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RESEARCH ARTICLE

The ADNI4 Digital Study: A novel approach to recruitment, screening, and assessment of participants for AD clinical research

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Abstract

INTRODUCTION: We evaluated preliminary feasibility of a digital, culturally-informed approach to recruit and screen participants for the Alzheimer's Disease Neuroimaging Initiative (ADNI4).

Data used in preparation of this article were obtained from the Alzheimer's Disease Neuroimaging Initiative (ADNI) database (adni.loni.usc.edu). As such, the investigators within the ADNI contributed to the design and implementation of ADNI and/or provided data. Some ADNI investigators participated in analysis or writing of this report. A complete listing of ADNI investigators can be found at: http://adni.loni.usc.edu/wp-content/uploads/how_to_apply/ADNI_Acknowledgement_List.pdf

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METHODS: Participants were recruited using digital advertising and completed digital surveys (e.g., demographics, medical exclusion criteria, 12-item Everyday Cognition Scale [ECog-12]), Novoic Storyteller speech-based cognitive test). Completion rates and assessment performance were compared between underrepresented populations (URPs: individuals from ethnoculturally minoritized or low education backgrounds) and non-URPs.

RESULTS: Of 3099 participants who provided contact information, 654 enrolled in the cohort, and 595 completed at least one assessment. Two hundred forty-seven participants were from URPs. Of those enrolled, 465 met ADNI4 inclusion criteria and 237 evidenced possible cognitive impairment from ECog-12 or Storyteller performance. URPs had lower ECog and Storyteller completion rates. Scores varied by ethnocultural group and educational level.

DISCUSSION: Preliminary results demonstrate digital recruitment and screening assessment of an older diverse cohort, including those with possible cognitive impairment, are feasible. Improving engagement and achieving educational diversity are key challenges.

KEYWORDS
Alzheimer's disease (AD), Alzheimer's disease clinical trials, Alzheimer's Disease Neuroimaging Initiative (ADNI), digital assessment, digital recruitment, participant screening, underrepresented populations

Highlights

- A total of 654 participants enrolled in a digital cohort to facilitate ADNI4 recruitment.
- Culturally-informed digital ads aided enrollment of underrepresented populations.
- From those enrolled, 42% were from underrepresented ethnocultural and educational groups.
- Digital screening tools indicate > 50% of participants likely cognitively impaired.
- Completion rates and assessment performance vary by ethnocultural group and education.

1 | BACKGROUND

The ability to identify older adults at risk of developing Alzheimer's disease (AD) is increasingly important for America's aging population as we enter the AD disease-modifying treatment era.[1–3] AD and related dementias disproportionately affect older Black/African American (Black) and Latino/a/x/e (heretofore Latinx) adults but these communities remain underrepresented in research studies.[4,5] The lack of diverse socioeconomic, educational, and ethnocultural representation in AD research hampers efforts to develop accurate diagnostic tools and effective treatments, and has significant ethical implications.[6–9]

Clinical sites are typically tasked with the work of identifying and recruiting potential participants, as well as carrying out the research protocol. Participant pools at local clinical centers may not represent the full range of communities in the region, in part reflecting differential access to healthcare resources. This may further exacerbate a lack of diverse representation among participants. Previous studies have demonstrated the great potential of online recruitment and Web-based study portals to enroll participants into scientific research, especially as these are often scalable, efficient, and accessible to more people.[10–17] Remote recruitment with referral to clinic-based studies may enhance representation and inclusion while also reducing site staff burden.

The Alzheimer's Disease Neuroimaging Initiative (ADNI4), whose primary aim is to validate biomarkers for AD clinical trials, has committed to a goal of enrolling 50%–60% of new participants in the clinic-based cohort as individuals from historically underrepresented populations (URPs; those from ethnoculturally minoritized backgrounds such as American Indian, Asian, African-American, Latinx, etc., and/or with 12 or fewer years of education).[3] Additional enrollment goals are 40%

with mild cognitive impairment (MCI) and 80% elevated AD biomarkers across diagnostic groups. To aid in achieving these goals, ADNI4 is using a sequential outreach and recruitment plan. At the first stage, culturally informed digital marketing will recruit up to 20,000 participants, especially URPs, to join an online study cohort (Remote Digital Cohort). The Remote Digital Cohort will then be used to screen and prioritize participants for referral for subsequent remote blood collection to obtain plasma AD biomarkers, and for enrollment in in-clinic ADNI4.[3]

With up to 65 clinical sites across the United States (including three in Canada), ADNI4 will ultimately recruit and enroll participants into the Remote Digital Cohort at a national scale. Past experiences in recruitment of participants into an online study, the Brain Health Registry (BHR),[10,11] as well as focused digital marketing recruitment of URP individuals (ADNI3 Diversity Task Force efforts[18,19]) have informed ADNI4's digital recruitment approach. ADNI4 aims to improve our engagement and enrollment of URP participants through a culturally-informed, community-engaged research approach,[18,19] led by the Engagement Core, working in partnership with ADNI's new Community Scientific Partnership Board (CSPB) to help guide our outreach and marketing strategies as well as support the retention of participants after they join (see Rivera Mindt and Arentoft et al., this special issue). The ADNI4 In-Clinic Cohort (up to 1500 participants including participants from previous ADNI phases, heretofore rollovers) will continue to gather the detailed data that ADNI is known for (clinical assessments, magnetic resonance imaging [MRI], positron emission tomography [PET], biofluids, genetics, neuropathology via future brain donation, etc.) across three diagnostic arms (~40% cognitively unimpaired [CU]; ~40% MCI; ~20% AD dementia). ADNI4 is aiming for the eventual In-Clinic Cohort to have ~80% amyloid positivity by PET.[3]

The goal of this study is to investigate the feasibility and preliminary effectiveness of the approach for enrolling and screening individuals, especially those from URP backgrounds, into the ADNI4 Digital Cohort study. Here, we report the initial baseline visit results for the Digital Cohort, including descriptive statistics, task completion, and evidence for cognitive impairment.

RESEARCH IN CONTEXT

1. **Systematic review**: We reviewed the literature using electronic databases (e.g., PubMed) and search engines (Google Scholar). Many Alzheimer's disease (AD) and related dementias studies under-include those from historically underrepresented populations (URPs). Culturally informed community engaged research strategies and remote, digital methods are promising approaches.
2. **Interpretation**: Our results support the feasibility of a culturally informed, digital recruitment and screening approach to enroll, screen, and remotely-assess older adults from underrepresented populations for subsequent enrollment in an in-clinic observational study, the Alzheimer's Disease Neuroimaging Initiative (ADNI4). Remaining challenges are improving participant engagement (especially for URPs) and increasing educational diversity.
3. **Future directions**: Future research will examine feasibility of scaled-up, national efforts; investigate comparative effectiveness of specific recruitment strategies; investigate feasibility of a multitier screening and enrichment approach for enrollment in Remote Digital, Remote Blood, and In-Clinic studies; and validate digital assessments and plasma biomarkers to identify participants with mild cognitive impairment and elevated AD biomarkers.

2 | METHODS

2.1 | Participants

Data used in the preparation of this article were obtained from the ADNI database (http://adni.loni.usc.edu). The ADNI program was launched in 2003 as a public-private partnership, led by Principal Investigator Michael W. Weiner, MD. The primary goal of ADNI has been to test whether serial MRI, PET, other biological markers, and clinical and neuropsychological assessment can be combined to measure the progression of MCI and early AD.

