

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16

Supplemental Online Content

Wilkins CH, Windon CC, Dilworth-Anderson P, et al. Racial and ethnic differences in amyloid PET positivity in individuals with mild cognitive impairment or dementia: a secondary analysis of the Imaging Dementia–Evidence for Amyloid Scanning (IDEAS) cohort study. *JAMA Neurol.* Published online October 3, 2022. doi:10.1001/jamaneurol.2022.3157

- eMethods**
- eResults**
- eReferences**

This supplemental material has been provided by the authors to give readers additional information about their work.

17 **eMethods**

18

19 *Inclusion and Exclusion Criteria in IDEAS*

20 The inclusion criteria for the IDEAS study included: 1) 65 and older; 2) Medicare beneficiary with
21 Medicare as primary insurance; 3) Diagnosis of MCI or dementia, according to DSM-IV and/or
22 National Institutes of Aging-Alzheimer's Association criteria, verified by a dementia specialist
23 within 24 months¹⁻³; 4) Meets Appropriate use criteria (Cognitive complaint with objectively
24 confirmed impairment; The etiologic cause of cognitive impairment is uncertain after a
25 comprehensive evaluation by a dementia specialist, including general medical and neurological
26 examination, mental status testing including standard measures of cognitive impairment,
27 laboratory testing, and structural neuroimaging as below; Alzheimer's disease is a diagnostic
28 consideration; Knowledge of amyloid PET status is expected to alter diagnosis and
29 management.); 5) Head MRI and/or CT within 24 months prior to enrollment; 6) Clinical
30 laboratory assessment (complete blood count [CBC], standard blood chemistry profile, thyroid
31 stimulating hormone [TSH], vitamin B12) within the 12 months prior to enrollment; 7) Able to
32 tolerate amyloid PET required by protocol, to be performed at a participating PET facility; 8)
33 English or Spanish speaking (for the purposes of informed consent); 9) Willing and able to
34 provide consent. Consent may be by proxy.

35 Exclusion criteria for IDEAS included: 1) Normal cognition or subjective complaints that are not
36 verified by cognitive testing; 2) Knowledge of amyloid status, in the opinion of the referring
37 dementia expert, may cause significant psychological harm or otherwise negatively impact the
38 patient or family; 3) Amyloid status already known to patient or referring clinician based on prior
39 amyloid imaging or cerebrospinal fluid analysis; 4) Current or previous enrollment in an anti-
40 amyloid therapeutic trial; 5) Scan is being ordered solely based on a family history of dementia,
41 presence of apolipoprotein E (APOE) 4, or in lieu of genotyping for suspected autosomal
42 mutation carriers; 6) Scan being ordered for nonmedical purposes (e.g., legal, insurance
43 coverage, or employment screening); 7) Cancer requiring active therapy (excluding non-

44 melanoma skin cancer); 8) Hip/pelvic fracture within the 12 months prior to enrollment; 9) Body
45 weight exceeds PET scanner weight limit; 10) Life expectancy less than 24 months based on
46 medical co-morbidities; 11) Residence in a skilled nursing facility.

47 (https://cdn.jamanetwork.com/ama/content_public/journal/jama/937922/joi190021supp1_prod.pdf?Expires=1659472364&Signature=WjHQR89YuHwGKKecqwqX5cl8h~fF0O0cTUcmhm3T9KJYHweyQqPaxRrV0n66VJjVeTEJ-BvemHRvoCTh8qlz~bt4pgp4PSUVnF3nBKRHTx4ciXbimeaSBaWTngFGPiwEvlb5dSDil4dHFfNwctlygtPnLAnDBiS6vKFw4si1Qo~3OSeQHv5z6honakNNYbTr9O1h3qYDjiYJpyT1wY3wU-b4xEIDEDf9kNubb9GQ3HKXy53VCYVGyD5St7qBNhnx0Ju5rbNxaIw7pePLRAwVLTOQFOKnJpGUZXPOzmrChDXAoSWwmqSpFfkZ6H8ZAUxjD2NysW15zvOUotKSKMmiOw &Key-Pair-Id=APKAIE5G5CRDK6RD3PGA).

