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Amyloid PET imaging in self-identified non-Hispanic Blacks from the Anti-Amyloid in Asymptomatic Alzheimer's Disease (A4) Study – Supplementary Data

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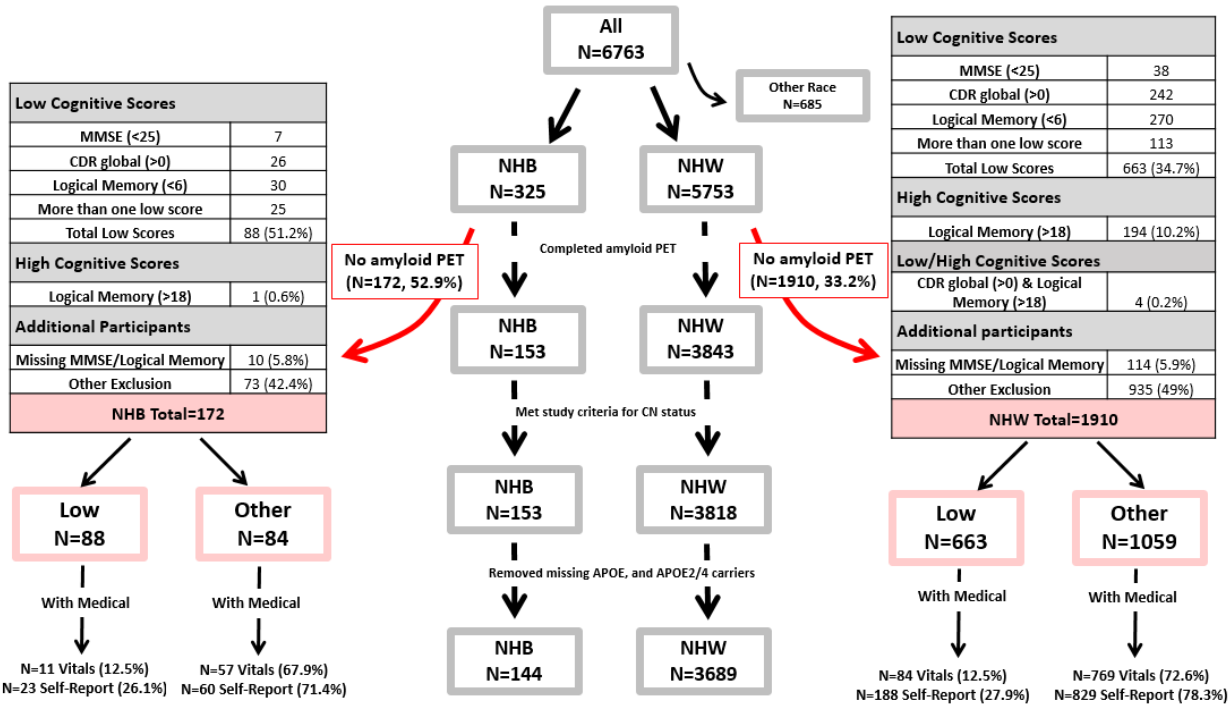
Abstract
The goal of the manuscript was to examine whether amyloid PET in CN individuals that were screened for the Anti-Amyloid in Asymptomatic AD (A4) study differed across self-identified, non-Hispanic White and Black (NHW and NHB) groups. We examined 3685 NHW and 144 NHB that passed initial screening for the A4 study and underwent amyloid PET. The effect of race on amyloid PET was examined using logistic (dichotomous groups) and linear (continuous values) regression controlling for age, sex, and number of *APOE ε4* and *APOE ε2* alleles. Lifestyle factors and medical conditions were available for the majority of individuals that received an amyloid PET scan. Additional sensitivity analyses were run to examine potential effects between amyloid and lifestyle as well as self-reported medical conditions that differed by race. Reduced amyloid was observed in self-identified non-Hispanic Blacks that passed initial eligibility criteria for the A4 Study, but lifestyle and vascular factors did not impact this effect. This work stresses the importance of investigating AD biomarkers in ancestrally diverse samples as well as the need for careful consideration regarding study eligibility criteria in AD prevention trials.