Currently, individuals who are between the ages of 55 and 90 years old, live within 150 miles of an ADNI4 clinical site, and can read English are able to register and join the Remote Digital Cohort. We report on the available results (consented participants who joined between June 21, 2023, and April 2, 2024) from 595 participants who are presently enrolled in the Remote Digital Cohort (Table 1) and answered at least one question about themselves (demographics questions are the first seen during the participant experience). Given the emphasis on identifying eligible participants for referral to clinical sites, those participants who self-report exclusionary criteria related to the ADNI4 in-clinic protocol (such as metal in the body that would preclude MRI) are included in Table 1 but are exempt from further analyses. Study partners are not required for Remote Digital Cohort participation, and current data indicate only 11% of participants have a study partner who is actively participating in the Remote Digital Study Partner component. Given the very small sample size of study partners to date, this factor will be further explored in a future publication.

2.2 | Digital advertising

ADNI4 marketing materials including advertisements and websites are developed in conjunction with the marketing firm Alaniz Marketing, the ADNI Engagement and Administrative Cores, and ADNI's CSPB (see Rivera-Mindt et al., this special issue). Wording and images used in advertising are culturally sensitive and tailored to relate to a specific

TABLE 1 Participants included in the ADNI4 Remote Digital Cohort (data as of April 2, 2024).

	All participants (*N* = 595)			Participants who did not indicate ADNI exclusions[a] (*N* = 465)		
Parameter	**Total (*N* = 595)**	**Non-URP (*N* = 348)**	**URP (*N* = 247)**	**Total (*N* = 465)**	**Non-URP (*N* = 275)**	**URP (*N* = 190)**
Age	68 (62, 73)	69 (63, 75)	66 (62, 71)	67 (62, 73)	69 (63, 75)	67 (62, 71)
Gender						
Female	449 (75%)	258 (74%)	191 (77%)	346 (74%)	199 (72%)	147 (77%)
Male	145 (24%)	89 (26%)	56 (23%)	118 (25%)	75 (27%)	43 (23%)
Prefer not to say	1 (0.2%)	1 (0.3%)	0 (0%)	1 (0.2%)	1 (0.4%)	0 (0%)
Education						
< or = 12 years	25 (4%)	0 (0%)	25 (10%)	14 (3%)	0 (0%)	14 (7%)
> 12 years	569 (96%)	348 (100%)	221 (89%)	450 (97%)	275 (100%)	175 (93%)
Unknown	1 (0.1%)	0 (0%)	1 (0.4%)	1 (0.2%)	0 (0%)	1 (0.5%)
Ethnicity						
Latino	553 (93%)	340 (98%)	213 (86%)	16 (3%)	0 (0%)	16 (8%)
Not Latino	27 (5%)	0 (0%)	27 (11%)	437 (94%)	269 (98%)	168 (88%)
Unknown	15 (3%)	8 (2%)	7 (3%)	12 (2%)	8 (3%)	6 (3%)
Race						
African American	183 (31%)	0 (0%)	183 (74%)	149 (32%)	0 (0%)	149 (78%)
Asian	12 (2%)	0 (0%)	12 (5%)	12 (3%)	0 (0%)	12 (6%)
Multiple selections	13 (2%)	0 (0%)	13 (5%)	8 (1.7%)	0 (0%)	8 (4%)
Prefer not to say	4 (0.7%)	2 (0.6%)	2 (0.8%)	2 (0.4%)	2 (0.7%)	0 (0%)
Unknown	6 (1%)	3 (0.9%)	3 (1%)	3 (0.6%)	2 (0.7%)	1 (0.5%)
White	375 (63%)	343 (99%)	32 (13%)	291 (63%)	271 (99%)	20 (11%)
Native American	1 (0.2%)	0 (0%)	1 (0.4%)	0 (0%)	0 (0%)	0 (0%)
Pacific Islander	1 (0.2%)	0 (0%)	1 (0.4%)	0 (0%)	0 (0%)	0 (0%)
Self-reported diagnosis	130 (100%)	73 (100%)	57 (100%)	64 (15%)	54 (21%)	10 (6%)
Self-reported MCI diagnosis						
No	447 (75%)	245 (70%)	202 (82%)	358 (77%)	195 (71%)	163 (86%)
Yes	84 (14%)	66 (19%)	18 (7%)	59 (13%)	51 (16%)	8 (4%)
Don't know	30 (5%)	18 (5%)	12 (5%)	14 (3%)	10 (4%)	4 (2%)
Prefer not to say	2 (0.3%)	1 (0.2%)	1 (0.4%)	2 (0.4%)	1 (0.4%)	1 (0.6%)
Unknown	32 (5%)	18 (5%)	14 (6%)	32 (7%)	18 (7%)	14 (7%)
Self-reported AD diagnosis						
No	522 (88%)	301 (87%)	221 (90%)	405 (87%)	234 (85%)	171 (90%)
Yes	23 (4%)	19 (6%)	4 (2%)	16 (3%)	16 (6%)	0 (0%)
Don't know	17 (3%)	9 (3%)	8 (3%)	12 (3%)	7 (3%)	5 (3%)
Prefer not to say	1 (0.2%)	1 (0.3%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Unknown	32 (5%)	18 (5%)	14 (6%)	32 (7%)	18 (7%)	14 (7%)
Self-reported dementia diagnosis						
No	513 (86%)	295 (84%)	218 (88%)	399 (86%)	231 (84%)	168 (88%)
Yes	22 (4%)	18 (5%)	4 (2%)	15 (3%)	13 (5%)	2 (1%)
Don't know	21 (4%)	13 (4%)	8 (3%)	14 (3%)	10 (4%)	4 (2%)
Prefer not to say	7 (1%)	4 (1%)	3 (1%)	5 (1%)	3 (1%)	2 (1%)
Unknown	32 (5%)	18 (5%)	14 (6%)	32 (7%)	18 (7%)	14 (7%)

(Continues)

TABLE 1 (Continued)

Parameter	All participants (*N* = 595)			Participants who did not indicate ADNI exclusions[a] (*N* = 465)		
	Total (*N* = 595)	Non-URP (*N* = 348)	URP (*N* = 247)	Total (*N* = 465)	Non-URP (*N* = 275)	URP (*N* = 190)
Self-reported memory concern						
No	218 (37%)	134 (39%)	84 (34%)	183 (39%)	112 (41%)	71 (37%)
Yes	330 (56%)	191 (55%)	139 (56%)	239 (51%)	143 (52%)	96 (51%)
Prefer not to say	11 (2%)	5 (1%)	6 (2%)	10 (2%)	4 (1%)	6 (3%)
Unknown	36 (6%)	18 (5%)	18 (7%)	33 (7%)	16 (6%)	17 (9%)
Self-reported memory decline						
No	377 (63%)	222 (64%)	155 (63%)	313 (67%)	185 (67%)	128 (67%)
Yes	170 (29%)	104 (30%)	66 (27%)	111 (24%)	72 (28%)	39 (20%)
Prefer not to say	9 (2%)	4 (1%)	5 (2%)	5 (1%)	2 (0.8%)	3 (2%)
Unknown	39 (7%)	18 (5%)	21 (9%)	36 (8%)	16 (6%)	20 (11%)
Prescribed medication for cognitive impairment						
No	491 (83%)	283 (81%)	208 (84%)	384 (83%)	220 (80%)	164 (86%)
Yes	48 (8%)	37 (11%)	11 (5%)	35 (8%)	31 (11%)	4 (2%)
Don't know	13 (2%)	6 (2%)	7 (3%)	4 (0.9%)	2 (0.7%)	2 (1%)
Unknown	43 (7%)	22 (6%)	21 (9%)	42 (9%)	22 (8%)	20 (11%)
Family history of AD/dementia						
No	212 (36%)	107 (31%)	105 (43%)	173 (37%)	90 (33%)	83 (44%)
Yes	315 (53%)	196 (56%)	119 (48%)	233 (50%)	147 (53%)	86 (45%)
Don't know	32 (5%)	24 (7%)	8 (3%)	24 (5.2%)	18 (7%)	6 (3.2%)
Prefer not to say	2 (0.3%)	2 (0.6%)	0 (0%)	1 (0.2%)	1 (0.4%)	0 (0%)
Unknown	34 (6%)	19 (6%)	15 (6%)	34 (7%)	19 (7%)	15 (8%)
Self-reported ADNI4 exclusionary conditions						
Indicated any medical exclusion	130 (22%)	73 (21%)	57 (23%)	0 (0%)	0 (0%)	0 (0%)
Lives in a nursing home						
No	559 (94%)	329 (95%)	230 (93%)	430 (92%)	256 (93%)	174 (92%)
Prefer not to say	1 (0.2%)	0 (0%)	1 (0.4%)	0 (0%)	0 (0%)	0 (0%)
Unknown	35 (6%)	19 (5%)	16 (6%)	35 (8%)	19 (7%)	16 (8%)
Diagnosed with schizophrenia, bipolar disorder, or major depression						
No	498 (84%)	295 (85%)	203 (82%)	430 (92%)	256 (93%)	174 (92%)
Yes	58 (10%)	32 (9%)	26 (11%)	0 (0%)	0 (0%)	0 (0%)
Prefer not to say	4 (0.7%)	2 (0.5%)	2 (0.8%)	0 (0%)	0 (0%)	0 (0%)
Unknown	35 (6%)	19 (5%)	16 (6%)	35 (8%)	19 (7%)	16 (8%)
Diagnosed with Parkinson's disease, Huntington's disease, brain tumor, seizure disorder, or multiple sclerosis						
No	535 (96%)	313 (90%)	222 (90%)	430 (92%)	256 (93%)	174 (92%)
Yes	24 (4%)	15 (4%)	9 (4%)	0 (0%)	0 (0%)	0 (0%)
Prefer not to say	1 (0.2%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Unknown	35 (6%)	19 (5%)	16 (6%)	35 (8%)	19 (7%)	16 (8%)

