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Referral Sources Across Racial and Ethnic Groups at Alzheimer's Disease Research Centers

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Abstract.
Background: Despite the need to increase engagement of underrepresented groups (URG) in Alzheimer's disease and related dementias (ADRD) studies, enrollment remains low.
Objective: Compare referral sources across racial and ethnic groups among participants enrolled in ADRC studies.
Methods: Data for this cross-sectional secondary analysis were extracted from the National Alzheimer's Coordinating Center Uniform Data Set. We performed mixed effects logistic regression models using generalized estimating equations for professional referral versus non-professional referral by racial and ethnic group, adjusted for age, gender, education, visit year, and Clinical Dementia Rating scale (CDR) with a random effect for study site.
Results: Included in the analysis were 48,330 participants across 46 ADRCs (mean [SD] age, 71.3 [10.5] years; 20,767 female [57%]; 4,138 Hispanic [8.6%]; 1,392 non-Hispanic Asian [2.9%]; 6,766 non-Hispanic Black [14%] individuals; and 676 individuals [1.4%] of other races. Non-Hispanic Black and Asian participants had lower odds of being referred by a professional contact compared to non-Hispanic White participants (Black: adjusted OR = 0.61, 95% CI = 0.44–0.86, $p = 0.005$; Asian: adjusted OR = 0.65, 95% CI, $p = 0.004$). In participants who had completed an MRI, there was no significant difference in referral source across ethnic and racial groups.

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Conclusions: Further studies are needed to better understand the systemic and structural factors that contribute to differences in referral sources and disparities in recruitment of URG into ADRD studies.

Keywords: Alzheimer's disease, diversity, language, race and ethnicity, recruitment

INTRODUCTION

It is estimated that 6.9 million Americans are living with Alzheimer's disease and related dementias (ADRD).[1] In the United States of America (US), higher prevalence and incidence of dementia have been observed in underrepresented groups (URG) compared to individuals who identify as non-Hispanic White.[2–4] According to the National Institute of Health, URG are a subgroup of the population whose representation is disproportionately low relative to their numbers in the general population.[5] In the context of clinical research, this may include people with disabilities, people from disadvantaged backgrounds, or people from minoritized racial and ethnic groups. The population growth of older adults from minoritized groups, as defined by the US Census Bureau as racial and ethnic groups other than non-Hispanic White, is expected to grow from approximately 20% to 45% of the US population over the next few decades, outpacing the growth of nonminority populations.[6] Given the expected growth in ADRD burden, particularly in minoritized populations, enrollment of participants from URG to ADRD studies is critical in understanding why these racial and ethnic differences in disease prevalence and incidence exist and in reducing disease burden.

Despite the growing need, URG participation in clinical research studies remains disproportionately low. Over 94% of participants in ADRD drug trials and 87% of participants in ADRD neuroimaging (e.g., magnetic resonance imaging, computerized tomography, single photon emission computed tomography, positron emission tomography) studies identify as non-Hispanic White.[7,8] The recruitment of URG into studies with neuroimaging is particularly pertinent to prevention studies, where neuroimaging is commonly required for early-stage biomarker characterization and clinical drug trials. The under-recruitment of URG has significant implications, including the generalizability of findings on AD processes, diagnostic cutoffs, and effectiveness of AD treatments. Recruitment into trials focused on the prevention of ADRD is especially needed to reduce the impact of disparities in dementia risk.