Supplementary Figure 1: Flowchart of study design showing all screening data used throughout the manuscript. Among "screen-fail" participants not eligible for amyloid PET, additional data is shown regarding screen-fail as a function of neuropsychological cut offs. Participants are listed for exclusion based on individual testing criteria if exclusion was based on single criteria, and classified as more than 1 if excluded based on 2 or more criteria (MMSE, CDR, and/or Logical Memory). Participants that were excluded for exceeding the upper bound of allowable logical memory scores are also listed. Remaining participants that were excluded but had testing scores within the eligible range are listed as unknown and could be due to co-morbid conditions, participant withdrawal, etc.

	NHB	NHW full	NHW Matched
N	144	3689	288
Age (years)	70.77 (4.87)	71.24 (4.67)	70.72 (4.44)
Education[1] (years)	16.10 (2.76)	16.65 (2.83)	16.27 (2.63)
Sex (Female)[1]	105 (72.9)	2199 (59.6)	215 (74.7)
Lifestyle Factors			
Endorse current Smokers[1]	5 (3.5)	45 (1.2)	4 (1.4)
Endorse current Alcohol[1, 2]	34 (23.8)	1886 (51.1)	141 (49.0)
Systolic BP[1, 2]	139.98 (16.76)	136.50 (16.32)	136.07 (15.96)
Diastolic BP[1, 2]	79.56 (9.88)	76.41 (9.34)	76.39 (8.67)
BMI[1, 2]	30.17 (6.17)	27.54 (5.03)	27.37 (4.89)
Self-Reported Medical Conditions, N (%)			
Psychiatric[1, 2]	25 (17.4)	1093 (29.6)	99 (34.4)
Neurologic (other than AD)[1]	31 (21.5)	1139 (30.9)	83 (28.8)
Head, Eyes, Ears, Nose, Throat[1,2]	66 (45.8)	2023 (54.8)	164 (56.9)
Cardiovascular[1, 2]	106 (73.6)	2399 (65.0)	178 (61.8)
Respiratory	22 (15.3)	814 (22.1)	59 (20.5)
Hepatic	6 (4.2)	120 (3.3)	5 (1.7)
Dermatologic-Connective Tissue[1, 2]	24 (16.7)	1198 (32.5)	102 (35.4)
Musculoskeletal	101 (70.1)	2596 (70.4)	219 (76.0)
Endocrine-Metabolic	75 (52.1)	1910 (51.8)	157 (54.5)
Gastrointestinal[1, 2]	53 (36.8)	1723 (46.7)	144 (50.0)
Hematopoietic-Lymphatic	14 (9.7)	354 (9.6)	26 (9.0)
Renal-Genitourinary	47 (32.6)	1488 (40.3)	104 (36.1)
Allergies or Drug Sensitivities	55 (38.2)	1420 (38.5)	124 (43.1)
Smoking, Alcohol Use, and/or Drug Use	7 (4.9)	229 (6.2)	16 (5.6)
Malignancy	23 (16.0)	430 (11.7)	36 (12.5)
Major Surgical Procedures[1]	94 (65.3)	2718 (73.7)	205 (71.2)
Other	33 (22.9)	984 (26.7)	79 (27.4)
None indicated[1, 2]	0 (0.0)	5 (0.1)	1 (0.3)

Supplementary Table 1: Vascular lifestyle factors and self-reported medical conditions in NHB and NHW groups. Mean (standard deviation) are listed for continuous values. N and percentages are listed for categorical variables. For endorsing current smoking and alcohol consumption, as well as all self-reported medical conditions, the number and percentages of participants endorsing each category are listed (irrespective of the total number of conditions indicated within a