(Continues)

TABLE 1 (Continued)

Parameter	All participants (*N* = 595)			Participants who did not indicate ADNI exclusions[a] (*N* = 465)		
	Total (*N* = 595)	Non-URP (*N* = 348)	URP (*N* = 247)	Total (*N* = 465)	Non-URP (*N* = 275)	URP (*N* = 190)
Diagnosed with alcohol or drug use disorder in the past 2 years						
No	550 (98%)	326 (94%)	224 (90%)	430 (92%)	256 (93%)	174 (92%)
Yes	9 (2%)	3 (0.8%)	6 (2%)	0 (0%)	0 (0%)	0 (0%)
Prefer not to say	1 (0.2%)	0 (0%)	1 (0.4%)	0 (0%)	0 (0%)	0 (0%)
Unknown	35 (6%)	19 (5%)	16 (6%)	35 (8%)	19 (7%)	16 (8%)
Has a pacemaker, implanted medical device, metal fragments, or other foreign objects in their body						
No	511 (86%)	301 (86%)	210 (85%)	427 (92%)	254 (92%)	173 (91%)
Yes	49 (8%))	28 (8%)	21 (9%)	0 (0%)	0 (0%)	0 (0%)
Prefer not to say	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Unknown	35 (6%)	19 (5%)	16 (6%)	38 (8%)	21 (8%)	17 (9%)
Willingness to participate in subsequent ADNI study activities						
Wiling to participate in a 5-year study with memory and thinking tests						
No	7 (1%)	3 (0.8%)	4 (2%)	5 (1%)	2 (0.7%)	3 (2%)
Yes	549 (92%)	325 (93%)	224 (91%)	422 (92%)	254 (92%)	168 (88%)
Prefer not to say	4 (0.6%)	1 (0.2%)	3 (1%)	3 (0.6%)	0 (0%)	3 (2%)
Unknown	35 (6%)	19 (5%)	16 (6%)	30 (7%)	19 (7%)	16 (8%)
Willing to undergo a blood draw procedure						
No	5 (0.8%)	0 (0%)	5 (2%)	5 (1%)	0 (0%)	5 (3%)
Yes	552 (93%)	328 (94%)	224 (91%)	422 (91%)	255 (93%)	167 (87%)
Prefer not to say	3 (0.5%)	1 (0.2%)	2 (0.8%)	3 (0.7%)	1 (0.3%)	2 (1%)
Unknown	35 (6%)	19 (5%)	16 (6%)	35 (8%)	19 (7%)	16 (8%)
Willing to participate in a 5-year study with MRI and PET scans						
No	8 (1%)	3 (0.9%)	5 (2%)	6 (1%)	1 (0.03%)	5 (3%)
Yes	545 (92%)	323 (93%)	222 (90%)	419 (91%)	253 (92%)	166 (87%)
Prefer not to say	7 (1%)	3 (0.8%)	4 (2%)	5 (1%)	2 (0.7%)	3 (2%)
Unknown	35 (6%)	19 (5%)	16 (6%)	30 (7%)	19 (7%)	16 (8%)
Experiences claustrophobia						
No	511 (86%)	303 (87%)	208 (84%)	396 (86%)	240 (87%)	156 (820%)
Yes	21 (4%)	8 (2%)	13 (5%)	13 (3%)	3 (1%)	10 (5%)
Don't know	27 (5%)	17 (5%)	10 (4%)	20 (4%)	12 (4%)	8 (4%)
Prefer not to say	1 (0.1%)	1 (0.2%)	0 (0%)	1 (0.2%)	1 (0.3%)	0 (0%)
Unknown	35 (6%)	19 (5%)	16 (6%)	30 (7%)	19 (7%)	16 (8%)
Technology access						
Has regular access to internet						
No	0 (0%)	0 (0%)	1 (0.4%)	0 (0%)	0 (0%)	1 (0.5%)
Yes	559 (93%)	329 (95%)	230 (993%)	429 (92%)	256 (93%)	173 (91%)
Prefer not to say	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Unknown	35 (6%)	19 (5%)	16 (6%)	35 (8%)	19 (7%)	16 (8%)
Has a computer, smartphone, or tablet device						
No	0 (0%)	0 (0%)	1 (0.4%)	0 (0%)	0 (0%)	0 (0%)
Yes	554 (93%)	327 (94%)	227 (92%)	427 (92%)	254 (92%)	173 (91%)
Prefer not to say	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Unknown	40 (7%)	21 (6%)	19 (8%)	38 (8%)	21 (8%)	17 (9%)

(Continues)

TABLE 1 (Continued)

Parameter	All participants (*N* = 595)			Participants who did not indicate ADNI exclusions[a] (*N* = 465)		
	Total (*N* = 595)	Non-URP (*N* = 348)	URP (*N* = 247)	Total (*N* = 465)	Non-URP (*N* = 275)	URP (*N* = 190)
Cognitive assessments						
Self-report ECog-12						
Score	1.36 (1.09, 1.82)	1.42 (1.17, 1.82)	1.33 (1.08, 1.83)	1.33 (1.08, 1.67)	1.36 (1.17, 1.75)	1.25 (1.08, 1.50)
Completed	545 (92%)	327 (94%)	218 (88%)	421 (91%)	257 (93%)	164 (86%)
Unknown/Did not complete	50 (8%)	21 (6%)	29 (12%)	44 (9%)	18 (7%)	26 (14%)
Study Partner-Report ECog-12 Score						
Score	1.25 (1.00, 1.75)	1.25 (1.00, 1.69)	1.39 (1.10, 1.94)	1.33 (1.04, 1.79)	1.29 (1.02, 1.74)	1.55 (1.08, 2.00)
Completed	81 (14%)	67 (19%)	14 (5.7%)	67 (14%)	58 (21%)	9 (5%)
Unknown/Did not complete	514 (86%)	281 (81%)	233 (90%)	398 (86%)	217 (79%)	181 (95%)
Novoic Storyteller						
Score	56 (43, 64)	59 (47, 66)	47 (41, 61)	59 (46, 67)	60 (48, 69)	55 (44, 63)
Completed	315 (53%)	216 (62%)	99 (40%)	250 (54%)	174 (63%)	76 (40%)
Unknown/Did not complete	280 (47%)	132 (38%)	147 (60%)	215 (46%)	101 (37%)	114 (60%)
Self-Report ECog-12 score suggestion of impairment (score greater than or equal to 1.36)						
Not likely impaired	272 (46%)	153 (44%)	119 (48%)	234 (50%)	128 (47%)	106 (56%)
Likely impaired	273 (46%)	174 (50%)	99 (40%)	187 (40%)	129 (47%)	58 (30%)
Unknown/Did not complete	50 (8%)	21 (6%)	29 (12%)	44 (10%)	18 (6%)	26 (14%)
Novoic Storyteller score suggestion of impairment (score less than 49.4)						
Not likely impaired	214 (36%)	155 (45%)	59 (24%)	174 (37%)	125 (45%)	49 (26%)
Likely impaired	101 (17%)	61 (18%)	40 (16%)	76 (16%)	49 (18%)	27 (14%)
Unknown/Did not complete	280 (47%)	132 (38%)	148 (60%)	215 (46%)	101 (37%)	114 (60%)