Race is a socially constructed category and proxy for structural and social factors related to dementia that need to be considered when studying ADRD. Multiple reasons for the disparities in recruitment have been suggested, including eligibility excluding individuals with psychiatric illness, cardiovascular disease, cerebrovascular disease, specific cognitive screening test scores, and requiring caregiver attendance, which may disproportionately exclude racially and ethnically diverse groups.[7,9] While successful strategies for enhancing URG recruitment have been described using recruitment from clinics with high populations of interest, community organizations, employment of bilingual staff, and providing translated recruitment materials,[10] major barriers remain due to the low quantity and quality of evidence for best practices in URG recruitment and retention.[10,11]

To our knowledge, studies directly examining differences in referral source by racial and ethnic groups have been mostly limited to patterns observed in individual studies.[12–14] A secondary analysis of the Preventing Alzheimer's with Cognitive Training trial found that White participants were more likely to be recruited via newspaper, while participants of other races were more likely to be recruited by mailed postcards, and Hispanic participants were more likely to be recruited by friends or family compared to non-Hispanic participants.[12] In the Anti-Amyloid in Asymptomatic Alzheimer's Disease Study, local site efforts and local earned media, as opposed to centralized recruitment efforts, was found to be more effective in the recruitment of non-Hispanic Black, non-Hispanic Asian and Hispanic participants.[13] A retrospective study of newly enrolled participants at the Knight ADRC found that social media recruitment yielded mainly non-Hispanic White enrollees, while speaking engagements, word-of-mouth, and traditional print media were successful for both African American and Non-Hispanic White enrollees.[14] While these analyses were limited to individual ADRCs or studies, they point to differences in recruitment preferences across racial and ethnic groups. One study included non-Hispanic Black and White participants from 37 US-based

ADRCs observed that non-Hispanic Black participants were less likely to be recruited by a health professional,[15] but excluded participants of other races and ethnicities.

To better understand potential reasons why individuals from URGs participate at lower rates, we completed a secondary analysis of the National Alzheimer's Coordinating Center (NACC) Uniform Data Set (UDS). Specifically, our aims were to compare the source of referral for participants enrolled in Alzheimer's disease research center (ADRC) studies across racial and ethnic groups (1) overall; (2) in individuals with early-stage ADRD,[16] to reflect the target population of most ongoing observational and clinical trials;[17] and (3) in individuals who have completed magnetic resonance imaging (MRI). While MRI completion is not equivalent to full biomarker characterization, it was used as a proxy for participation in procedures needed for biomarker characterization (e.g. cerebrospinal fluid or positron emission tomography amyloid and tau).

METHODS

National Alzheimer's Coordinating Center Uniform Data Set

Data for this secondary analysis were obtained from the NACC UDS Version 3.0.[18] The NACC database is comprised of standardized research data collected from National Institute of Aging-funded ADRCs across the United States and reflects the total enrollment of ADRCs since 2005.

Data collection was approved by the institutional review board at each participating Alzheimer's Disease Research Center. Written informed consent was obtained from all participants and co-participants.

Recruitment and participant evaluation are described in detail elsewhere.[18] Briefly, participants were enrolled by each ADRC according to their own protocol and criteria. Data for the UDS were collected using standardized evaluation forms. Participants across the cognitive spectrum were included in the NACC UDS, including those with normal cognition, mild cognitive impairment (MCI), and dementia.

Participant selection

These secondary analyses considered all participants enrolled in the NACC UDS between June 2005 and May 2023 with data available for variables related to race and ethnicity.

Demographic, cognitive and clinical variables

Demographic, cognitive, and clinical variable data were extracted from participants' initial visit records. Race (categorized in NACC UDS as White, Black or African American, Asian, American Indian or Alaska Native, Native Hawaiian or Other Pacific Islander, multiracial, or unknown), ethnicity (Hispanic or Latino, non-Hispanic) and primary language were determined by self-report. Five racial ethnic groups were created: non-Hispanic White, Hispanic, non-Hispanic Black, non-Hispanic Asian and Other race. Participants who were classified as Hispanic were included in the Hispanic group, regardless of their race. Participants who were classified as multiracial and selected Black or African-American were included as non-Hispanic Black. Next, non-Hispanic Asians were included similarly. Other race included American Indian or Alaska Native, Native Hawaiian or Other Pacific Islander, and remaining multi-racial participants who did not also identify as non-Hispanic Black or non-Hispanic Asian.