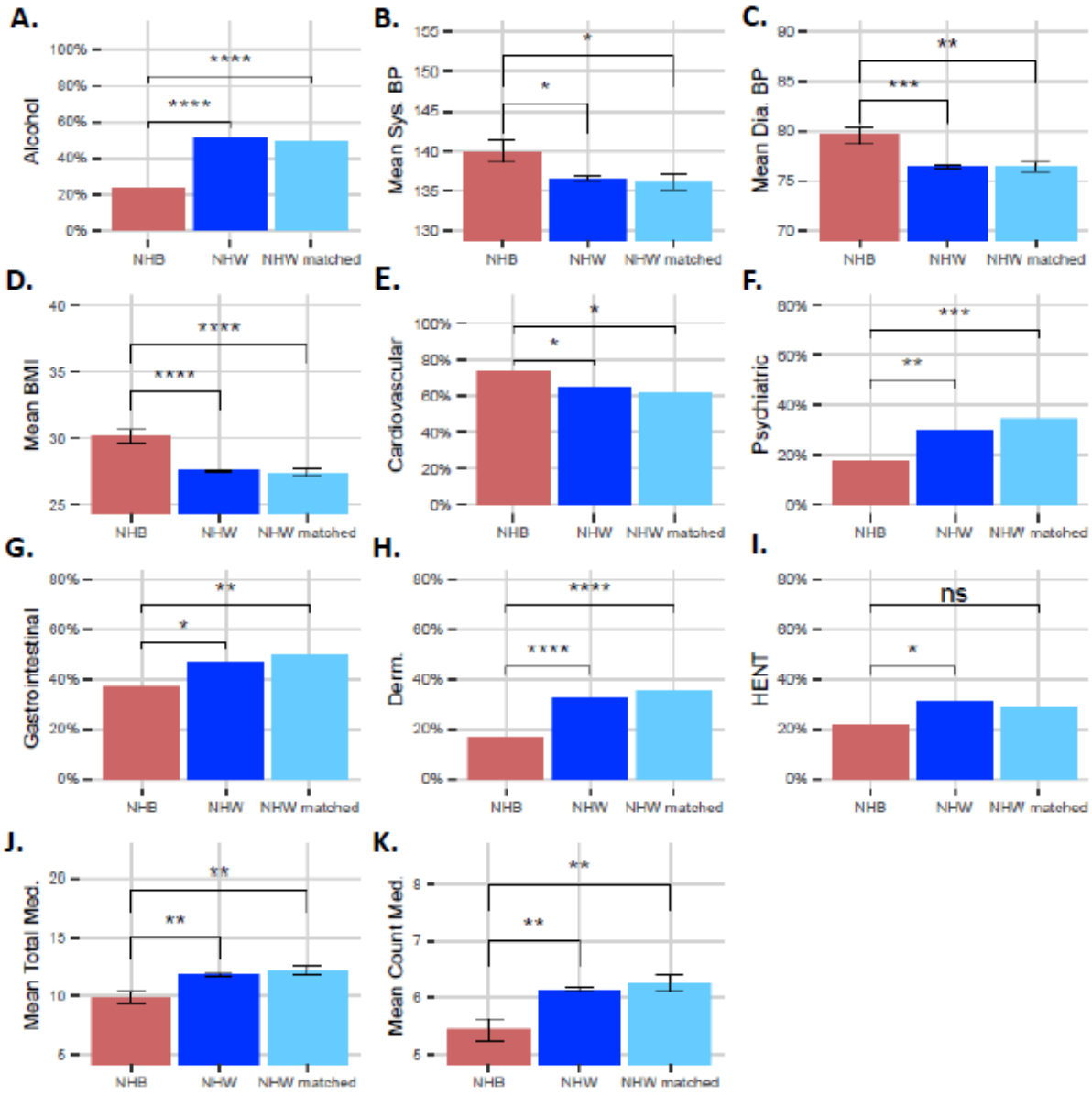
category). Lifestyle factors and medical conditions were examined using self-report during the initial screening visit for some participants (see S. Figure 1 to show patterns of missingness). For vascular lifestyle factors, we examined the “SMOKE” (endorsing current smoking) and “ALCOHOL” (endorsing current drinking) variables from the data sheet titled “HABITS.csv” sheet. These variables were treated as binary in our analysis (yes/no). We additionally examined “STDWT” (weight), “STDHT” (height), “VSBPSYS” (systolic blood pressure), “VSBPDIA” (diastolic blood pressure) variables from the “VITALS.csv” sheet. Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared. For self-reported medical conditions, we examined the data sheet titled “INITHEALTH.csv” sheet, and used the variable called ‘IHSYMPTOM’ that describes health symptoms across multiple categories spanning 17 categories. Differences between groups for continuous variables (age, education, blood pressure, and BMI) were performed with t-tests. Differences between groups for categorical variables (sex, endorse smoking, endorse drinking, and all self-reported medical conditions) were performed with chi-squared tests. We examined the following two contrasts (with significance at $p<0.05$ and indicated by numerical superscripts): [1]NHB and full NHW. [2]NHB and matched NHW.

