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RESEARCH ARTICLE

Reasons for undergoing amyloid imaging among diverse enrollees in the A4 study

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Abstract

INTRODUCTION: Understanding attitudes toward participation among diverse preclinical Alzheimer's disease (AD) trial participants could yield insights to instruct future recruitment.

METHODS: Using data from the Anti-Amyloid Treatment in Asymptomatic AD (A4) Study, we examined differences among mutually exclusive racial and ethnic groups in views and perceptions of amyloid imaging (VPAI), a measure of motivations to undergo amyloid biomarker testing in the setting of preclinical AD. We used linear regression to quantify differences at baseline.

RESULTS: Compared to non-Hispanic or Latino (NH) White participants, Hispanic or Latino (3.52 points, 95% confidence interval [CI]: [2.61, 4.42]); NH Asian (2.97 points, 95% CI: [1.71, 4.22]); and NH Black participants (2.79 points, 95% CI: [1.96, 3.63]) participants demonstrated higher levels of endorsement of the VPAI items at baseline.

DISCUSSION: Differences may exist among participants from differing ethnic and racial groups in motivations to undergo biomarker testing in the setting of a preclinical AD trial.

KEYWORDS
disclosure, diversity, preclinical, recruitment

Highlights

- Representative samples in AD clinical trials are vital to result in generalizability.
- We assessed motivations to undergo amyloid imaging in a preclinical AD trial.
- Racial and ethnic minority groups showed higher endorsement of VPAI items.
- Differences were driven by perceived risk, plan/prepare, and curiosity domains.
- Few observations among racial and ethnic groups changed after biomarker disclosure.

1 | BACKGROUND

The prevalence of dementia and mild cognitive impairment (MCI) differ among some racial and ethnic groups.[1] For example, Hispanic and African American individuals are estimated to have higher risk for dementia and MCI, compared to non-Hispanic White individuals.[2] The underlying cause of this difference is unknown and must be addressed. Alzheimer's disease (AD) is the most common cause of MCI and

dementia and differentially impacts minority communities. Research will be key to addressing the burden of AD in these groups, yet these communities remain underrepresented in most studies, particularly trials of new therapies hoped to ameliorate disease burden.[3–5] Underrepresented communities may face additional barriers to participation in AD clinical trials.[6–10] Individuals from minority races and ethnicities, on average, may have less access to medical resources, expert diagnoses, and the locations in which the clinical trials are conducted.[11,12] Despite these challenges, some individuals from these communities overcome the barriers to participate in studies; these individuals may offer key insights into means to improve inclusivity in trials.

Preclinical AD is characterized by detectable AD brain changes in the absence of overt cognitive impairment[13,14] and is anticipated to represent a key stage for intervention with disease-delaying interventions.[15] Essential to ensuring equitable outcomes for preclinical AD trials will be efforts to ensure representation of underserved communities,[16,17] yet these trials have unique barriers to participant recruitment.[18,19] Chief among the unique requirements in preclinical AD trials is the need for participants to undergo biomarker testing to determine their eligibility. While disclosing amyloid biomarker results was not found to have short-term adverse psychological effects in cognitively unimpaired preclinical AD trial participants,[20] biomarker information is sensitive, associated with risk of stigma and discrimination,[21] and few studies have explicitly examined potential differences among racial, ethnic, and cultural groups in interest or willingness to undergo biomarker testing or the personal and sociocultural implications of receiving the results.[22–25]

Analyses of intrapersonal reflections of participants in preclinical AD trials from historically underrepresented backgrounds may provide insights to factors that contributed to participation and/or can highlight key differences between racial and ethnic subgroups. To better understand why diverse enrollees chose to participate in a preclinical AD trial and the associated required amyloid biomarker testing, we analyzed participant responses on the views and perceptions of amyloid imaging (VPAI) questionnaire from the Anti-Amyloid Treatment in Asymptomatic Alzheimer's (A4) Study.[26,27] Though the A4 trial did not recruit a representative sample, it did include a large sample and a more diverse population than most AD trials before it. This created the opportunity to perform exploratory, hypothesis-generating analyses of potential subgroup differences on key outcomes. In this study, we tested the hypothesis that racial and ethnic groups enrolled in the A4 Study differed in VPAI prior to amyloid biomarker testing and that change in VPAI would differ after learning biomarker status.

RESEARCH IN CONTEXT

1. **Systematic review**: To review the literature, the authors utilized traditional methods of PubMed and Google Scholar. This literature suggests that, to increase the recruitment of minority groups, researchers need to invest in communities but also engage in a science of recruitment.[4,17,35]
2. **Interpretation**: The findings of this study indicated differences in the perceived motivations of mutually exclusive racial and ethnic groups to undergo amyloid imaging in the setting of a preclinical Alzheimer's disease (AD) trial. We observed higher motivations to undergo amyloid imaging in a setting of a preclinical AD trial among underrepresented groups compared to non-Hispanic or Latino (NH) White participants.
3. **Future directions**: Future work should test the generalizability of our findings through replication of our study in other trials.

