

**Supplemental Table 1:** Distribution of baseline characteristics between included and excluded participants in the United States Retirement Study

Characteristic	Overall N = 8,781 <sup>1</sup>	Included N = 5,143 <sup>1</sup>	Excluded N = 3,638 <sup>1</sup>	p-value <sup>2</sup>
<b>Cognitive Status</b>				
Incident dementia	795 (15%)	795 (15%)	NA	
Cognitively normal	4,348 (85%)	4,348 (85%)	NA	
<b>Baseline CRP</b> ( $\mu\text{g/mL}$ )	4.55 (8.14)	4.18 (7.70)	5.09 (8.69)	<b>&lt;0.001</b>
<b>Age</b> (years)	68.12 (10.38)	66.36 (9.90)	70.60 (10.52)	<b>&lt;0.001</b>
<b>Race</b>				
Non-Hispanic Black	1,057 (12%)	488 (9.5%)	569 (16%)	
Hispanic	794 (9.0%)	376 (7.3%)	418 (11%)	
Non-Hispanic Other	189 (2.2%)	0 (0%)	189 (5.2%)	
Non-Hispanic White	6,741 (77%)	4,279 (83%)	2,462 (68%)	
<b>Gender</b>				
Female	5,290 (60%)	3,189 (62%)	2,101 (58%)	
Male	3,491 (40%)	1,954 (38%)	1,537 (42%)	
<b>Education Category</b>				
> College	812 (9.2%)	602 (12%)	210 (5.8%)	
College/Some	1,575 (18%)	1,109 (22%)	466 (13%)	
HS or <	6,394 (73%)	3,432 (67%)	2,962 (81%)	
<b>Alcohol</b> (# drinks/day when drinks)	0.70 (1.41)	0.74 (1.27)	0.64 (1.59)	<b>0.002</b>
<b>Smoking</b>				
Current/Former	4,950 (56%)	2,835 (55%)	2,115 (58%)	
Never	3,831 (44%)	2,308 (45%)	1,523 (42%)	
<b>Body Mass Index</b> ( $\text{kg}/\text{m}^2$ )	28.33 (5.88)	28.46 (5.75)	28.16 (6.05)	<b>0.018</b>
<b>Chronic Conditions</b>				
At least 1	7,465 (85%)	4,223 (82%)	3,242 (89%)	
No	1,316 (15%)	920 (18%)	396 (11%)	
<b><i>APOE-ε4</i></b>				
At least 1	2,373 (27%)	1,363 (27%)	1,010 (28%)	
No copy	6,408 (73%)	3,780 (73%)	2,628 (72%)	
<b>Wave</b>				
2006	4,178 (48%)	2,597 (50%)	1,581 (43%)	
2008	4,603 (52%)	2,546 (50%)	2,057 (57%)	

<sup>1</sup>n (%); Mean (SD)

<sup>2</sup>Pearson's Chi-squared test; One-way ANOVA

CRP: C-reactive protein; *APOE-ε4*: apolipoprotein E ε4 allele carrier status

**Supplemental Table 2:** Distribution of baseline sample characteristics by racialized social groups in the Health and Retirement Study, 2006 and 2008