	Frontal amyloid SUVR		Precuneus amyloid SUVR	
	Full NHW vs NHB	**Matched NHW vs NHB**	**Full NHW vs NHB**	**Matched NHW vs NHB**
Race (NHW vs NHB)	0.022 (0.014) p=0.107	0.048 (0.017) p=0.006	0.075 (0.019) p<0.0001	0.095 (0.023) p<0.0001
Gender (Female v Male)	0.041 (0.005) p<0.0001	0.063 (0.018) p=0.001	-0.001 (0.008) p=0.906	0.02 (0.025) p=0.416
Age (Years)	0.005 (0.001) p<0.0001	0.004 (0.002) p=0.023	0.01 (0.001) p<0.0001	0.006 (0.002) p=0.012
APOE4 (0, 1, 2)	-0.015 (0.008) p=0.055	-0.007 (0.024) p=0.78	-0.029 (0.011) p=0.008	-0.03 (0.033) p=0.352
APOE2 (0, 1, 2)	0.12 (0.005) p<0.0001	0.130 (0.015) p<0.0001	0.163 (0.007) p<0.0001	0.16 (0.02) p<0.0001

Supplementary Table 2. Linear regression models summarizing effect of race on amyloid regions. We examined frontal and precuneus brain regions since these are regions that show early deposition. NHB showed significantly reduced amyloid compared to NHW, with the exception of the contrast of NHB versus the full NHW sample for frontal.

A) Logistic Regression Predicting Amyloid group. Odds ratio (95% CI)		
	Full NHW Sample vs NHB	**Matched NHW Sample vs NHB**
Race (NHW v NHB)	1.98 (1.24-3.25) p=0.005	2.33 (1.35-4.16) p=0.003
Gender (Female v Male)	1.2 (1.02-1.42) p=0.024	1.37 (0.78-2.48) p=0.283
Age (years)	1.1 (1.08-1.12) p<0.0001	1.09 (1.04-1.15) p=0.001
APOE2 **(0, 1, 2)**	0.69 (0.51-0.91) p=0.012	1.12 (0.45-2.49) p=0.794
APOE4 **(0, 1, 2)**	4.74 (4.1-5.5) p<0.0001	5.67 (3.62-9.13) p<0.0001
MMSE	0.93 (0.87-0.99) p<0.0001	0.99 (0.81-1.22) p=0.92
B) Linear Regression Predicting Continuous Amyloid SUVR. Beta estimate (standard error)		
	Full NHW Sample vs NHB	**Matched NHW Sample vs NHB**
Race (NHW v NHB)	0.049 (0.015) p=0.001	0.065 (0.018) p<0.0001
Gender (Female v Male)	0.018 (0.006) p=0.002	0.0364 (0.019) p=0.062
Age (years)	0.007 (0.001) p<0.0001	0.0052 (0.002) p=0.006
APOE2 **(0, 1, 2)**	-0.021 (0.008) p=0.013	-0.016 (0.026) p=0.538
APOE4 **(0, 1, 2)**	0.133 (0.005) p<0.0001	0.137 (0.016) p<0.0001
MMSE	-0.01 (0.002) p<0.0001	0.0029 (0.007) p=0.69

Supplementary Table 3. Regression models summarizing effect of race on amyloid, controlling for MMSE score.