The principal referral source was based on participant self-report. Referral sources were categorized in the NACC UDS as 'professional', 'non-professional', 'other', and 'unknown' referral. Further details on the source of referral beyond these categories were not available in the dataset. Referrals from clinicians, nurses, doctors, other health care providers, or other staff (ADRC and non-ADRC) were categorized as 'professional' referrals, while referrals from self, family or friends were categorized as 'non-professional' referrals. Self-referral included participants who directly contacted the ADRC requesting to join a study. The category of 'other' referrals was comprised of individuals referred through ADRC solicitation, non-ADRC study, population sample, or a non-ADRC media appeal.

Criteria for cognitive status are detailed elsewhere.[18,19] The Cognitive Dementia Rating scale (CDR)[20] score is derived from clinician rating of cognition and function, where a score of 0, 0.5, 1, 2, and 3 corresponds to no impairment, mild cognitive impairment, mild dementia, moderate dementia, and severe dementia respectively. A subgroup of individuals with MCI or dementia and CDR 0.5 or 1 was created to reflect the target population of most current early-stage ADRD observational and clinical trials.[17]

Magnetic resonance imaging (MRI) was available for a subset of participants. MRI data were voluntarily submitted by ADRCs, thus may not reflect the full scope of MRI availability. Participants were considered to have completed an MRI if they had at least one MRI in the database at any time point.

Statistical analysis

One-way analysis of variance (ANOVAs) and Fisher's exact tests were used to compare demographic and clinical variables across racial and ethnic groups. Additional Fisher's exact tests were used to compare each racial and ethnic group to non-Hispanic white participants.

Mixed effects logistic regression models using generalized estimating equations (GEE) were used to examine the association of racial and ethnic group and professional versus non-professional referral. Non-Hispanic White was used as the reference group. This association was examined across the (1) entire sample, (2) in individuals with MCI or dementia and global CDR 0.5 or 1 at baseline, (3) individuals who had completed magnetic resonance imaging (MRI) at any time point, and (4) individuals who had MCI or dementia and global CDR 0.5 or 1 at baseline and had completed MRI at any time point. The analyses were adjusted for age, gender, education, visit year, and CDR score as a categorical variable with a random effect to adjust for study site. Mixed effects logistic regression models using GEE and a study site random effect were used to compare the percentages of participants from study sites with MRI and those without MRI for each racial and ethnic group.

Because a larger proportion of Hispanic and non-Hispanic Asian participants reported a primary language outside of English compared to non-Hispanic White and Black participants, *post-hoc* exploratory analysis examining the association between primary language and referral source in Hispanic and Asian participants were completed using similar models. The mixed effects logistic regression model using GEE was repeated in these two subgroups with language as the main independent variable. In Hispanic participants, comparisons were made between those whose primary language was English versus Spanish. In non-Hispanic Asian participants, comparisons were made between those whose primary language was English versus language other than English.

Statistical analyses were completed using SAS version 9.4. Significance was set at $alpha = 0.05$.

RESULTS

Participant characteristics

These analyses included data from 48,330 participants across 46 ADRCs (Table 1), after excluding 275 participants who did not have race and ethnicity documented. It included 4,138 (8.6%) Hispanic, 1,392 (2.9%) non-Hispanic Asian, 6,766 (14%) non-Hispanic Black, 35,358 (73.2%) non-Hispanic White participants, and 676 (1.4%) participants of other races. 20,412 (42.2%) were referred by a professional contact, 15,380 (31.8%) by a non-professional contact, 11,389 (23.6%) by an 'other' referral source, and 1,149 (2.4%) by an unknown referral source. Due to the heterogeneity of the 'other' referrals group, which included referrals made from ADRC solicitation, non-ADRC study, population sample, or a non-ADRC media appeal, it was excluded from subsequent analyses. The breakdown of racial and ethnic participants across the excluded referral groups ('other' and 'unknown') are shown in Table 1.