2 | METHODS

2.1 | Data source

The A4 Study was a phase 3 preclinical AD trial conducted—in the United States, Canada, and Japan.[26,28] The A4 Study randomized participants in a 1:1 fashion to receive either solanezumab, an investigational anti-amyloid treatment, or placebo. The study demonstrated that solanezumab did not slow cognitive decline in preclinical AD.[29] Trial exclusion criteria consisted of previous significant health conditions, psychiatric disorders, diagnosis of dementia or MCI and use of AD medications. Participants were required to be within the ages of 65–85 and to have a study partner with whom they had weekly communication.[26] Participants needed to meet criteria for being cognitively unimpaired, including scoring 25–30 on the Mini-Mental State Examination (MMSE), having a Global Clinical Dementia Rating (CDR) score of 0, and a Logical Memory II score 6–18.[5] As a means of restricting our analyses to participants in North America, we limited to individuals who participated in the A4 Study in English or Spanish language.[24]

Otherwise, eligible A4 participants underwent amyloid positron emission tomography (PET) imaging to determine whether they met biomarker criteria for preclinical AD.[13] A protocol defined approach was taken to educate, counsel, ensure informed consent, and disclose biomarker results to participants. The disclosure approach was implemented consistently across sites and has been described previously.[19,20] It included explicit guidance related to psychological screening, pre-biomarker testing education, assurance of informed consent, and in-person delivery of biomarker results. Participants were informed they had either "elevated" or "not elevated" amyloid.[19] Psychological assessments were collected to determine appropriateness of disclosure of participant measurements and as assessments of safety.[20]

The VPAI questionnaire[28] was collected at initial screening (screening visit 1) and immediately after biomarker disclosure (screening visit 3). VPAI items include potential contributing motivators in the decision to undergo amyloid imaging in a preclinical trial. Participants rated nine presented motivations for undergoing amyloid imaging in a preclinical

TABLE 1 VPAI items.

Domain	VPAI Items
Perceived risk	2. To put my mind at ease if I found out I do not have elevated amyloid on my PET scan
(domain score range: 2–10)	7. To confirm the feeling that I might already be developing symptoms of AD dementia
Altruism/contribute to research	4. To be able to participate in anti-amyloid clinical trials (such as the A4 trial)
(domain score range: 2–10)	5. The desire to contribute to research on AD
Plan/prepare	1. To seek information on preventative measures (e.g., change diet, exercise, or other lifestyle changes)
(domain score range: 3–15)	6. To arrange my personal affairs
	8. To prepare my family for my possible illness in the future
Curiosity	3. To know more about my risk of developing AD dementia
(domain score range: 2–10)	9. Curiosity

Note: VPAI items using original VPAI ordering.
Abbreviations: A4, Anti-Amyloid Treatment in Asymptomatic AD Study; AD, Alzheimer's disease; PET, positron emission tomography; VPAI, views and perceptions of amyloid imaging.

trial using 5-point Likert scales (1, "Not at all"; 5, "Extremely"), with a total score ranging from 9 to 45. An additional free response question was excluded for the purpose of these analyses.

We grouped the VPAI items into four domains, as done previously.[28] The four constructs were perceived risk (items 2 and 7; domain score range: 2–10), altruism/contribute to research (items 4 and 5; domain score range: 2–10), plan/prepare (items 1, 6, and 8; domain score range: 3–15) and curiosity (items 3 and 9; domain score range: 2–10).[28] The domains were based on scientific and logical/natural groupings of questions.[28] The range for the domain scores were dependent on the number of questions within the grouping. Table 1 lists VPAI items and illustrates domain specific groupings.

2.2 | Data analyses

Based on self-reported race and ethnicity that were collected separately, we assigned participants to five mutually exclusive groups including a Hispanic or Latino (Hispanic/Latino) (HL) group, a NH Asian group, a NH Black group, a NH White group, and a NH Other (Other) group. Relatively few individuals identified as American Indian or Alaskan Native (n = 10), Native Hawaiian or other Pacific Islander (n = 3), more than one race (n = 38) or did not report a race or did not report an ethnicity (n = 47). These individuals were placed into the NH Other group. For cases of re-screening, we utilized patients' most recent data for analysis and previous records for imputation, if applicable. Study partner type (spouse, adult child or child-in-law, friend or companion, other) was defined using study partner data collected at screening. We created a dichotomized family history of AD variable where participants who had one or more biological parents, full sibling, or half sibling with AD diagnoses were classified as having a family history.