Supplementary Figure 2. Lifestyle factors and medical conditions that were significantly different between PET eligible NHB and NHW (either full or matched) as identified in S. Table 1. Each participant self-reported medical conditions during the initial screening visit, as listed in S. Table 1. Mean Total Med. = The y-axis shows the mean total number of total medical conditions reported by each participant collapsed across categories listed in S. Table 1. NHW reported more medical conditions compared to NHB (NHB vs NHW, p=0.001; NHB vs NHW matched, p=0.002). No difference was observed between screen-fail groups within each race (NHB fail vs NHB, p=0.631; NHW fail vs NHW, p=0.277). Mean Count Med. = Total number of medical conditions reported by each participant (score = 1 for each condition reported in Table 1; range=0-17). NHW reported more co-morbid medical conditions compared to NHB (NHB vs NHW, p<0.001; NHB vs NHW matched, p=0.0004). Within racial groups, NHW and NHB reported more co-morbid medical conditions compared to the screen-fail group (NHW fail vs NHW, p<0.001; NHB fail vs NHB, p<0.001). *p<0.05; **p<0.01; ***p<0.001; ****p<0.0001; Sys. = Systolic; Dia.= Diastolic; BP=blood pressure; BMI=body mass index; Derm.=dermatology; HENT = Head, Eyes, Nose, Throat.

Logistic Regression Predicting Amyloid Group. Odds ratio (95% CI)		
	Full NHW Sample vs NHB	**Matched NHW Sample vs NHB**
Race (NHW v NHB)	1.99 (1.24-3.32) p=0.006	2.49 (1.38-4.64) p=0.003
Gender (Female v Male)	1.17 (0.99-1.38) p=0.063	1.43 (0.8-2.64) p=0.234
Age (years)	1.1 (1.08-1.12) p<0.0001	1.08 (1.03-1.14) p=0.003
APOE2 (0, 1, 2)	0.71 (0.52-0.94) p=0.021	1.22 (0.49-2.73) p=0.652
APOE4 (0, 1, 2)	4.75 (4.1-5.51) p<0.0001	5.87 (3.72-9.54) p<0.0001
Cardiovascular (Yes v No)	1.11 (0.94-1.32) p=0.213	1.44 (0.85-2.47) p=0.18
Alcohol (Yes v No)	0.99 (0.85-1.16) p=0.922	1.13 (0.68-1.88) p=0.622
Systolic BP	1.00 (1-1.01) p=0.403	1.00 (0.99-1.02) p=0.593
Diastolic BP	1.00 (0.99-1.01) p=0.57	1.01 (0.98-1.04) p=0.732
BMI	0.99 (0.97-1) p=0.148	0.99 (0.94-1.04) p=0.614
Unadjusted effect of race		
Race (NHW v NHB)	1.94 (1.22-3.19) p=0.007	2.33 (1.35-4.13) p=0.003
Linear Regression Predicting Amyloid Group. Beta estimate (standard error)		
	Full NHW Sample vs NHB	**Matched NHW Sample vs NHB**
Race (NHW v NHB)	0.046 (0.015) p=0.002	0.066 (0.020) p=0.001
Gender (Female v Male)	0.016 (0.006) p=0.008	0.038 (0.020) p=0.055
Age (years)	0.007 (0.001) p<0.0001	0.005 (0.002) p=0.012
APOE2 (0, 1, 2)	-0.019 (0.009) p=0.024	-0.015 (0.026) p=0.564
APOE4 (0, 1, 2)	0.133 (0.005) p<0.0001	0.137 (0.016) p<0.0001
Cardiovascular (Yes v No)	0.009 (0.006) p=0.131	0.012 (0.018) p=0.53
Alcohol (Yes v No)	0.001 (0.006) p=0.889	0.008 (0.018) p=0.67
Systolic BP	0.0001 (0.0002) p=0.708	0.0001 (0.001) p=0.841
Diastolic BP	-0.00005 (0.0004) p=0.895	0.0004 (0.001) p=0.689
BMI	0 (0.001) p=0.504	-0.001 (0.002) p=0.622
Unadjusted effect of race		
Race (NHW v NHB)	0.046 (0.015) p=0.002	0.066 (0.018) p=0.0003

Supplementary Table 4: Regression models summarizing effect of vascular risk factors on amyloid. Smoking was excluded because of the small number of participants that endorse current smoking for NHB (N=5) and NHW matched (N=2). Lifestyle variables that were significantly different in NHB and NHW were added to models predicting amyloid to determine whether race remained significantly associated with amyloid. BP=blood pressure; BMI=body mass index. Overall, race remained significantly association with amyloid. There was no association between any lifestyle variable and amyloid. The effect of race on amyloid from the manuscript (without adjustment for lifestyle variables) is listed for reference.