MRI data were available in 7,582 (15.7%) participants (Table 1). Non-Hispanic Black (13.6%) and Asian (11.3%) participants were less likely to have an MRI scan available compared to non-Hispanic White participants (15.9%; both $p < 0.0001$). More Hispanic participants (18.9%) had at least one MRI available compared to non-Hispanic White participants ($p < 0.0001$). There was no difference in MRI availability between non-Hispanic White participants and participants in the 'other race' group ($p = 0.0890$). Sites that submitted MRI data had a significantly lower percentage of participants of other races ($p = 0.0398$), but a greater percentage of non-Hispanic Asian participants than sites that did not submit MRI data ($p = 0.0214$; Supplementary Table 1).

Professional versus non-professional referral

When all participants were considered, non-Hispanic Black and non-Hispanic Asian participants had significantly lower odds of being referred by a professional contact compared to non-Hispanic White participants (Table 2). This pattern remained when considering only participants who had a diagnosis of MCI or dementia and a global CDR of 0.5 or 1 (Table 2). In participants who had completed an MRI, there was no significant difference between professional and non-professional referrals across ethnic and racial groups, both when all cognitive statuses

Table 1
Participants demographics stratified by race and ethnicity

	Hispanic (n = 4,138)		Non-Hispanic Asian (n = 1,392)		Non-Hispanic Black (n-6,766)		Non-Hispanic White (n = 35,358)		Other race (n = 676)		
Characteristics	N	Statistics	N	Statistics	N	Statistics	N	Statistics	N	Statistics	Overall p
Age (y), mean ± sd	4,138	70.3 ± 10.3	1,392	69.8 ± 10.5	6,766	71.5 ± 9.1	35,358	71.5 ± 10.7	676	67.9 ± 10.5	<0.0001
Female, *n* (%)	4,138	2,727 (65.9%)	1,392	824 (59.2%)	6,766	4,862 (71.9%)	35,358	18,744 (53.0%)	676	406 (60.1%)	<0.0001
Years of Education, mean ± sd	4,138	12.7 ± 10.8	1,392	17.0 ± 10.0	6,766	14.6 ± 6.9	35,358	16.4 ± 7.4	676	14.3 ± 5.6	<0.0001
Years of Education, *n* (%)	4,138		1,392		6,766		35,358		676		<0.0001
<12 y		1,483 (35.8%)		94 (6.8%)		875 (12.9%)		980 (2.8%)		77 (11.4%)	
12 + y		2,655 (64.2%)		1,298 (93.2%)		5,891 (87.1%)		34,378 (97.2%)		599 (88.6%)	
Primary language, *n* (%)	4,109		1,386		6,763		35,308		676		<0.0001
English		1,410 (34.3%)		685 (49.4%)		6,730 (99.5%)		34,748 (98.4%)		657 (97.2%)	
Non-English*		2,699 (65.7%)		701 (50.6%)		33 (0.5%)		560 (1.6%)		19 (2.8%)	
Cognitive status at UDS visit, *n* (%)	4,138		1,392		6,766		35,358		676		<0.0001
Normal cognition		1,468 (35.5%)		612 (44.0%)		3,010 (44.5%)		13,932 (39.4%)		281 (41.6%)	
Impaired - Not MCI		271 (6.5%)		56 (4.0%)		450 (6.7%)		1,314 (3.7%)		31 (4.6%)	
MCI		994 (24.0%)		353 (25.4%)		1,642 (24.3%)		7,590 (21.5%)		120 (17.8%)	
Dementia		1,405 (34.0%)		371 (26.7%)		1,664 (24.6%)		12,522 (35.4%)		244 (36.1%)	
Global CDR, *n* (%)	4,138		1,392		6,766		35,358		676		<0.0001
0.0		1,457 (35.2%)		600 (43.1%)		3,206 (47.4%)		13,878 (39.2%)		248 (36.7%)	
0.5		1,513 (36.6%)		515 (37.0%)		2,325 (34.4%)		13,119 (37.1%)		274 (40.5%)	
1.0		672 (16.2%)		182 (13.1%)		724 (10.7%)		5,631 (15.9%)		105 (15.5%)	
>1		496 (12.0%)		95 (6.8%)		511 (7.6%)		2,730 (7.7%)		49 (7.2%)	
Indicator of first-degree family member with cognitive impairment, *n* (%)	3,470	1,949 (56.2%)	1,201	616 (51.3%)	5,590	2,948 (52.7%)	31,670	18,960 (59.9%)	584	323 (55.3%)	<0.0001
Principal referral source, *n* (%)	4,138		1,392		6,766		35,358		676		<0.0001
Non-professional contact		1,124 (27.2%)		455 (32.7%)		2,554 (37.7%)		11,066 (31.3%)		181 (26.8%)	
Professional contact		1,935 (46.8%)		506 (36.4%)		1,967 (29.1%)		15,679 (44.3%)		325 (48.1%)	
Other referral		993 (24.0%)		404 (29.0%)		2,117 (31.3%)		7,711 (21.8%)		164 (24.3%)	
Unknown		86 (2.1%)		27 (1.9%)		128 (1.9%)		902 (2.6%)		6 (0.9%)	
Has at least one MRI scan available, *n* (%)	4,138	784 (18.9%)	1,392	157 (11.3%)	6,766	919 (13.6%)	35,358	5,631 (15.9%)	676	91 (13.5%)	<0.0001
Visit Year, *n* (%)	4,138		1,392		6,766		35,358		676		<0.0001
2005		177 (4.3%)		27 (1.9%)		212 (3.1%)		1,530 (4.3%)		16 (2.4%)	
2006–2007		944 (22.8%)		264 (19.0%)		1,789 (26.4%)		10,180 (28.8%)		135 (20.0%)	
2008–2012		1,091 (26.4%)		352 (25.3%)		1,902 (28.1%)		9,594 (27.1%)		258 (38.2%)	
2013–2017		851 (20.6%)		310 (22.3%)		1,324 (19.6%)		7,195 (20.3%)		169 (25.0%)	
2018–2019		434 (10.5%)		184 (13.2%)		702 (10.4%)		3,497 (9.9%)		47 (7.0%)	
2020–2021		209 (5.1%)		119 (8.5%)		378 (5.6%)		1,700 (4.8%)		21 (3.1%)	
2022–2023		432 (10.4%)		136 (9.8%)		459 (6.8%)		1,662 (4.7%)		30 (4.4%)	