In our first analysis, we sought to assess whether VPAI total scores differed among the racial and ethnic groups prior to biomarker testing and disclosure using a linear regression model. We utilized complete cases of the VPAI at screening visit 1 (n = 5472), excluding n = 18 individuals due to missingness of VPAI components. We conducted a sensitivity analysis in which we imputed scores for individuals with missing questions and found that point estimates were consistent with the estimates from our complete case analysis. The primary predictor of interest was mutually exclusive racial and ethnic groups. We adjusted the model for a priori specified adjustment covariates, including participant age, sex, education, family history of AD, and study partner type. Adjustment covariates were chosen a priori, as we hypothesized that the covariates would have distributional imbalances by race and ethnicity groups, while not explicitly in the mediating pathway, and associated to VPAI score. We intentionally set the reference group as NH White, to compare the motivations of groups underrepresented in preclinical AD trials to those who are overrepresented, with the goal of understanding potential group differences and instructing future efforts to improve representation of these communities. Education was treated as a continuous variable in our primary analysis; however, we also conducted the analysis treating education as a categorical covariate ($\leq$ 12 years, $>$ 12 and $\leq$ 16 years, and $>$ 16 years) to aid in interpretation and assess potential non-linearities. Study partner types were grouped into four categories: spouse, adult child or child in law, friend or companion, and other (consisting of other relative (n = 288), paid caregiver (n = 2), or other (n = 111)). Family history of AD was a binary indicator. Key secondary analyses examined domain scores using linear models with the same predictors of interest and adjustment covariates. For all models, inference utilized the Huber-White robust variance estimator[30] to guard against potential violations of the homoscedasticity assumption in model residuals.

We next assessed the change in VPAI total score after disclosure of amyloid results. We stratified our linear model by elevated versus not elevated amyloid result. The sample for the post-disclosure analysis consisted of participants with complete VPAI data pre- and post-disclosure (n = 4254), with 32 individuals excluded for missingness. We used a linear regression model, regressing the change in the total VPAI score after disclosure on the indicators of racial and ethnic groups. The linear model had similar adjustment covariates to the pre-disclosure model apart from also adjusting for baseline VPAI score. Key

TABLE 2 Characteristics/demographics of pre-disclosure analysis participants.

Parameter	Hispanic/Latino *n* = 205	NH Asian *n* = 94	NH Black *n* = 234	NH White *n* = 4841	Other *n* = 98
Sex					
Male	84 (41.0%)	40 (42.6%)	64 (27.4%)	1985 (41.0%)	34 (34.7%)
Female	121 (59.0%)	54 (57.4%)	170 (72.6%)	2856 (59.0%)	64 (65.3%)
Study partner type					
Spouse	104 (50.7%)	56 (59.6%)	75 (32.1%)	3021 (62.4%)	62 (63.3%)
Adult child or child in law	43 (21.0%)	19 (20.2%)	40 (17.1%)	558 (11.5%)	6 (6.1%)
Friend or companion	38 (18.5%)	14 (14.9%)	71 (30.3%)	902 (18.6%)	23 (23.5%)
Other	19 (9.3%)	5 (5.3%)	40 (17.1%)	333 (6.9%)	4 (4.1%)
Missing	1 (0.5%)	0 (0.0%)	8 (3.4%)	27 (0.6%)	3 (3.1%)
Family history of AD					
No	123 (60.0%)	66 (70.2%)	143 (61.1%)	2739 (56.6%)	56 (57.1%)
Yes	77 (37.6%)	22 (23.4%)	79 (33.8%)	2025 (41.8%)	37 (37.8%)
Missing	5 (2.4%)	6 (6.4%)	12 (5.1%)	77 (1.6%)	5 (5.1%)
Education level					
≤ 12 years	25 (12.2%)	7 (7.4%)	39 (16.7%)	466 (9.6%)	13 (13.3%)
> 12 and ≤ 16	116 (56.6%)	36 (38.3%)	108 (46.2%)	2019 (41.7%)	37 (37.8%)
> 16	63 (30.7%)	51 (54.3%)	86 (36.8%)	2348 (48.5%)	48 (49.0%)
Missing	1 (0.5%)	0 (0.0%)	1 (0.4%)	8 (0.2%)	0 (0.0%)
Education (numeric)	15.77 (2.85)	17.15 (2.76)	15.78 (3.01)	16.63 (2.85)	16.56 (3.17)
Age	71.76 (4.76)	71.78 (5.02)	70.83 (4.67)	71.42 (4.79)	71.55 (4.72)
VPAI total score	34.58 (6.46)	33.43 (5.92)	34.19 (6.22)	30.77 (6.57)	32.67 (7.93)

Note: Continuous variables are summarized by mean (standard deviation) and categorial variables are summarized by frequency (proportion).
Abbreviations: AD, Alzheimer's disease; NH, non-Hispanic or Latino; VPAI, views and perceptions of amyloid imaging.

secondary analyses included assessing the change in domain scores using stratified linear models. All inference utilized the Huber–White robust variance estimator. To address multiplicity, we used a Bonferroni–Holm correction.[31] Model diagnostics were performed using residual versus fitted value plots, residual normal QQ plots, delta betas versus observation number plots, and delta betas versus leverage plots. We did not observe strong evidence of inadequate or influential points. Data were analyzed using R version 4.1.1.[32]

3 | RESULTS

3.1 | Study participants

Table 2 describes the demographics of the study participants at baseline, before disclosure of amyloid imaging results. There was a majority of female participants overall, and particularly among the NH Black group. The NH Black group had the lowest proportion of participants enrolled with a spouse study partner and the highest proportion enrolled with a friend or companion. The NH Asian group had the highest mean level of education and the lowest frequency of AD family history.