Note: Median (IQR) for continuous variables; *N* (%) for categorical variables.
Abbreviations: AD, Alzheimer's disease; ADNI, Alzheimer's Disease Neuroimaging Initiative; ECog-12, Everyday Cognition 12-item questionnaire; MCI, mild cognitive impairment; MRI, magnetic resonance imaging; PET, positron emission tomography; URP, underrepresented populations.
[a]includes *N* = 38 who did not complete exclusion prescreen questions.

theme (such as community or family focus, educational or aspirational messaging). Digital marketing was deployed on the Meta (Facebook and Instagram) social media platforms to recruit participants residing near eight of the ADNI4 clinical sites: Mayo Clinic, University of Kansas, University of Kentucky, Wake Forest University, University of California San Francisco, University of California Los Angeles, Butler Hospital, and Georgetown University. Ads placed on social media platforms direct interested individuals to the ADNI4 study website (adni4.org) where more information is provided about the study, as well as a form to register and establish an account on our study platform. Once registered, individuals review an electronic consent form and, if they agree, they are then directed to begin answering questions about themselves.

2.3 | Digital infrastructure

The ADNI online platform for participant and study partner consenting and data collection is designed and operated by the ADNI Administrative Core utilizing the Ebisu software developed for the BHR (registered software with the University of California, San Francisco).[10,11] Technical support is available to all participants via the ADNI Community Research Navigators (see Rivera-Mindt et al., this special issue), who can be contacted by email, phone, and chat. Communications with participants are facilitated using Zendesk software, which aids ADNI study staff in tracking participant support and feedback requests.

2.4 | Study tasks

Participants are asked to provide information about their location, including the option to provide a complete address. The participant is presented with a list of all ADNI4 clinical sites located within a 150-mile radius of the zip code they provide. If more than one site is within this radius, they are asked to indicate which, if any, sites they would be willing to travel to, and which would be their preferred site. Participants complete the following questionnaires and tasks: (1) demographics (self-reported gender, ethnicity, race, and education);

(2) screening questions which include (i) self-report medical history (metal in the body, recent diagnoses of mental health conditions, etc.), (ii) interest in participating in study related activities (blood draw, visiting a clinic for a 5-year study, MRI and PET), and (iii) self-report MCI or AD diagnosis and/or medication for cognitive impairment; (3) self-report memory concern and memory decline questions; (4) the self-report Everyday Cognition 12-item questionnaire (ECog-12)[20,21]; (5) the objective Novoic Storyteller test[22–24]; (6) Study Partner invitation task. For the Study Partner task, participants can list the name and contact information to invite someone to be their study partner in the Remote Digital Cohort. If this information is provided, the ADNI Ebisu platform automatically sends the potential study partner an email with a unique link to register, allowing the participant and study partner data to be connected on the backend. This remote, online baseline visit takes 15–20 min to complete. Participants have 30 days after signing consent to finish these study tasks and are prompted by automated emails to return to the study website if they have outstanding tasks. A study partner is not required for participation in the Remote Digital Cohort but is encouraged. If a study partner consents to join, they are asked subjective questions about the corresponding participant's cognition and functional abilities (informant-reporting on the associate participant's memory concern and decline; ECog-12 informant/study partner report). Longitudinal follow-up will track these participants at 6-month increments and include repetition of the self-report memory concern/decline questions, the ECog-12, and Novoic Storyteller. Longitudinal follow-up with study partners at 6-month intervals includes repetition of questions about their associated partner's memory concern/decline, as well as the informant report ECog-12. From the data collected on participants in the Remote Digital Cohort, select participants are invited to join the Remote Blood Cohort and/or referred directly to a clinical site to be screened to join the in-clinic Cohort.

2.5 | Novoic Storyteller

The Remote Digital Cohort study tasks include Novoic Ltd.'s Storyteller, which is a speech-based objective cognitive assessment.[22–24] The participant is asked if they have about 10 min to complete the Storyteller test, as well as if they are in a quiet location, wearing glasses or hearing aids if they use them, and is prompted with encouragement to try their best on the task. The participant is asked to provide microphone access via their device so that their voice responses to the questions may be recorded. A quality control sound check is performed to ensure the microphone and speakers on the device are working and that background noise is minimal to capture a decent recording, and then the participant begins the test. There is currently no performance threshold below which the Novoic score is considered invalid, though individual scores of "0" are manually checked for quality to determine if that score is valid or should be invalidated due to poor audio quality. Further details about the Storyteller test can be found in Skirrow et al., this special issue. Completion rates, discussed below, may be impacted by an issue specific to Android users who sign up for the Remote Digital Cohort via ads on Meta's Facebook platform. Unfortunately, that user experience pathway will not allow the participant microphone access, which is required to complete the Storyteller test. A workaround has been implemented (June 2024) and asks participants who are on Android devices and using the Facebook platform to log into the ADNI study portal via a different Web browser (Chrome, Firefox, Safari, etc.). The ADNI4 Ebisu platform is linked to the Novoic platform via an application programming interface (API), and results are quickly transmitted between systems. Storyteller includes immediate recalls of two different stories from the Automated Story Recall Task (ASRT),[25] followed by a category fluency distractor task, and the delayed recall of the first story presented. Novoic's automated speech analysis pipeline transcribes participant responses to story recall tasks to produce a "G-match score" which automatically quantifies the similarity between the participant's recollection and the original story source (see Skirrow et al., this special issue). The ADNI study team receives the Storyteller G-match score (between 0 and 100) as well as a binary recommendation output (true = possibly cognitively impaired; false = not likely cognitively impaired). The current cutoff score, provided by Novoic, divides the recommendation outcomes at 49.4, where scores less than this value indicate likely cognitive impairment.

2.6 | Defining possible/probable cognitive impairment

Individuals who self-report a diagnosis of MCI, AD, dementia, and/or indicate they have been prescribed a medication for cognitive impairment or memory problems are identified as having possible cognitive impairment (see Table 1). The ECog-12 total score is also used as an indicator of possible cognitive impairment, with those scoring greater than or equal to 1.36 as possibly impaired. The cutoff score was calculated as the threshold of a derived ECog-12 score that best distinguished those with and without cognitive impairment in past ADNI data. Participants who complete the Novoic Storyteller test are also flagged as possibly cognitively impaired if their score is less than or equal to 49.4. The self-report ECog-12 and Storyteller cutoff scores may be revised in the future as more data are collected and analyzed.