UDS, Uniform Data Set; MCI, mild cognitive impairment; CDR, Clinical Dementia Rating scale; MRI, magnetic resonance imaging; y, years; sd, standard deviation. *for Hispanic participants, Non-English = Spanish, as the language comparisons made in this ethnic group were limited to English versus Spanish. 24 subjects from the Hispanic group were excluded as they reported primary languages outside of English and Spanish, such as Portuguese, Italian etc. For participants of other ethnic groups, Non-English = any language outside of English. Other race = American Indian or Alaska Native, Native Hawaiian or Other Pacific Islander, and remaining multi-racial participants who did not also identify as non-Hispanic Black or non-Hispanic Asian.

Table 2
Results from mixed effects logistic regression models using generalized estimating equations for professional referral versus non-professional referral by racial and ethnic group, adjusted for age, gender, education, visit year, and CDR with a random effect for study site

	All participants ($n = 35,792$)			Mild cognitive impairment or dementia and a global CDR or 0.5 or 1 ($n = 17,476$)		
Racial-Ethnic Group	Odds Ratio	95% CI	p	Odds Ratio	95% CI	p
Hispanic	0.96	0.81–1.13	0.6065	0.93	0.80–1.09	0.3937
Non-Hispanic Asian	0.65	0.49–0.87	0.0035	0.73	0.57–0.95	0.0174
Non-Hispanic Black	0.61	0.44–0.86	0.0045	0.58	0.42–0.82	0.0015
Other race	1.44	0.65–3.20	0.3742	1.45	0.60–3.49	0.4122
Non-Hispanic White	1.00	reference	—	1.00	reference	—

Reference group = non-professional referral. CDR = clinical dementia rating scale, professional = referrals made by healthcare professionals, non-professional=self, family and friends. Other race = American Indian or Alaska Native, Native Hawaiian or Other Pacific Islander, and remaining multi-racial participants who did not also identify as non-Hispanic Black or non-Hispanic Asian.