3.2 | Pre-disclosure of amyloid imaging results

Table 3 describes the differences among the groups in pre-disclosure total VPAI scores. Hispanic/Latino, NH Asian, and NH Black participants scored higher, on average, compared to NH White participants after adjustment (Hispanic/Latino: 3.52 points, 95% confidence interval [CI]: [2.61, 4.42], $p < 0.001$; NH Asian: 2.97 points, 95% CI: [1.71, 4.22], $p < 0.001$; NH Black: 2.79 points, 95% CI: [1.96, 3.63], $p < 0.001$). A multivariate Wald test confirmed that the difference among the racial and ethnic groups was statistically significant ($p < 0.001$).

Figure 1 illustrates the domain-specific scores pre-disclosure of amyloid imaging results. Hispanic/Latino, NH Asian, and NH Black participants all scored higher, on average, in the perceived risk domain, compared to NH White participants (Hispanic/Latino: 1.24 points, 95% CI: [0.94, 1.55], $p < 0.001$; NH Asian: 1.14 points, 95% CI: [0.71, 1.58], $p < 0.001$; NH Black: 0.97 points, 95% CI: [0.68, 1.25], $p < 0.001$). Participants in each of these groups also scored higher than NH White participants, on average, in the plan/prepare domain-specific score (Hispanic/Latino: 1.63 points, 95% CI: [1.20, 2.05], $p < 0.001$; NH Asian: 1.59 points, 95% CI [0.98, 2.20], $p < 0.001$; NH Black: 1.39 points, 95% CI [0.98, 1.79], $p < 0.001$). Hispanic/Latino and NH Black participants scored higher, on average, compared to NH White participants in the

TABLE 3 Regression summary table of pre-disclosure total score.

Covariate	Estimate	95% CI	*p*-value
Race and ethnicity			
NH White	Reference		
Hispanic/Latino	3.52	(2.61, 4.42)	<0.001
NH Asian	2.97	(1.71, 4.22)	<0.001
NH Black	2.79	(1.96, 3.63)	<0.001
Other	1.45	(−0.12, 3.03)	0.070
Age (per 10 years)	0.32	(−0.06, 0.70)	0.099
Sex			
Female versus male	1.27	(0.89, 1.64)	<0.001
Family history of AD			
Yes versus no	0.74	(0.38, 1.09)	<0.001
Education			
Education (numeric)	−0.28	(−0.34, −0.22)	<0.001
≤ 12 years	Reference		
> 12 and ≤ 16	−1.08	(−1.71, −0.45)	0.001
> 16 years	−2.33	(−2.95, −1.71)	<0.001
Study partner type			
Spouse	Reference		
Adult child or child in law	0.14	(−0.41, 0.69)	0.618
Friend or companion	0.34	(−0.15, 0.82)	0.172
Other	0.43	(−0.27, 1.13)	0.227

Note: Estimated regression estimates, 95% confidence intervals, and *p*-values of pre-disclosure primary analysis quantifying the associations between mutually exclusive race and ethnicity groups and total VPAI score. Abbreviations: AD, Alzheimer's disease; CI, confidence interval; NH, non-Hispanic or Latino; VPAI, views and perceptions of amyloid imaging.

curiosity domain-specific score (Hispanic/Latino: 0.50 points, 95% CI: [0.27, 0.73], $p < 0.001$; NH Black: 0.63 points, 95% CI: [0.41, 0.84], $p < 0.001$). No differences among the groups were observed for the altruism domain. The appendix Figure A.1 contains analysis results of standardized domain-specific scores pre-disclosure of amyloid imaging results.

3.3 | Post-disclosure of amyloid imaging results

Table 4 describes the change in total VPAI score after biomarker disclosure. We observed overall significant effects of race and ethnicity in the not elevated ($p = 0.005$) but not the elevated amyloid group ($p = 0.713$). Among those with a not elevated amyloid result, NH Asian participants were estimated to have a mean change 1.37 points greater than that of NH White participants (95% CI: [0.08, 2.66], $p = 0.038$), and NH Black participants were estimated to have a mean change 1.21 points greater than NH White participants (95% CI: [0.22, 2.20], $p = 0.016$). Although the corresponding *p*-values for these pairwise comparisons were 0.038 and 0.016, respectively, they were not significant after Bonferroni–Holm correction with an overall familywise type I error at 0.05. We found no significant evidence of a differential effect of race and ethnicity on the change in total score by amyloid status ($p = 0.811$ for the test of interaction).

