences of discrimination: validity and reliability of a self-report measure for population health research on racism and health. *Soc Sci Med 1982*. 2005;61:1576–1596.
12. Rubright JD, Cary MS, Karlawish JH, et al. Measuring how people view biomedical research: reliability and validity analysis of the Research Attitudes Questionnaire. *J Empir Res Hum Res Ethics*. 2011;6:63–68.
13. Anderson LN, McCaul KD, Langley LK. Common-sense beliefs about the prevention of Alzheimer's disease. *Aging Ment Health*. 2011;15:922–931.
14. Roberts JS, Connell CM. Illness representations among first-degree relatives of people with Alzheimer disease. *Alzheimer Dis Assoc Disord*. 2000;14:129–136; discussion 127–128.
15. Whitfield KE, Allaire JC, Belue R, et al. Are comparisons the answer to understanding behavioral aspects of aging in racial and ethnic groups? *J Gerontol B Psychol Sci Soc Sci*. 2008;63: P301–P308.
16. R Core Team. *R: A Language and Environment for Statistical*. R Foundation for Statistical Computing; 2020. Available at: https://www.R-project.org/.
17. Mayring P. Qualitative content analysis: theoretical background and procedures. In: Bikner-Ahsbahs A, Knipping C, Presmeg N, eds. *Approaches to Qualitative Research in Mathematics Education: Examples of Methodology and Methods Advances in Mathematics Education*. The Netherlands: Springer; 2015:365–380.
18. Saldaña J. *The Coding Manual for Qualitative Researchers*. Thousand Oaks, CA: Sage; 2009.
19. Gleason CE, Norton D, Zuelsdorff M, et al. Association between enrollment factors and incident cognitive impairment in Blacks and Whites: Data from the Alzheimer's Disease Center. *Alzheimers Dement J Alzheimers Assoc*. 2019;15:1533–1545.
20. George S, Duran N, Norris K. A systematic review of barriers and facilitators to minority research participation among African Americans, Latinos, Asian Americans, and Pacific Islanders. *Am J Public Health*. 2014;104:e16–e31.
21. Hussain-Gambles M, Atkin K, Leese B. Why ethnic minority groups are under-represented in clinical trials: a review of the literature. *Health Soc Care Community*. 2004;12:382–388.
22. Shavers VL, Lynch CF, Burmeister LF. Racial differences in factors that influence the willingness to participate in medical research studies. *Ann Epidemiol*. 2002;12:248–256.
23. Blazel MM, Lazar KK, Van Hulle CA, et al. Factors associated with lumbar puncture participation in Alzheimer's disease research. *J Alzheimers Dis*. 2020;77:1559–1567.
24. Muroff JR, Hoerauf SL, Kim SYH. Is psychiatric research stigmatized? An experimental survey of the public. *Schizophr Bull*. 2006;32:129–136.
25. Karlawish J, Rubright J, Casarett D, et al. Older adults' attitudes toward enrollment of non-competent subjects participating in Alzheimer's research. *Am J Psychiatry*. 2009;166: 182–188.
26. Garza MA, Quinn SC, Li Y, et al. The influence of race and ethnicity on becoming a human subject: factors associated with participation in research. *Contemp Clin Trials Commun*. 2017;7: 57–63.
27. Luebbert R, Perez A. Barriers to clinical research participation among African Americans. *J Transcult Nurs*. 2016;27:456–463.
28. Scharff DP, Mathews KJ, Jackson P, et al. More than Tuskegee: understanding mistrust about research participation. *J Health Care Poor Underserved*. 2010;21:879–897.
29. Elliott LK, Bami H, Gelkopf MJ, et al. Patient and caregiver engagement in research: factors that influence co-enrollment in research. *Pediatr Rheumatol Online J*. 2019;17:85.
30. Leslie M, Khayatzadeh-Mahani A, MacKean G. Recruitment of caregivers into health services research: lessons from a user-centred design study. *Res Involv Engagem*. 2019;5:17.