Table 3
Results from mixed effects logistic regression models using generalized estimating equations for professional referral versus non-professional referral by racial and ethnic group in participants with an MRI scan. Adjusted for age, gender, education, visit year, and CDR with a random effect for study site

	All participants ($n = 5,318$)			Mild cognitive impairment or dementia and a global CDR or 0.5 or 1 ($n = 2,329$)		
Racial-Ethnic Group	Odds Ratio	95% CI	p	Odds Ratio	95% CI	p
Hispanic	0.84	0.68–1.04	0.1021	0.84	0.60–1.17	0.2973
Non-Hispanic Asian	1.05	0.57–1.93	0.8742	0.93	0.49–1.75	0.8206
Non-Hispanic Black	0.97	0.79–1.18	0.7376	0.82	0.51–1.34	0.4349
Other race	0.97	0.61–1.55	0.9067	1.40	0.62–3.15	0.4209
Non-Hispanic White	1.00	reference	–	1.00	reference	–

Reference group = non-professional referral. CDR = clinical dementia rating scale, professional = referrals made by healthcare professionals, non-professional=self, family and friends. Other race = American Indian or Alaska Native, Native Hawaiian or Other Pacific Islander, and remaining multi-racial participants who did not also identify as non-Hispanic Black or non-Hispanic Asian.

were considered, and when only participants with a diagnosis of MCI or dementia and a global CDR of 0.5 or 1 were considered (Table 3).

Primary language

Fewer non-Hispanic Black participants than non-Hispanic White participants reported a non-English primary language (Table 1; $p < 0.0001$). More Hispanic and non-Hispanic Asian participants reported a non-English primary language than non-Hispanic White participants (Table 1; $p < 0.0001$).

In *post-hoc* exploratory analysis examining the effects of primary language on referral source, no differences were observed between Hispanic participants who reported English (34.3%) versus Spanish (65.7%) as their primary language (Supplementary Table 2; OR = 0.87, 95% CI = 0.65–1.12, $p = 0.28$). In non-Hispanic Asian participants, participants who reported their primary language as English (49.4%) had higher odds of being referred by a professional contact than a non-professional contact compared to those who reported their primary language as a language other than English (Supplementary Table 3; OR = 1.46, 95% CI = 1.03–2.07, $p = 0.03$).

DISCUSSION

In this large sample of well-characterized clinical research participants from ADRC studies across the US, non-Hispanic Black and non-Hispanic Asian participants were less likely to be referred to an ADRC study by a professional contact and more likely to be referred by a non-professional contact than non-Hispanic White participants. These observations were not accounted for by participant differences between study sites. This pattern was not observed in Hispanic participants, who had no differences in referrals by professional versus non-professional contacts compared to non-Hispanic White participants. Our findings extend the current limited literature and are consistent with prior reports of differences in patterns of recruitment source across racial and ethnic groups, that URG were more likely to be recruited by family or friends,[12] local earned media (e.g., local news, non-paid con-

tent on television or radio, in print or web-based), local site efforts,[13] word-of-mouth, and speaking engagements[14] than non-Hispanic White participants. These prior studies have focused primarily on recruitment materials, which our dataset did not have sufficient detail to examine. Additionally, these methods of recruitment may have been categorized in the NACC UDS as 'other referrals', thus may have been excluded from the final analyses, limiting direct comparison of results.