Figure 2 describes the key secondary outcomes for the change in domain specific VPAI scores after biomarker disclosure. Among participants with elevated amyloid, we found no significant differences among the groups in the average changes in domain scores. Among participants with not elevated amyloid, compared to NH White participants, NH Black participants were estimated to have a mean change 0.45 points greater in the curiosity domain (95% CI [0.19, 0.72], $p = 0.001$). This result remained statistically significant after Bonferroni-Holm correction at target type 1 error level of 0.05. The appendix Figure A.2 contains analysis results of standardized change in domain-specific scores post-disclosure of amyloid imaging results.

4 | DISCUSSION

In this study, we examined differences among racial and ethnic groups in perceived motivations to undergo amyloid imaging in the setting of a preclinical AD trial. Among individuals enrolled in a preclinical AD trial, we found that Hispanic/Latino, NH Asian, and NH Black participants scored VPAI items higher than did NH White participants after adjustment for covariates. These differences appeared to be driven by specific domains of perceived risk, plan/prepare, and curiosity, whereas the groups were similar in their altruistic motivations. After biomarker disclosure, we found an overall association between race and ethnicity groups and change in VPAI score only in those with a not elevated result. Pairwise comparisons across race and ethnicity groups were, however, not statistically significant after multiple comparison adjustment.

Inclusive recruitment into AD clinical trials is critical for the generalizability of results, exploration of heterogeneity in treatment effects,[5,33] and to ensuring trust and willingness to take approved medications.[17] There is conflicting evidence regarding whether individuals of minority races and ethnicities are as willing as NH White individuals to engage in biomedical research.[8,34–39] It has been observed, however, that at least some underrepresented groups experience greater barriers that must be overcome in order to participate in AD clinical trials.[6–10] Preclinical AD trials require participants to undergo amyloid biomarker testing to assess eligibility and ensure appropriateness for treatment.[40] Hispanic/Latino, NH Asian, and NH Black participants who enrolled in the A4 Study scored VPAI items higher than their NH White counterparts, perhaps indicating a higher motivation to participate in the A4 trial and the elements required to do so.

Figure 1 provides insight into the distribution of domain-specific scores by racial and ethnic groups at baseline and contextualizes the findings from our key secondary outcomes. The score distributions illustrate that altruism and curiosity domains drove VPAI scores, regardless of race and ethnicity. From Figure 1, we also infer that more frequent agreement or strong agreement occurred in domain-specific scores of perceived risks, plan/prepare, and curiosity among