2.7 | Selection criteria for referrals to Remote Blood and/or In-Clinic Cohorts

Clinical site capacity to screen new participants is the primary factor in timing the launch of digital marketing efforts to recruit into the Remote Digital Cohort as well as the subsequent cadence of referrals to sites. As clinical sites indicate readiness to receive referrals, results from the Remote Digital and/or Blood Cohorts are used to prioritize participant referrals from URP backgrounds, and/or those who may be cognitively impaired across multiple indicators (self-report data and/or the Novoic Storyteller data), and/or plasma AD biomarker data, if available. The goal is to utilize the Remote cohorts to enrich the In-Clinic Cohort with new participants who are likely to have MCI and/or be amyloid positive

by PET, as well as provide sites with individuals from URP backgrounds to help ADNI meet its inclusion/diversification goals.

The Remote Digital Cohort already includes more participants than the clinical sites can currently enroll. Since current clinical referral prioritization emphasizes referring URP individuals as well as those with multiple indicators of potential cognitive impairment, Remote Digital Cohort participants who do not have these characteristics may instead be offered the opportunity to join the Remote Blood Cohort. Participants with at least one indicator of possible cognitive impairment (such as a high ECog-12 score or a low Novoic Storyteller score) are referred to the Remote Blood Cohort when possible. The Remote Blood Cohort involves a participant visiting a Quest Diagnostics Patient Service Center (Quest PSC) location for a blood draw. Currently, individuals under consideration for referral to the Remote Blood Cohort must live within 25 miles of a Quest PSC. Future publications will discuss these referral processes and subsequent data from these cohorts in greater detail.

2.8 | Statistical methods

A logistic regression model was used to measure the association between a set of participant demographic factors (age, gender, race, ethnicity, and education level), with completion of the Novoic storyteller task. Completion rates of the ECog-12 task were sufficiently high (91%), such that a logistic regression model with the same set of independent variables underwent complete separation,[26] and failed to provide meaningful results.

We examined the association between these same demographic factors and self-reported evidence of cognitive impairment. Three separate univariate logistic regression models were constructed, with one of the following items included as the response variable in each model: (1) subjective memory concern; (2) self-reported decline in memory; and (3) self-reported a diagnosis of MCI, AD, dementia, or indication they have been prescribed a medication for cognitive impairment or memory problems.

For those participants who did complete the Novoic Storyteller task, a linear regression model was used to examine the association between these demographic factors and a score derived from performance on the Storyteller task. A generalized linear model (GLM) assuming a gamma likelihood[27] was used to evaluate the association between demographic factors and participant ECog-12 score. This model was chosen over the more conventional Gaussian GLM to better capture the association with a response that is both right-skewed and supported on a narrow range of strictly positive values.

3 | RESULTS

3.1 | Participants

A total of 3099 individuals provided contact information within the registration page of the study website. Of those, 654 (21%) enrolled in the Remote Digital Cohort, and 595 (91% of those enrolled) provided at least basic demographic information. In the entire enrolled cohort who answered demographic questions ($N = 595$), participants had a median age of 68, 75% were female, and 96% had > 12 years of education (Table 1). A total of 247 (42%) self-reported an ethnocultural and/or educational URP background.

Of those enrolled, 465 (78%) did not indicate any ADNI exclusions and are therefore likely to be eligible for ADNI4 in-clinic participation (Figure 1). The subset of likely-eligible participants had a median age of 67, 74% were female, and 97% had > 12 years of education. (Table 1). There was no difference between URP and non-URP groups in the percent who indicated exclusion criteria ($p = 0.61$). The remainder of the analyses are limited to the cohort that did not endorse ADNI exclusion criteria ($N = 465$).

3.2 | Completion rates

Completion rates were 91% for self-report ECog-12, 14% for study partner-report ECog-12, and 54% for Novoic Storyteller. URP participants had lower completion rates than non-URP participants for both tasks (Table 2). Completion rates were then compared for URP groups defined separately by race, ethnicity, and education (Tables S1–S3). Comparing completion rates in different race groups, those identifying as Black or Other race (a composite category including those who identify as Asian, multiple race selections, Native American, Pacific Islander, and Other) had lower Novoic Storyteller completion rates compared to those who identified as White ($p < 0.001$). Black participants had lower completion rates of study partner ECog-12 compared to White and other race groups ($p < 0.001$). There were no differences in completion rates in any assessment for Latinx versus non-Latinx participants but note that all study tasks were completed in English. Comparing completion rates by education, those with less than or equal to 12 years of education had lower completion rates for self-report ECog-12 ($p = 0.032$) and Novoic Storyteller ($p = 0.054$). In regression models including age, education, race, ethnicity, and evidence for cognitive impairment, self-identifying as Black/African American and older age were associated with lower odds of completing Novoic Storyteller (Figure 2).

3.3 | Evidence for cognitive impairment

Two main assessments, Novoic Storyteller and the self-reported ECog-12, were used to identify participants with likely cognitive impairment. A total of 73 participants (out of 250 completers; 30%) were likely impaired according to the Novoic Storyteller cutoff, and 188 (out of 421 completers; 45%) were likely impaired according to the ECog-12 cutoff. In a subset of 247 participants who completed both Storyteller and ECog-12, scores for the two assessments were correlated with Spearman's *rho* = −0.27 (Figure 3, Table 3). Agreement between Novoic Storyteller and ECog-12 was 68% (19% for both scores indicating impairment, 49% for neither score indicating impairment). (Table 3 and Figure 4). The relationship between Novoic Storyteller or self-report ECog-12 and additional indicators of cognitive impairment