56 *Race and Ethnicity Reporting in IDEAS*

57 In IDEAS, race and ethnicity of participants was recorded by dementia specialists into a
58 minimum of 1 race category (American Indian, Alaskan Native, Asian, Black or African
59 American, Native Hawaiian or Pacific Islander, White, Not reported, Unknown) and a minimum
60 of 1 ethnicity category (Hispanic or Latino, not Hispanic or Latino, not reported, unknown).
61 Dementia specialists were not given instruction by the study protocol or registration form on how
62 race and ethnicity were to be determined⁴, therefore, we do not if or which participants were
63 directly asked to self-identify race and ethnicity.

65 *Amyloid PET Scan Interpretation and Communication of Results in IDEAS*

66 In the IDEAS study, amyloid PET scans were interpreted by radiologists or nuclear medicine
67 physicians at respective PET facilities that agreed to participate in the IDEAS study. Each
68 radiologist or nuclear medicine physician provided a dichotomized interpretation of the amyloid
69 PET scan (positive or negative). All radiologists and nuclear medicine physicians who
70 participated in the interpretation of PET scans had completed vendor-provided online or in-
71 person training courses specific to the amyloid imaging agent(s) used at his or her PET facility.
72 Amyloid PET scan reads were then uploaded to the IDEAS database within 7 days of

73 completing the PET scan read. Additional information regarding PET scan interpretation and
74 report submission can be found in the original protocol

75
76 (https://cdn.jamanetwork.com/ama/content_public/journal/jama/937922/joi190021supp1_prod.pdf?Expires=1659472364&Signature=WjHQR89YuHwGKKecqwqX5cl8h~fF0O0cTUcmhm3T9KJYHweyQqPaxRrV0n66VJjVeTEJ-BvemHRvoCTh8glz~bt4pgp4PSUVnF3nBKRHTx4ciXbimeaSBaWTngFGPiwEvlb5dSDil4dHFfNwctlygtPnLAnDBiS6vKfw4si1Qo~3OSeQHv5z6honakNNYbTr9O1h3qYDjiYJpyT1wY3wU-b4xEIDEDf9kNubb9GQ3HKXy53VCYVGyD5St7gBNhnx0Ju5rbNxaW7pePLRAwVLTOQFOKnJpGUZXPOzmrChDXAoSWwmqSpFfkZ6H8ZAUxjD2NysW15zvOUotKSKMmiOw_&Key-Pair-Id=APKAIE5G5CRDK6RD3PGA).

85 *Optimal Matching Strategy*

86 To compare the amyloid PET positivity rate between racial and ethnic minority groups and
87 White participants, optimal 1:1 matching (Black to White, Hispanic to White, Asian to White; all 3
88 White groups unique) to obtain minimal distances between matches using network flow
89 optimization methods⁵⁻⁷ created balanced groups with respect to their baseline characteristics.
90 Variables used for matching were recorded in case report forms at IDEAS study entry and
91 included age (matching within ± 3 years), sex, highest level of education attained, living
92 arrangement (with whom do you reside; coded into alone/not alone for purposes of analyses),
93 history of hypertension, history of diabetes, family history of dementia, and level of impairment
94 (MCI or dementia).

95

96

97 **eResults**

98 Because higher percentages of Black, Hispanic/Latinx and Asian patients had vascular disease
 99 risk factors (e.g., diabetes) and were more likely to have dementia (vs MCI) relative to White
 100 patients, we examined whether there were differences in ADRD subtype across racial and
 101 ethnic categories. Past medical history of stroke, TIA, and CVD were similar across racial and
 102 ethnic groups (Supplemental Table 5). Pre-PET diagnosis of vascular cognitive impairment was
 103 similar across the groups, however, pre-PET diagnosis of mixed AD pathology was higher
 104 among Black (15.75%) and Hispanic (13.15%) participants compared to White (10.78%) and
 105 Asian (10.28%) (Supplemental Table 6). No additional imaging data is available to examine
 106 cerebrovascular disease.