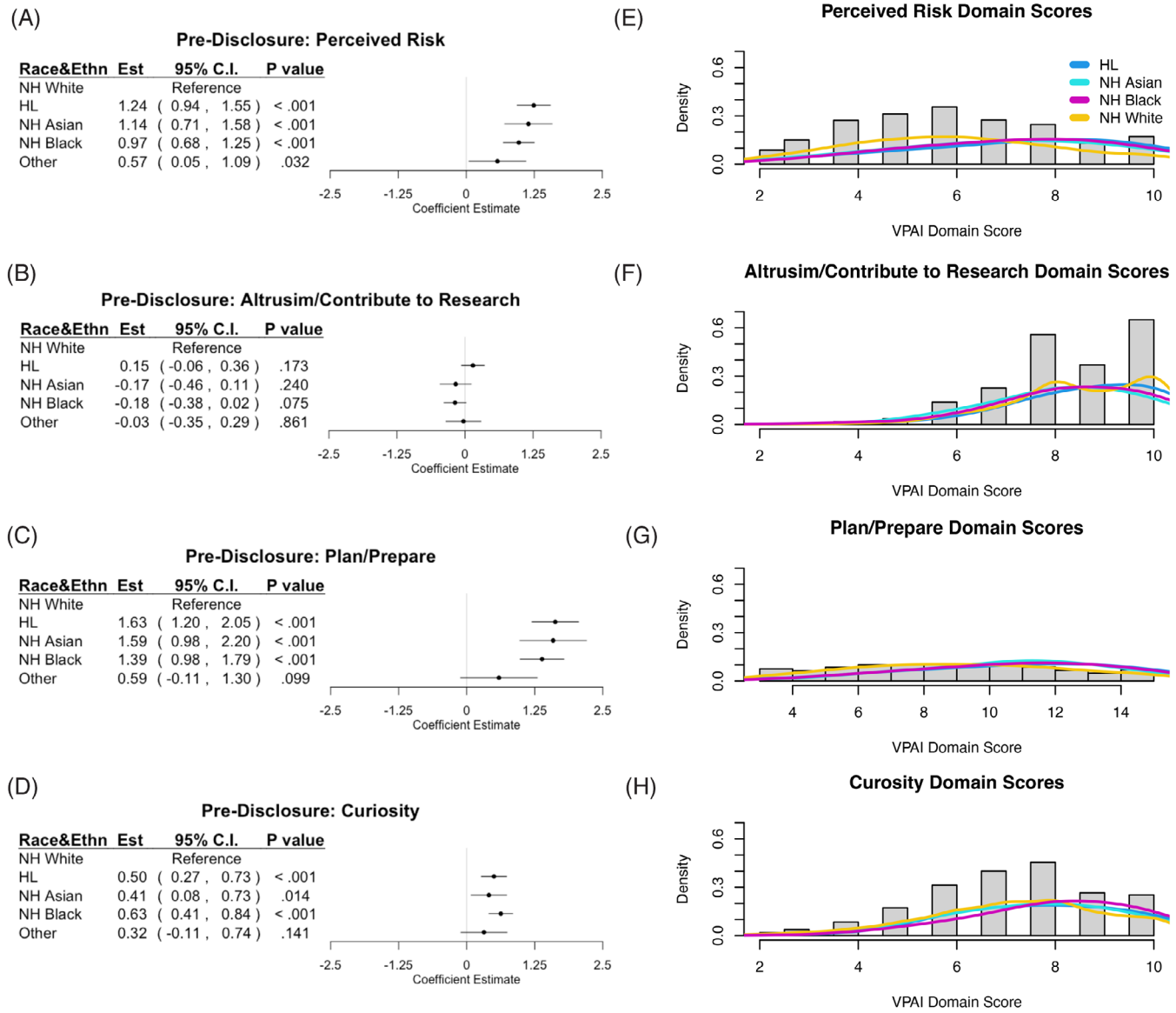

FIGURE 1 Pre-disclosure mean difference and distributions. Estimated regression estimates of pre-disclosure key secondary outcomes (left panels) qualifying the associations between mutually exclusive race and ethnicity groups and domain-specific scores of perceived risk (A), altruism/contribute to research (B), plan and prepare (C), and curiosity (D). The estimate is illustrated by a point which represents the average domain score difference of the mutually exclusive race and ethnicity groups relative to the reference group (NH White participants) and its corresponding uncertainty is illustrated by the horizontal lines which represent the 95% confidence interval. Additionally, distributions of domain scores for perceived risk (E), altruism/contribute to research (F), plan and prepare (G), and curiosity (H) with fitted density curves corresponding to mutually exclusive race and ethnicity groups (right panels). HL, Hispanic or Latino; NH, non-Hispanic or Latino.

Hispanic/Latino, NH Asian, and NH Black subgroups, and led to differences from the more neutral NH White group. The subtle differences led to the notable relationships of race and ethnicity groups and VPAI total and domain-specific scores. Though results come from individuals who were already enrolled in a study, they may instruct future recruitment efforts for preclinical AD trials, and particularly efforts to recruit members of underrepresented communities. Specifically, the data suggest that recruitment efforts that emphasize altruism but also the opportunity to gain personal information that could be valuable to planning and preparing for the future may be effective in underrepresented communities.

Interestingly, these findings may contrast previous literature in which Black and Hispanic adults were deemed more likely than NH White adults to view AD cognitive decline as an unavoidable and normal aspect of aging.[41–43] These differences could have several explanations. It is possible that community awareness and understanding of AD risk are changing with time. AD is prominent in the news media, including stories about risk among diverse communities. In fact, specific efforts have been undertaken to increase understanding of AD and other causes of dementia in diverse communities.[44] Alternatively, though not mutually exclusive, the current study was limited to those enrolled in an investigational drug trial, a potentially uniquely

TABLE 4 Regression summary table of change in post-disclosure total score.

	Elevated amyloid ($n = 1281$)			Not elevated amyloid ($n = 2973$)		
Covariate	**Estimate**	**95% CI**	***p*-value**	**Estimate**	**95% CI**	***p*-value**
Race and ethnicity**						
NH White	Reference			Reference		
Hispanic/Latino	0.98	(−1.09, 3.06)	0.353	0.46	(−0.76, 1.68)	0.458
NH Asian	0.13	(−2.44, 2.71)	0.921	1.37	(0.08, 2.66)	0.038
NH Black	0.92	(−0.91, 2.75)	0.324	1.21	(0.22, 2.20)	0.016
Other	0.68	(−1.57, 2.92)	0.555	2.01	(0.33, 3.69)	0.019
Age	−0.72	(−1.34, −0.10)	0.024	−0.26	(−0.72, 0.20)	0.269
Sex						
Female versus male	0.49	(−0.10, 1.08)	0.106	0.73	(0.33, 1.13)	<0.001
Family history of AD						
Yes versus no	−0.42	(−0.99, 0.14)	0.141	0.58	(0.20, 0.97)	0.003
Education						
Education (numeric)	−0.12	(−0.22, −0.02)	0.023	−0.10	(−0.17, −0.03)	0.004
≤ 12 years	Reference			Reference		
> 12 and ≤ 16	−0.69	(−1.72, 0.34)	0.189	−0.04	(−0.73, 0.64)	0.908
> 16 years	−0.83	(−1.85, 0.20)	0.115	−0.53	(−1.20, 0.14)	0.124
Study partner type						
Spouse	Reference			Reference		
Adult child or child in law	0.01	(−0.93, 0.95)	0.983	0.50	(−0.10, 1.11)	0.103
Friend or companion	−0.41	(−1.17, 0.35)	0.294	−0.19	(−0.68, 0.30)	0.446
Other	0.75	(−0.53, 2.02)	0.252	−0.35	(−1.16, 0.46)	0.394
Previous score	−0.38	(−0.43, −0.33)	<0.001	−0.37	(−0.40, −0.34)	<0.001