Logistic Regression Predicting Amyloid Group. Odds ratio (95% CI)		
	Full NHW Sample vs NHB	**Matched NHW Sample vs NHB**
Race (NHW v NHB)	1.86 (1.17-3.06) p=0.012	2.46 (1.39-4.49) p=0.002
Gender (Female v Male)	1.16 (0.99-1.37) p=0.075	1.43 (0.81-2.6) p=0.199
Age (years)	1.1 (1.08-1.12) p<0.0001	1.09 (1.03-1.15) p=0.002
APOE2 (0, 1, 2)	0.69 (0.51-0.91) p=0.012	1.18 (0.48-2.64) p=0.649
APOE4 (0, 1, 2)	4.71 (4.07-5.46) p<0.0001	6.05 (3.81-9.93) p=<0.0001
Psychiatric (Yes v No)	1.1 (0.92-1.3) p=0.298	0.69 (0.39-1.18) p=0.168
HENT (Yes v No)	1.23 (1.05-1.45) p=0.012	1.61 (0.97-2.69) p=0.052
Dermatology (Yes v No)	1.05 (0.89-1.25) p=0.542	1 (0.63-1.87) p=0.118
GI (Yes v No)	1.02 (0.87-1.2) p=0.768	0.81 (0.49-1.33) p=0.854
Unadjusted effect of race		
Race (NHW v NHB)	1.94 (1.22-3.19) p=0.007	2.33 (1.35-4.13) p=0.003
Linear Regression Predicting Amyloid Group. Beta estimate (standard error)		
	Full NHW Sample vs NHB	**Matched NHW Sample vs NHB**
Race (NHW v NHB)	0.044 (0.015) p=0.003	0.062 (0.019) p=0.001
Gender (Female v Male)	0.014 (0.006) p=0.019	0.039 (0.020) p=0.05
Age (years)	0.007 (0.001) p<0.0001	0.005 (0.002) p=0.011
APOE2 (0, 1, 2)	-0.021 (0.008) p=0.015	-0.017 (0.026) p=0.509
APOE4 (0, 1, 2)	0.133 (0.005) p<0.0001	0.138 (0.016) p<0.0001
Psychiatric (Yes v No)	0.009 (0.006) p=0.155	-0.005 (0.019) p=0.79
HENT (Yes v No)	0.011 (0.006) p=0.063	0.017 (0.018) p=0.334
Dermatology	-0.002 (0.006) p=0.789	0.024 (0.020) p=0.228
GI	-0.002 (0.006) p=0.678	-0.008 (0.017) p=0.662
Unadjusted effect of race		
Race (NHW v NHB)	0.046 (0.015) p=0.002	0.066 (0.018) p=0.0003

Supplementary Table 5: Regression models summarizing effect of medical health conditions on amyloid. Medical conditions that were significantly different in NHB and NHW were added to models predicting amyloid to determine whether race remained significantly associated with amyloid. HENT=head, eyes, ears, nose, throat; GI=gastrointestinal. Overall, race remained significantly association with amyloid. There was no association between any medical condition and amyloid. The effect of race on amyloid from the manuscript (without adjustment for medical conditions) is listed for reference.