107

108

109

110 **Supplemental Table 1 – Recoding Separate IDEAS Race and Ethnicity Questions**

IDEAS race and ethnicity questions		Race and Ethnicity used for the analysis
Race (Select all that apply)	Hispanic origin	
White only	Not Hispanic or Latino, Not reported, or Unknown	White
Black or African American only	Not Hispanic or Latino, Not reported, or Unknown	Black
Asian only	Not Hispanic or Latino, Not reported, or Unknown	Asian
Only one of <ul style="list-style-type: none"> • American Indian • Alaska Native • Native Hawaiian or Pacific Islander 	Not Hispanic or Latino, Not reported, or Unknown	Indigenous

<p>Only one of:</p> <ul style="list-style-type: none"> • White • Black or African American • Asian • American Indian • Alaska Native • Native Hawaiian or Pacific Islander • Not reported • Unknown 	Hispanic or Latino	Hispanic
<p>More than one of:</p> <ul style="list-style-type: none"> • White • Black or African American • Asian • American Indian • Alaska Native • Native Hawaiian or Pacific Islander 	Any ethnicity	Multiracial
Not reported or Unknown	Not Hispanic or Latino, Not reported, or Unknown	Not reported or Unknown

111
112
113

114 **Supplemental Table 2 - Results From Optimal 1:1 Matching**
 115

Variable	Matched participants		Matched participants		Matched participants	
	Asian (n=313)	White (n=313)	Black (n=615)	White (n=615)	Hispanic (n=780)	White (n=780)
Age, median (range), years	76 (65-91)	76 (65-91)	75 (65-95)	75 (65-93)	76 (65-93)	76 (65-92)
Sex, No. (%)						
Male	150 (47.9)	150 (47.9)	226 (36.7)	226 (36.7)	303 (38.8)	303 (38.8)
Female	163 (52.1)	163 (52.1)	389 (63.3)	389 (63.3)	477 (61.2)	477 (61.2)
Education, No. (%)						
Less than high school	40 (12.8)	40 (12.8)	101 (16.4)	101 (16.4)	279 (35.8)	279 (35.8)
High school (including equivalency)	62 (19.8)	62 (19.8)	215 (35.0)	215 (35.0)	201 (25.8)	201 (25.8)
Some college or associate degree	40 (12.8)	40 (12.8)	129 (21.0)	129 (21.0)	149 (19.1)	149 (19.1)
Bachelor's degree	98 (31.3)	98 (31.3)	88 (14.3)	88 (14.3)	74 (9.5)	74 (9.5)
Master's degree	29 (9.3)	29 (9.3)	55 (8.9)	55 (8.9)	42 (5.4)	42 (5.4)
Doctorate	44 (14.1)	44 (14.1)	27 (4.4)	27 (4.4)	35 (4.5)	35 (4.5)
Living arrangement, No. (%)						
Patient lives alone	35 (11.2)	35 (11.2)	146 (23.7)	146 (23.7)	115 (14.7)	115 (14.7)
Patient lives with at least one other person	278 (88.8)	278 (88.8)	469 (76.3)	469 (76.3)	665 (85.3)	665 (85.3)
History of hypertension, No. (%)						
No	169 (54.0)	169 (54.0)	193 (31.4)	193 (31.4)	351 (45.0)	351 (45.0)

Yes	144 (46.0)	144 (46.0)	422 (68.6)	422 (68.6)	429 (55.0)	429 (55.0)
History of diabetes, No. (%)						
No	240 (76.7)	240 (76.7)	448 (72.8)	448 (72.8)	595 (76.3)	595 (76.3)
Yes	73 (23.3)	73 (23.3)	167 (27.2)	167 (27.2)	185 (23.7)	185 (23.7)
Family history of dementia, No. (%)						
No	273 (87.2)	273 (87.2)	516 (83.9)	516 (83.9)	647 (82.9)	647 (82.9)
Yes	40 (12.8)	40 (12.8)	99 (16.1)	99 (16.1)	133 (17.1)	133 (17.1)
Impairment level, No. (%)						
MCI	168 (53.7)	168 (53.7)	302 (49.1)	302 (49.1)	356 (45.6)	356 (45.6)
Dementia	145 (46.3)	145 (46.3)	313 (50.9)	313 (50.9)	424 (54.4)	424 (54.4)

116 MCI = mild cognitive impairment
117
118

119
120
121

Supplemental Table 3 – Race and ethnicity of participants that did not have an amyloid PET scan performed

	Eligible (N=21,630)	Amyloid PET scan not performed (N=3,337)
Race or Ethnicity	N	N (%)
Asian	394	73 (18.5)
Black	806	169 (21.0)
Hispanic	1,119	290 (25.9)
White	17,801	2,452 (13.8)
Other	41	9 (22.0)
Multiracial	37	6 (16.2)
Not reported or Unknown	1,432	338 (23.6)

122
123

Note: Percentages are out of the number of participants in each race or ethnicity that are eligible.