Abbreviations: AD, Alzheimer's disease; CI, confidence interval; NH, non-Hispanic or Latino; VPAI, views and perceptions of amyloid imaging.
**Multivariate Wald test for test of interaction between mutually exclusive race and ethnicity groups and amyloid status was not significant ($p = 0.811$).
Estimated regression estimates, 95% confidence intervals, and *p*-values of post-disclosure primary analysis quantifying the associations between mutually exclusive race and ethnicity groups and the change in total VPAI score post-disclosure to pre-disclosure of amyloid imaging results (screening visit 3 total score—screening visit 1 total score).

informed and motivated population compared more broadly to the larger community.

We also found an overall association between racial and ethnic groups in our analyses of changes in VPAI score after disclosure, though these differences were observed only in the participants receiving a not-elevated amyloid biomarker result. This may suggest that the impact of learning an elevated amyloid result in a preclinical trial may be similar among racial and ethnic groups,[24] and less subject to cultural differences. Although pairwise comparisons across race and ethnicity groups were not statistically significant after multiple comparison adjustment, we observed that, among participants with not elevated amyloid results, NH Asian and NH Black participants demonstrated greater changes in total score than did NH White participants. When looking at the construct-specific change scores, it appeared that these greater changes resulted from trends observed in the perceived risk construct in both NH Asian and NH Black subgroups and the curiosity construct in NH Black subpopulation. Hence, a conjecture can be made that this result could be related to greater relief experienced by these participants compared to their NH White counterparts; however, this exploratory hypothesis will require further research.

Our study has important limitations. First, our analysis utilized data from participants in the A4 study, which was among the first ever preclinical AD trials. This inherently limits the implications to future recruitment efforts, which need to increase representation of individuals otherwise missing from trials. To the extent that trial awareness is a key barrier; however, these results may instruct messaging in broader recruitment campaigns. It has been demonstrated that the sources of participants in the A4 Study varied among diverse groups.[5] This further limits generalizability, not only to other trials, but potentially differentially among diverse groups. The VPAI questionnaire examines reasons to undergo amyloid imaging in the setting of a preclinical AD trial, and not specifically to either the choice to undergo amyloid imaging or to participate in a trial. We believe; however, that these results are relevant to gain insights into future preclinical AD trials that require amyloid imaging, such as the AHEAD 3–45 study.[45] Whether and how the results will be relevant to trials that incorporate cerebrospinal fluid