Model 1		
Logistic Regression Predicting Amyloid Group. Odds ratio (95% CI)		
	Full NHW Sample vs NHB	**Matched NHW Sample vs NHB**
Race (NHW v NHB)	1.84 (1.15-3.03) p=0.013	2.21 (1.28-3.95) p=0.006
Gender (Female v Male)	1.13 (0.96-1.33) p=0.149	1.33 (0.75-2.4) p=0.337
Age (years)	1.1 (1.08-1.12) p<0.0001	1.09 (1.03-1.15) p=0.001
APOE2 (0, 1, 2)	0.69 (0.51-0.92) p=0.014	1.08 (0.44-2.4) p=0.858
APOE4 (0, 1, 2)	4.69 (4.06-5.45) p<0.0001	5.59 (3.57-9) p=<0.0001
Endorsed Medical Categories	1.03 (1.02-1.04) p<0.0001	1.02 (0.99-1.06) p=0.181
Unadjusted effect of race		
Race (NHW v NHB)	1.94 (1.22-3.19) p=0.007	2.33 (1.35-4.13) p=0.003
Linear Regression Predicting Amyloid Group. Beta estimate (standard error)		
	Full NHW Sample vs NHB	**Matched NHW Sample vs NHB**
Race (NHW v NHB)	0.043 (0.015) p=0.004	0.063 (0.018) p=0.001
Gender (Female v Male)	0.013 (0.006) p=0.021	0.034 (0.02) p=0.082
Age (years)	0.007 (0.001) p<0.0001	0.0049 (0.002) p=0.009
APOE2 (0, 1, 2)	-0.02 (0.008) p=0.016	-0.019 (0.026) p=0.465
APOE4 (0, 1, 2)	0.132 (0.005) p<0.0001	0.136 (0.016) p<0.0001
Endorsed Medical Categories	0.001 (0) p=0.004	0.001 (0.001) p=0.297
Unadjusted effect of race		
Race (NHW v NHB)	0.046 (0.015) p=0.002	0.066 (0.018) p=0.0003
Model 2		
Logistic Regression Predicting Amyloid Group. Odds ratio (95% CI)		
	Full NHW Sample vs NHB	**Matched NHW Sample vs NHB**
Race (NHW v NHB)	1.85 (1.16-3.05) p=0.012	2.23 (1.29-3.99) p=0.005
Gender (Female v Male)	1.14 (0.97-1.34) p=0.113	1.35 (0.77-2.44) p=0.306
Age (years)	1.1 (1.08-1.12) p<0.0001	1.09 (1.04-1.15) p=0.001
APOE2 (0, 1, 2)	0.7 (0.52-0.93) p=0.016	1.1 (0.44-2.44) p=0.83
APOE4 (0, 1, 2)	4.7 (4.06-5.46) p<0.0001	5.61 (3.59-9.03) p<0.0001
Total Medical Conditions	1.07 (1.04-1.11) p<0.0001	1.06 (0.96-1.17) p=0.275
Unadjusted effect of race		
Race (NHW v NHB)	1.94 (1.22-3.19) p=0.007	2.33 (1.35-4.13) p=0.003
Linear Regression Predicting Amyloid Group. Beta estimate (standard error)		
	Full NHW Sample vs NHB	**Matched NHW Sample vs NHB**
Race (NHW v NHB)	0.044 (0.015) p=0.003	0.063 (0.018) p=0.001
Gender (Female v Male)	0.014 (0.006) p=0.015	0.036 (0.019) p=0.068
Age (years)	0.007 (0.001) p<0.0001	0.005 (0.002) p=0.008
APOE2 (0, 1, 2)	-0.02 (0.008) p=0.017	-0.018 (0.026) p=0.485
APOE4 (0, 1, 2)	0.132 (0.005) p<0.0001	0.1365 (0.016) p<0.0001
Total Medical Conditions	0.002 (0.001) p=0.043	0.004 (0.003) p=0.29
Unadjusted effect of race		
Race (NHW v NHB)	0.046 (0.015) p=0.002	0.066 (0.018) p=0.0003

Supplementary Table 6: Regression models summarizing effect of medical health conditions on amyloid. Model 1: Endorsed Medical Categories are the total number of medical categories endorsed by each participant (score = 1 for each condition reported in Table 1; range=0-17. Model

2: Total medical conditions is the number of total medical conditions reported by each participant collapsed across categories listed in S. Table 1. First, the total category and number of self-reported medical condition burden was shown to be significantly reduced in NHB compared to NHW (S. Figure 2 J-K). We therefore added medical condition burden to models predicting amyloid to determine whether race remained significantly associated with amyloid. The effect of race on amyloid from the manuscript (without adjustment for medical condition burden) is listed for reference.