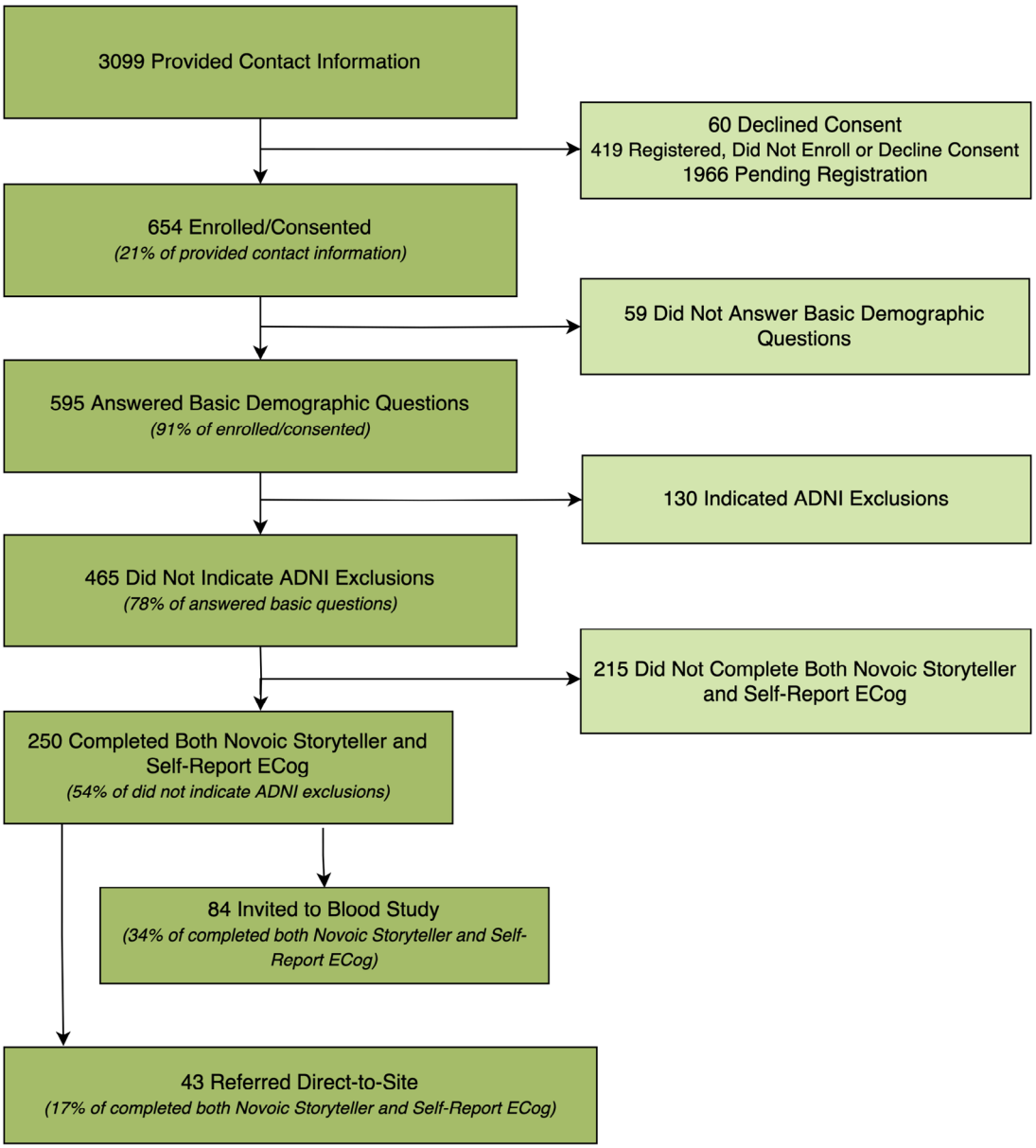

FIGURE 1 Consort diagram of participants included in the ADNI4 Remote Digital Cohort. ADNI, Alzheimer's Disease Neuroimaging Initiative; ECog-12, Everyday Cognition 12-item questionnaire.

(i.e., subjective memory concern, subjective memory change, self-report of diagnosed cognitive impairment) are shown in Figures S1 and S2.

3.4 | Association between evidence for cognitive impairment and participant demographics

In the multivariable gamma GLM, higher ECog-12 scores (indicating report of more subjective cognitive change) were associated with Black/African American ethnocultural status and more years of education. Higher (better) Novoic Storyteller scores were associated with younger age, identifying as female, more years of education, and White ethnocultural status compared to Black/African Americans. (Table S4). Those with fewer years of education had increased odds of endorsing a memory concern. Males had increased odds of endorsing a recent change in memory. Those who were younger and those who self-identified as Black/African American had reduced odds of reporting a diagnosis of MCI, AD, or dementia. (Figure S3A–C).

3.5 | Participant support and feedback

The study staff received a total of 274 questions/support requests via Zendesk, including 91 via email, 69 via online messaging, and 114 via telephone. The most frequent areas of support requested were for Remote Digital Cohort technical support and support for the Remote Blood Cohort. Breakdown of support requests by topic area are shown

TABLE 2 Completion rates of self-report ECog-12 and Novoic Storyteller tasks among participants who did not indicate ADNI exclusions, stratified by URP vs. non-URP.

Parameter	Total (*N* = 465)	Non-URP (*N* = 275)	URP (*N* = 190)	*p*-value[a]
Self-Report ECog-12	421 (91%)	257 (93%)	164 (86%)	<0.001
Study Partner-Report ECog-12	67 (14%)	58 (21%)	9 (5%)	<0.001
Novoic Storyteller	250 (54%)	174 (63%)	76 (40%)	0.010

Abbreviation: ADNI, Alzheimer's Disease Neuroimaging Initiative; ECog-12, Everyday Cognition 12-item questionnaire; URP, underrepresented populations.
[a]Pearson's chi-squared test.

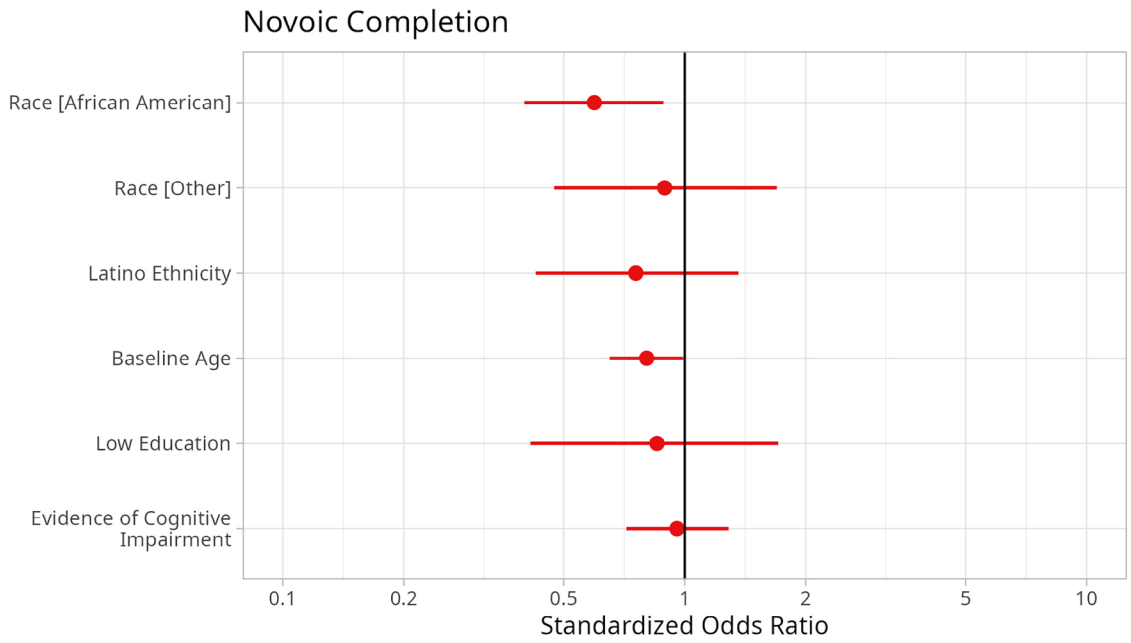

FIGURE 2 Association between demographic and cognitive characteristics and completion of Novoic Storyteller assessment. Results of logistic regression with completion of Novoic Storyteller as the dependent variable. Odds ratios and 95% confidence intervals for each independent variable are displayed.

in Table 4. All requests were responded to by ADNI's Community Research Navigators.

4 | DISCUSSION

The major findings of this study are (1) Digital recruitment, screening, and assessment of diverse cohort older adults are feasible using an online, unsupervised portal. Our culturally-informed digital recruitment efforts enrolled 42% URPs, defined by ethnocultural identity and/or education level. (2) Indication of ADNI4 in-clinic exclusion criteria did not differ by ethnocultural groups or education level. (3) Completion rates of key digital assessments (91% for self-report ECog-12, 54% for Novoic Storyteller) indicate overall good usability and compliance. Lower Novoic completion rates suggest that technical constraints and participant burden may limit compliance. (4) ECog-12 and Novoic Storyteller completion rates were lower for URPs, which may affect inclusion of diverse populations in subsequent study activities. (5) Recruitment of diverse older adults with likely cognitive impairment is feasible. Depending on criteria used, 29%–51% of eligible participants were likely to have cognitive impairment. (6) A large number of participant requests for additional technical support highlight the need to provide such assistance in digital assessment studies. Taken together, the results support the feasibility, acceptability, and usability of the approach. Key challenges are improving engagement strategies to maximize completion rates, especially for URPs; and achieving more educational diversity. Once validated as an effective method to enroll for in-clinic ADNI, this approach can be adapted to facilitate efficient recruitment, screening, prioritization, and assessment in other AD studies and trials, and in healthcare and public health settings.