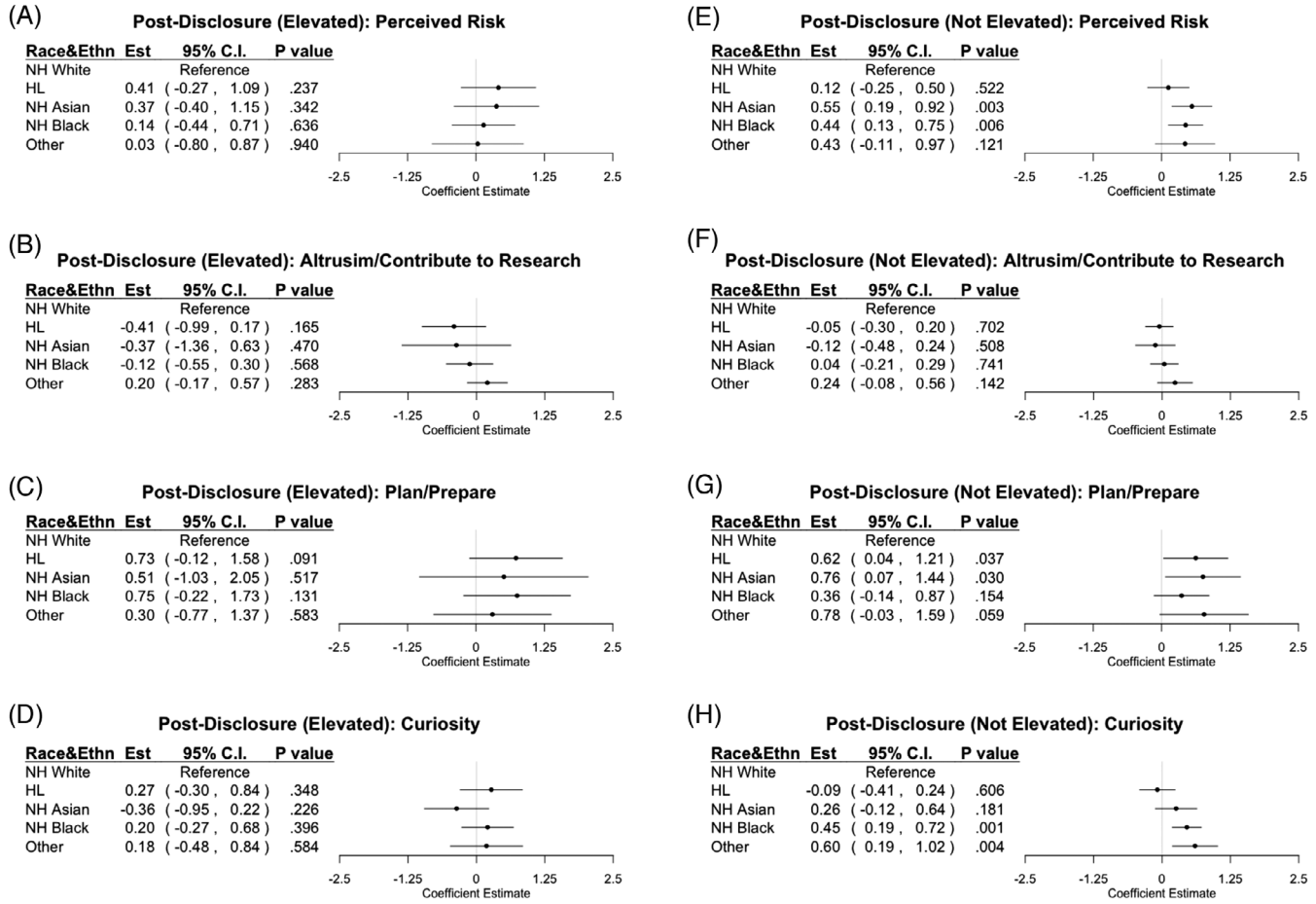

FIGURE 2 Post-disclosure change in score. Estimated regression estimates of post-disclosure key secondary outcomes qualifying the associations between mutually exclusive race and ethnicity groups and change of domain-specific scores (visit 3 domain score–visit 1 domain score) of perceived risk (A, E), altruism/contribute to research (B, F), plan and prepare (C, G), and curiosity (D, H) stratified by biomarker result. The estimate is illustrated by the point which represents the estimated difference in the change of domain score of the mutually exclusive race and ethnicity groups relative to the reference group (NH White participants), and its corresponding uncertainty is illustrated by the horizontal lines which represent the 95% confidence interval. HL, Hispanic or Latino; NH, non-Hispanic or Latino.

or blood biomarkers is unknown.[46] To our knowledge, few individuals dropped out of the trial before or after biomarker testing but prior to biomarker disclosure. Nevertheless, it would have been valuable to explore potential differences among racial and ethnic groups in their decisions to continue or withdraw at varying stages of the disclosure processes, had such data been available. Additionally, the differential exclusion rates based on psychological assessments among racial and ethnic groups could produce a bias in post-disclosure results as we only have data on individuals who underwent amyloid imaging. Last, as with any observational study, there is the potential for unmeasured covariates that are imbalanced by racial and ethnic groups and that also impact VPAI scores. These include measures of trust, past healthcare experiences, socioeconomic status, and acculturation, to name a few. Despite this, we were able to adjust for key demographic and disease-related factors when comparing groups.

Future work should attempt to replicate our results in different AD clinical trial samples. It would be valuable to know VPAI score differences that ultimately lead to trial recruitment and retention decisions. Applications of recruitment methods using the insights from this analysis could also be developed and rigorously tested for efficacy.[7] Prospective studies aiming to better understand biomarker disclosure outside of the trial setting remain needed. Finally, for each of these issues, assessing additional subcategories of races and ethnicities (e.g., specific nationalities or cultural groups, immigration status, spoken language) would be of interest and value.[47]

In conclusion, we found differences in endorsement of presented motivations to undergo amyloid imaging among racial and ethnic groups in a preclinical AD trial. This may inform targeted recruitment strategies for diverse populations in future trials. Post-disclosure changes in VPAI results indicated that there were no major differences among the racial and ethnic groups after learning biomarker results.

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CONFLICT OF INTEREST STATEMENT

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CONSENT STATEMENT

All human subjects provided informed consent into the A4 study.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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