There are many potential barriers that may explain the lower likelihood of referral to ADRD studies by professional contacts in URG. Patients from minoritized groups are less likely to receive specialist care,[21,22] which may limit their exposure to opportunities to learn about ADRD studies from healthcare professionals, or to be referred by a healthcare professional. A survey of Asian and Native Hawaiian patients diagnosed with Alzheimer's disease or MCI found that insufficient information about ADRD studies was the primary barrier to participation.[23] Black patients are also more likely to present to specialist care at later stages of dementia.[22] The delayed presentation to specialist care may preclude them from participation in ADRD studies that now primarily focus on prodromal and earlier stages of dementia. Our finding that non-Hispanic Black and Asian participants are less likely to be referred by a professional contact may reflect differences in access to care at tertiary centers, where ADRCs and referring professionals are typically located, which in turn causes selection bias. Selection bias is a substantial concern in the cohort composition of the NACC. A recent study found that the NACC cohort was not representative of the US population in key demographic and health factors.[24] Compared to the general US population, NACC participants tended to be, among other things, more educated, which is generally associated with higher healthcare access and utilization.[25] The authors found that these differences were further amplified between racial and ethnic groups.

Skepticism towards research, worry about experimental interventions, and potential physical harm of biomarker testing may also contribute to underrepresentation in trials.[26–29] Our findings were largely consistent with prior studies that non-Hispanic Black and Asian participants were less willing to be contacted for participate in ADRD trials,[29,30] while Hispanic participants were more willing to be contacted for studies with requirements typical of ADRD prevention trials [30] and clinical intervention studies in general.[31] While the underlying reasons for these observations are beyond the scope of this paper, future studies are needed to explore ways to improve willingness to participate in research, including ways that community outreach may be utilized.

An alternative interpretation of our findings is that non-Hispanic Black and Asian participants who participate in ADRD research have higher odds of being referred by non-professionals. It is possible that the non-professional referral pathway is capturing effects of community outreach, though there was insufficient detail in the dataset to confirm this. Qualitative studies exploring barriers for URG participation in ADRD research have cited lack of trust towards researchers and the healthcare system as a recurring theme.[11,32] This was largely consistent with findings from Raman et al who found that local site efforts and local earned media (e.g., local news, non-paid content on television or radio, in print or web-based) were more frequently the source of recruitment for Black, Hispanic and Asian participants, as opposed to centralized recruitment efforts.[13] This may indicate that trust was critical to clinical trial recruitment, and that community outreach and local earned media may be more effective in engaging in trustful communication and relationships with diverse communities. Future studies on recruitment strategies are needed to explore ways that ADRCs can strategically leverage their non-professional networks for outreach.

Our analyses did not find any differences across race and ethnicity and referral source when considering only participants with at least one MRI. It should be noted, however, that the sample with MRI was relatively small, and that MRI and other biomarker data in the NACC UDS were convenience samples, voluntarily submitted by ADRCs. We found that ADRCs which submitted MRI data had fewer non-Hispanic Black participants than ADRCs that did not submit MRI data, thus subject to potential reporting bias. The NACC UDS dataset did not include information on the characteristics of ADRCs, thus we were unable to explore potential factors that may explain these differences. To date, most biomarker research has been conducted in non-Hispanic White samples, who make up approximately 89% of participants in ADRD research overall.[33] Concerns about invasive procedures and negative psychological and physical effects of biomarker testing, and the stigma of being diagnosed with dementia have been previously reported as potential barriers for recruitment of URG

to biomarker studies.[26,28,30,34] Future studies are needed to better understand differences in URG participation and the potential contribution of site-based factors on the completion and reporting of biomarker data.