A major goal of this inclusion and engagement approach is to increase participation of those from historically under-included ethnocultural and educational groups in ADNI4. Our results support feasibility enrolling Black older adults. Of the 595 participants enrolled, 31% identified as Black/African American. However, we failed to adequately include those from other URP ethnocultural groups, including Latinx:

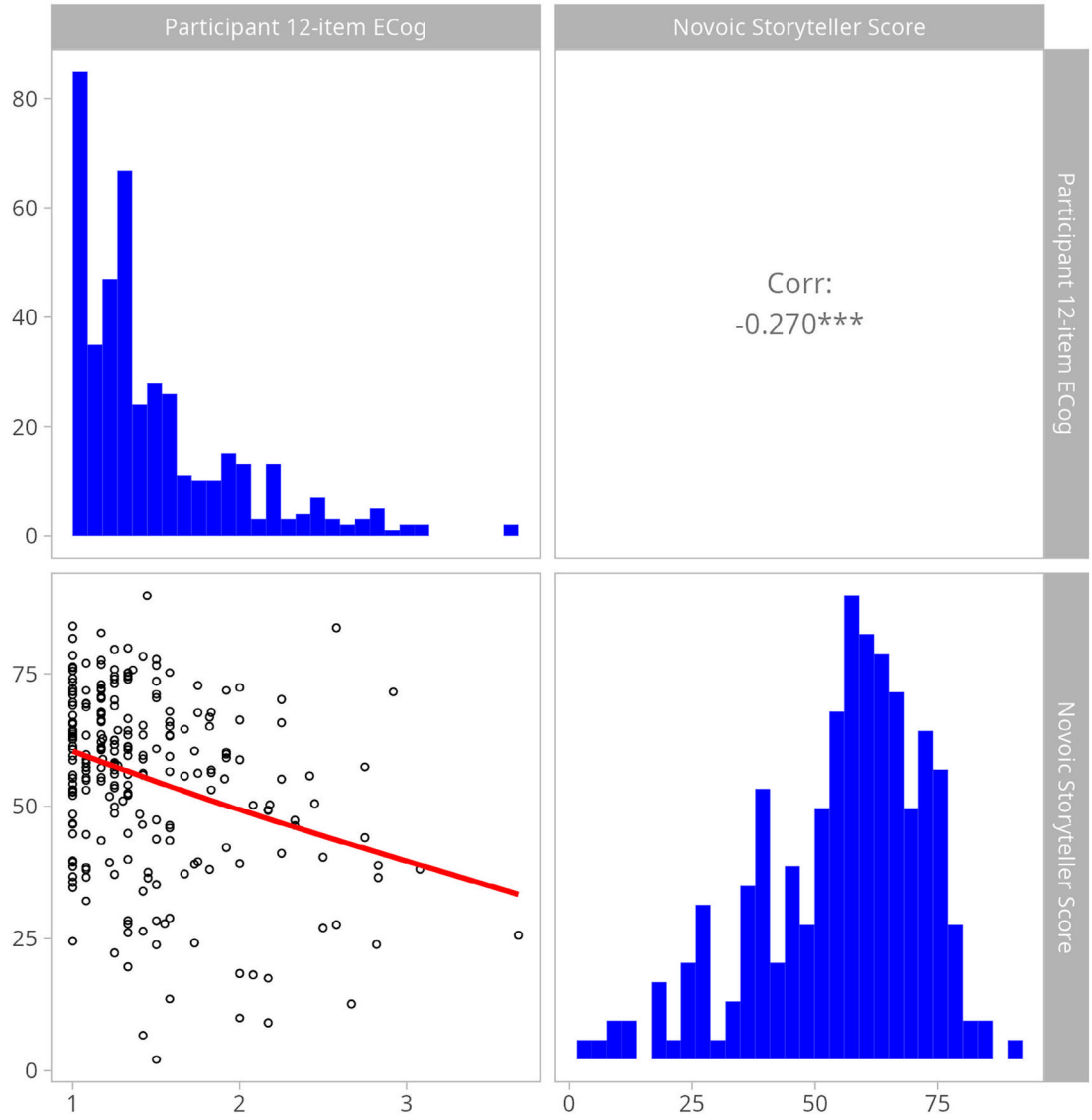

FIGURE 3 Score distributions and correlation between Novoic Storyteller and Self-Report ECog-12. Score distributions for Self-Report ECog-12 and Novoic Storyteller, with a scatter plot of assessment scores. Spearmans *rho* = –0.27. ECog-12, Everyday Cognition 12-item questionnaire.

TABLE 3 Table of agreement between Self-Report ECog-12 and Novoic Storyteller scores among participants who did not indicate ADNI exclusions, indicating likely/not likely cognitively impaired.

	Novoic Storyteller		
Self-Report ECog-12	*Not-impaired (n =)*	*Impaired (n =)*	*Total (n =)*
Not-impaired (n =)	121	27	148
Impaired (n =)	53	46	99
Total (n =)	174	73	247

Abbreviations: ADNI, Alzheimer's Disease Neuroimaging Initiative; ECog-12, Everyday Cognition 12-item questionnaire.

(5%) and other non-White (4%); and those with high school education or less (4%). Many factors likely contribute to these limitations, including the geographical reach of digital advertising and that currently the study is only available in English. Further, the initial recruitment efforts were limited to the catchment areas of the first of 65 ADNI sites ready to enroll new participants in-clinic (Mayo Clinic, Universities of Kansas and Kentucky), in which the population of Latinx older adults is quite low. Additional contributing factors are reliance on Meta as the sole platform for digital advertising, and use of email as our primary communication format. New approaches are being proposed to address Latinx inclusion moving forward. Our failure to recruit participants with low education levels is a general problem with many AD studies and trials. Future recruitment materials will be designed to reach those with lower educational levels. Also, further analysis of the comparative effectiveness of specific ads and other outreach efforts are needed to understand how to better include all URP groups.

The completion rates for study procedures (survey responses and the Storyteller assessment) provide insight into participant

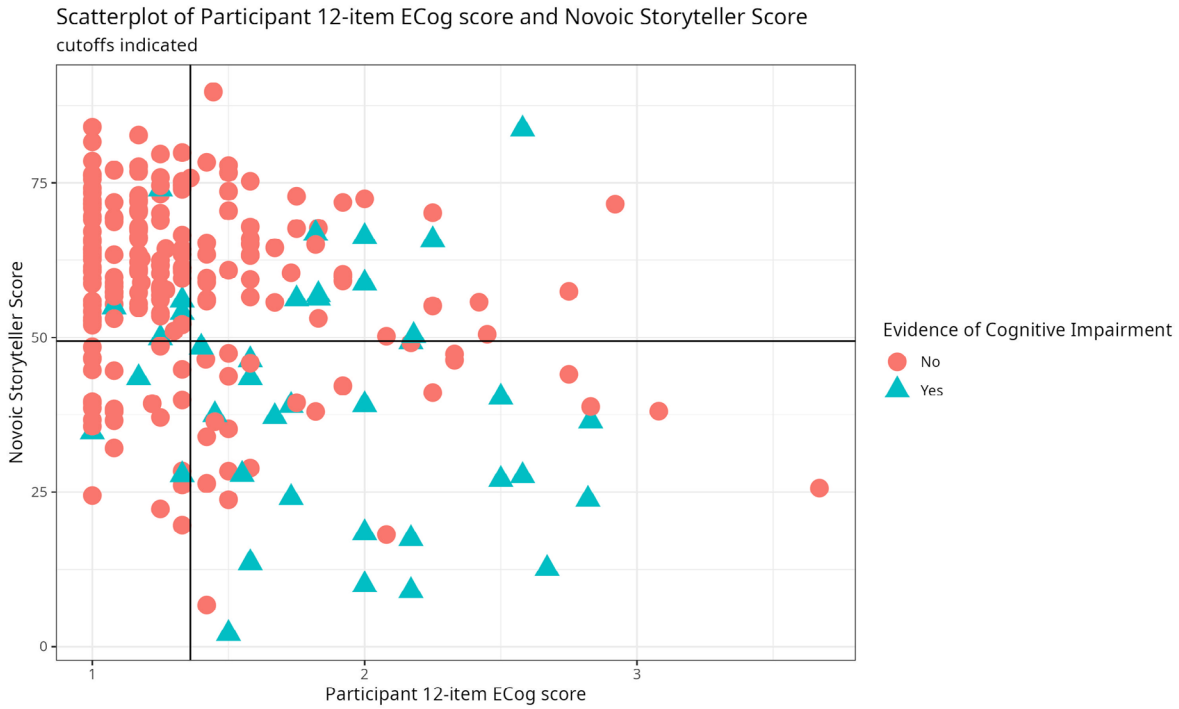

FIGURE 4 Evidence for cognitive impairment indicated by Novoic Storyteller and Self-Report ECog-12 scores. Scatter plot of Novoic Storyteller and Self-Report ECog-12 scores, with cut offs for likely impairment (49.4 for Novoic Storyteller G-match, 1.36 for total Self-Report ECog-12 score) indicated by black lines. Points are color coded according to whether the participant indicated additional evidence for cognitive impairment (self-report of MCI, dementia, or AD and/or taking a medication for cognitive impairment). AD, Alzheimer's disease; ECog-12, Everyday Cognition 12-item questionnaire; MCI, mild cognitive impairment.