124 **Supplemental Table 4 – Race/Ethnicity of participants that did not have an amyloid PET scan performed by**
 125 **highest level of education**

Education	Race and Ethnicity							Total
	Asian	Black	Hispanic	White	Other	Multiracial	Not reported or Unknown	
Less than high school	9 (12.3)	21 (12.4)	102 (35.2)	130 (5.3)	0 (0.0)	1 (16.7)	49 (14.5)	312 (9.3)
High school (including equivalency)	10 (13.7)	56 (33.1)	86 (29.7)	679 (27.7)	2 (22.2)	2 (33.3)	88 (26.0)	923 (27.7)
Some college or associate degree	13 (17.8)	44 (26.0)	37 (12.8)	614 (25.0)	3 (33.3)	2 (33.3)	62 (18.3)	775 (23.2)
Bachelor's degree	15 (20.5)	18 (10.7)	20 (6.9)	415 (16.9)	2 (22.2)	0 (0.0)	50 (14.8)	520 (15.6)
Master's degree	5 (6.8)	9 (5.3)	4 (1.4)	185 (7.5)	0 (0.0)	0 (0.0)	24 (7.1)	227 (6.8)
Doctorate	10 (13.7)	4 (2.4)	6 (2.1)	111 (4.5)	1 (11.1)	0 (0.0)	12 (3.6)	144 (4.3)
Missing	11 (15.1)	17 (10.1)	35 (12.1)	318 (13.0)	1 (11.1)	1 (16.7)	53 (15.7)	436 (13.1)
Total	73 (100.0)	169 (100.0)	290 (100.0)	2,452 (100.0)	9 (100.0)	6 (100.0)	338 (100.0)	3,337 (100.0)

126 Note: Percentages are column percentages

127

128 **Supplemental Table 5 – Select past/current medical history variables by race and**
 129 **ethnicity**

130
 131

Variable	Race and Ethnicity			
	White (n=15,322)	Hispanic/Latino (n=829)	Black/African American (n=635)	Asian (n=321)
History of stroke or TIA, No. (%)	1,606 (10.5)	75 (9.0)	67 (10.6)	31 (9.7)
History of CVD without stroke, No. (%)	794 (5.2)	56 (6.8)	35 (5.5)	16 (5.0)
Total	2,400 (15.7)	131 (15.8)	102 (16.1)	47 (14.7)

132
 133

134 **Supplemental Table 6 Primary pre-PET differential diagnosis by race and ethnicity**

135

Pre-PET primary differential diagnosis	Race and Ethnicity			
	Asian	Black/African American	Hispanic/Latino	White
Vascular cognitive impairment	19	37	45	839
	5.92%	5.83%	5.43%	5.48%
AD, mixed pathology	33	100	109	1,652
	10.28%	15.75%	13.15%	10.78%

136
 137
 138

139 **eReferences**

140 1. American Psychiatric Association. (2000). *Diagnostic and statistical manual of mental*
141 *disorders* (4th ed., text rev.).

142 2. McKhann GM, Knopman DS, Chertkow H, et al. The diagnosis of dementia due to
143 Alzheimer's disease: recommendations from the National Institute on Aging-Alzheimer's
144 Association workgroups on diagnostic guidelines for Alzheimer's disease. *Alzheimers*
145 *Dement.* 2011;7(3):263-269. doi:10.1016/j.jalz.2011.03.005

146 3. Albert MS, DeKosky ST, Dickson D, et al. The diagnosis of mild cognitive impairment
147 due to Alzheimer's disease: recommendations from the National Institute on Aging-
148 Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease.
149 *Alzheimers Dement.* 2011;7(3):270-279. doi:10.1016/j.jalz.2011.03.008

150 4. Rabinovici GD, Gatsonis C, Apgar C, et al. Association of Amyloid Positron Emission
151 Tomography With Subsequent Change in Clinical Management Among Medicare
152 Beneficiaries With Mild Cognitive Impairment or Dementia. *JAMA.* 2019;321(13):1286-
153 1294. doi:10.1001/jama.2019.2000

154 5. Rosenbaum P. Optimal Matching for Observational Studies. *Journal of the American*
155 *Statistical Association.* 1989; 84(408): 1024-1032.

156 6. Carre, B. (1979), *Graphs and Networks*, New York: Oxford University
157 Press

158 7. Ford, L., and Fulkerson, D. (1962), *Flows in Networks*, Princeton, NJ:
159 Princeton University Press
160