It should be emphasized again that race and ethnicity are proxy measures for many factors, including those related to psychosocial factors, such as cultural factors and social determinants of health. At the time that these analyses were completed, variables related to structural and social determinants (e.g., socioeconomic status, health insurance status, distance to ADRC, area deprivation index) were not available in the NACC UDS dataset, thus we were unable to further explore their correlation to race, ethnicity and referral sources. These variables are needed to fully understand potential barriers to study participation, including access to healthcare. A new form focused on social determinants of health will be included in the next version of the UDS (UDSv4). Our findings underscore the critical need to collect data related to structural and social determinants of health to further our understanding of representation and inclusion in ADRD studies. The missed nuances of relying solely on racial and ethnic categories is exemplified in our observation that non-English primary language was associated with lower likelihood of professional referrals in non-Hispanic Asian but not Hispanic participants who spoke Spanish. This may be explained by the vast heterogeneity in cultures and languages across individuals who identify as Asian. A qualitative study of participants who identified as Asian Americans and Pacific Islanders found variability across cultural and ethnic groups in their perspectives about research engagement and recruitment.[35] Assumptions that members of the same racial or ethnic group hold similar preferences regarding research participation may have the unintended consequence of exacerbating barriers to recruitment.[11]

Beyond variables related to psychosocial factors, refinement of data collection related to recruitment pathway is needed. In these analyses, the 'other' referrals pathway was excluded despite making up 24% of the cohort due to the heterogeneity of the group. Prior studies that have reported differences in recruitment sources across racial and ethnic groups used recruitment methods that may have fallen under the 'other' category in the UDS,[12,14] pointing to potentially missed opportunities to understand this group. Furthermore, in analyzing their marketing questionnaire data, Julbe-Delgado et al. found that participants could not always recall their referral source, or reported referral sources that were not possible.[12] Therefore, improvements in methods of determining the source of referrals beyond participant self-report are needed to ensure accuracy in quantifying referral sources.

This study has several limitations. First, we were unable to examine psychosocial factors and factors related to social determinants of health that may underlie our observations related to racial and ethnic groups. MRI was used as a proxy for biomarker studies in general. Other biomarker measures more specific to ADRD, such as cerebrospinal fluid biomarkers and positron emission tomography, were not included due to high variability in reporting across study sites. While MRI completion is not equivalent to full biomarker characterization in terms of clinical use, research use, and invasiveness, it provides insight into the likelihood of participants to complete other procedures needed for biomarker characterization. Additionally, MRI data was submitted voluntarily by study sites. Because of the anonymized nature of the NACC dataset, we were unable further explore site characteristics that may have contributed to differences in reporting. Finally, data related to referral source were based on self-report by the participant or their study partner and is therefore vulnerable to inaccuracies. Because the NACC UDS reported referral sources only as 'professional', 'non-professional', 'other', and 'unknown', we were unable to examine the referral source in greater detail, including whether participants were recruited from a clinic versus community outreach.

In conclusion, there is a need at a national level to develop recruitment strategies to increase URG representation. A lack of healthcare professional-facilitated recruitment may contribute to the disproportionately lower research participation in URG. Further efforts are needed to improve data collection of referral sources and variables related to cultural factors and social determinants of health to improve our understanding of barriers. Finally, improvements to the characterization of recruitment methodology are required to provide high quality evidence for actionable strategies to increase URG representation in ADRD studies.

AUTHOR CONTRIBUTIONS

Carol K. Chan (Conceptualization; Writing – original draft); Kathleen A. Lane (Data curation; Formal

analysis; Writing – review & editing); Sujuan Gao (Data curation; Formal analysis; Writing – review & editing); Omolola A. Adeoye-Olatunde (Writing – review & editing); Sarah Biber (Writing – review & editing); Crystal M. Glover (Writing – review & editing); David K. Johnson (Writing – review & editing); Shannon L. Risacher (Writing – review & editing); Andrew J. Saykin (Conceptualization; Supervision; Writing – review & editing); Sophia Wang (Conceptualization; Supervision; Writing – review & editing).

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CONFLICT OF INTEREST

Carol K. Chan and Andrew J. Saykin are Editorial Board members of this journal but were not involved in the peer-review process of this article nor had access to any information regarding its peer-review.

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DATA AVAILABILITY

The data supporting the findings of this study are available to eligible researchers from the National Alzheimer's Coordinating Center at https://naccdata.org.

SUPPLEMENTARY MATERIAL

The supplementary material is available in the electronic version of this article: https://dx.doi.org/10.3233/JAD-240485.

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