engagement, and feasibility of using this approach to screen and prioritize participants for inclusion in in-clinic ADNI. Overall completion rates for survey questions, including self-report ECog-12, were > 90%, indicating high compliance. Completion rates for study partner ECog-12 were low (14%), which is consistent with completion rates in BHR.[10] Since study partner information has been found to be a reliable and accurate source of information about the associated participant, we plan to develop and evaluate methods to improve study partner inclusion in future studies. Completion rates for Novoic Storyteller (54%) were much lower than for survey responses. This, too, is consistent with completion rates for digital neuropsychological assessments in BHR[10] and is likely influenced by many factors, including participant burden and technological constraints. The Storyteller assessment is one of the last tasks that participants encounter. It requires participants to enable microphone and speaker use on their device, and that participants are in a quiet place without distractions for ~10 min. An issue for Android users operating the Facebook in-app Web browser made them unable to access their microphone and unable to complete Storyteller. A solution has recently been implemented to redirect those participants to a new Web browser. For both ECog-12 and Storyteller, completion rates were lower for URP than non-URP participants. This is an important selection bias that limits the external validity and generalizability of results. We plan to explore strategies to increase completion rates, such as expanded use of Clinical Research Navigators[28] to remind participants to complete tasks and support those requiring assistance. In addition, we will develop and evaluate culturally informed participant communications to encourage task completion.

A major goal of this study is to enrich the sample for those with cognitive impairment, who are likely to qualify for enrollment in the MCI arm of in-clinic ADNI4. The goal is to enroll 40% with MCI into the ADNI4 In-Clinic study. However, digital recruitment strategies have known selection biases for cognitively unimpaired older adults.[10,29,30] Thus, we are deploying digital advertising directed towards those who may have cognitive impairment, such as ads with messages about memory concerns. ECog-12 and Storyteller were the main assessments chosen as indicators of possible cognitive impairment, based on past evidence of their ability to identify older adults with MCI.[25,31] A total of 51% of participants who completed either ECog-12 or Novoic had assessment scores meeting the cutoff for possible cognitive impairment, supporting the effectiveness of the approach to enrich for cognitive impaired individuals in the Digital Cohort.

Agreement between self-report ECog-12 and Storyteller in identifying cognitive impairment was 68%, with ECog-12 identifying more participants as cognitively impaired (47%) than Storyteller (30%). Many factors are likely to contribute to disagreement between the two assessments. The cutoffs used were not established in diverse populations due to lack of available data. Our approach provides an opportunity to validate ECog-12 and Novoic in URPs. Additional factors are likely to contribute to performance on these assessments, including many sociocultural and structural factors. Future studies are needed to more fully understand these influences. Further, ECog-12

TABLE 4 ADNI4 Zendesk support tickets received by topic.

Topic	Support tickets, (*N* = 274)
General study inquiries	
Study details (participant or non-participant)	15 (5%)
Digital study inquiries (non-technical)	
Joining the study	39 (14%)
Operational details (participant)[a]	32 (12%)
Digital study technical support	
Novoic Storyteller	20 (7%)
Other technical difficulties	55 (20%)
Referral studies	
Blood study	72 (26%)
In-Clinic study	20 (7%)
Other topics	
Feedback and non-study related comments[b]	21 (8%)

Abbreviations: ADNI, Alzheimer's Disease Neuroimaging Initiative.
[a]An example of "operational details" is participants who are outside of their 30-day window to complete assessments but reach out indicating they would still like to complete them.
[b]Examples of "feedback and non-study related comments" include messages thanking the study staff and requesting collaboration.

accuracy may be influenced by participant mood, personality traits, denial, and lack of awareness of cognitive impairment dementia.[32,33] Subjective cognitive decline may be overestimated by "worried well" participants who are motivated to join because of their worry. A crucial next step is to validate the approach in participants who are subsequently selected for in-clinic ADNI, by comparing results of digital assessment to confirmed clinical diagnosis and cognitive performance. Based on these findings, we plan to adjust criteria used to define cognitive impairment in the digital study.

Finally, we investigated the amount of individual support requested by participants to complete the digital study. We received a total of 274 support requests or study inquiries. Since a single participant can initiate multiple inquiries, we do not know the total percentage of participants who required support. However, the large number of inquiries suggests that it is important to provide such support in digital assessment protocols. Although this somewhat limits the scalability of the approach, it is crucial for inclusion and engagement of diverse populations. Further, many requests can be addressed using automated responses to limit resources needed. The most frequent inquiries were questions about the Remote Digital, Remote Blood, and/or In-Clinic studies. Requests for technical support (75 support tickets; 27% of total tickets), suggesting that diverse populations of older adults may face issues related to digital literacy that limit their inclusion in online studies.

This study has some limitations. The remote, digital approach causes a selection bias for those with access to an Internet-connected device and adequate familiarity with digital tools to complete enrollment and study tasks. The small number of participants from some ethnocultural groups (e.g., Asian, Latinx, Native American, Pacific Islander) limited our ability to investigate task completion and assessment results in these groups. Additionally, the ADNI online experience is limited to those who read and speak English but will expand to include Spanish-language participants in the future. Finally, a lack of validated cutoffs for the self-report ECog-12 and Novoic Storyteller test, including ethnoculturally and educationally diverse individuals, limits the robustness and interpretation of the current data.

For the remainder of ADNI4, we plan to expand this effort to facilitate national recruitment into in-clinic ADNI4 across 65 clinical sites, with the goal of enrolling 500 new participants: > 50% from URP groups and 40% with MCI. Based on responses to digital assessments, a subset of participants will be chosen to join the Remote Blood Cohort, in which they will get a blood draw at a local Quest Diagnostics Patient Service Center, and plasma will be analyzed for AD biomarkers. Based on the results of the Remote Cohorts, a subset will be referred to clinical ADNI sites, with the goal of enrolling 80% with elevated AD biomarkers across diagnostic groups. Future analyses will evaluate the "multi-tier" screening approach from the Remote Digital Cohort to Remote Blood to In-Clinic ADNI to enrich for URP participants and/or those with cognitive impairment and elevated AD biomarkers.

In conclusion, our results support the feasibility of a remote, digital, Internet-based approach for recruitment, screening, and assessment of diverse older adults for AD observational research. Important challenges are achieving more robust ethnocultural and educational diversity, and improving study task completion of all participants, especially URPs. Once validated and optimized, this approach can be adapted to facilitate recruitment, screening, and longitudinal assessment in other AD studies and trials and possibly serve as the framework for public health screening for AD and related cognitive disorders.

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CONFLICT OF INTEREST STATEMENT

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CONSENT STATEMENT

All human subjects provided informed consent.

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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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