Characteristic	Overall Sample N = 5,143 <sup>1</sup>	Non-Hispanic Black N = 488 <sup>1</sup>	Hispanic N = 376 <sup>1</sup>	Non-Hispanic White N = 4,279 <sup>1</sup>	p-value <sup>2</sup>
<b>Dementia</b>	<b>&lt;0.001</b>				
Incident dementia	795 (15%)	171 (35%)	103 (27%)	521 (12%)	
Cognitively normal	4,348 (85%)	317 (65%)	273 (73%)	3,758 (88%)	
<b>Baseline CRP (µg/mL)</b>	4.18 (7.70)	6.19 (11.15)	4.32 (6.29)	3.94 (7.28)	<b>&lt;0.001</b>
<b>Age (years)</b>	66.36 (9.90)	65.53 (9.68)	63.63 (10.33)	66.70 (9.85)	<b>&lt;0.001</b>
<b>Sex</b>	<b>0.002</b>				
Female	3,189 (62%)	338 (69%)	232 (62%)	2,619 (61%)	
Male	1,954 (38%)	150 (31%)	144 (38%)	1,660 (39%)	
<b>Educational Category</b>	<b>&lt;0.001</b>				
> College	602 (12%)	30 (6.1%)	11 (2.9%)	561 (13%)	
College/Some	1,109 (22%)	75 (15%)	45 (12%)	989 (23%)	
HS or <	3,432 (67%)	383 (78%)	320 (85%)	2,729 (64%)	
<b>Alcohol (# drinks/day when drinks)</b>	0.74 (1.27)	0.48 (1.14)	0.65 (1.41)	0.77 (1.27)	<b>&lt;0.001</b>
<b>Smoking</b>	0.496				
Current/Former	2,835 (55%)	279 (57%)	200 (53%)	2,356 (55%)	
Never	2,308 (45%)	209 (43%)	176 (47%)	1,923 (45%)	
<b>Body Mass Index (kg/m<sup>2</sup>)</b>	28.46 (5.75)	30.69 (6.50)	29.41 (5.50)	28.12 (5.61)	<b>&lt;0.001</b>
<b>Chronic Conditions</b>	<b>&lt;0.001</b>				
At least 1	4,223 (82%)	432 (89%)	291 (77%)	3,500 (82%)	
No	920 (18%)	56 (11%)	85 (23%)	779 (18%)	
<b><i>APOE-ε4</i></b>	<b>&lt;0.001</b>				
At least 1 copy	1,363 (27%)	185 (38%)	83 (22%)	1,095 (26%)	
No copy	3,780 (73%)	303 (62%)	293 (78%)	3,184 (74%)	
<b>Time (years)</b>	<b>&lt;0.001</b>				
2	302 (5.9%)	80 (16%)	39 (10%)	183 (4.3%)	
4	269 (5.2%)	52 (11%)	37 (9.8%)	180 (4.2%)	
6	4,572 (89%)	356 (73%)	300 (80%)	3,916 (92%)	

Characteristic	Overall Sample N = 5,143 <sup>1</sup>	Non-Hispanic Black N = 488 <sup>1</sup>	Hispanic N = 376 <sup>1</sup>	Non-Hispanic White N = 4,279 <sup>1</sup>	p-value <sup>2</sup>
<b>Wave</b>					<b>0.017</b>
2006	2,597 (50%)	224 (46%)	174 (46%)	2,199 (51%)	
2008	2,546 (50%)	264 (54%)	202 (54%)	2,080 (49%)	

<sup>1</sup>n (%) ; Mean (SD)

<sup>2</sup>Pearson's Chi-squared test; One-way ANOVA

CRP: C-reactive protein; *APOE-ε4*: apolipoprotein E *ε4* allele carrier status

**Supplemental Table 3:** Baseline levels of C-reactive protein (CRP) by racialized social groups and sex in the United States Health and Retirement Study, waves 2006 & 2008

Race/ethnicity	Sex	Observations	Mean	SD	Min	Max	25 <sup>th</sup>	50 <sup>th</sup>	75 <sup>th</sup>	IQR
Non-Hispanic Black	Female	338	6.28	9.04	0.04	81.1	1.42	3.60	7.77	6.34
Non-Hispanic Black	Male	150	6.00	14.9	0.03	125.0	1.14	2.49	5.86	4.72
Hispanic	Female	232	4.61	5.59	0.08	37.9	1.40	2.50	5.79	4.39
Hispanic	Male	144	3.85	7.28	0.04	66.7	0.99	1.89	4.04	3.06
Non-Hispanic White	Female	2619	4.27	7.57	0.04	173.0	1.01	2.13	4.91	3.90
Non-Hispanic White	Male	1660	3.40	6.77	0.02	121.0	0.79	1.55	3.30	2.51

**Supplemental Table 4:** Distribution of baseline sample characteristics by percentiles of C-reactive protein, United States Health and Retirement Study, 2006 and 2008

Characteristic	Overall N = 5,143 <sup>1</sup>	C-reactive protein (µg/mL) percentiles				p-value <sup>2</sup>
		25 <sup>th</sup> (<0.96) N = 1,282 <sup>1</sup>	25 <sup>th</sup> - 50 <sup>th</sup> (≥0.96 & <1.97) N = 1,267 <sup>1</sup>	50 <sup>th</sup> - 75 <sup>th</sup> (≥1.97 & <4.57) N = 1,306 <sup>1</sup>	75 <sup>th</sup> (≥4.57) N = 1,288 <sup>1</sup>	
<b>Dementia Status</b>						0.115
Incident dementia	795 (15%)	195 (15%)	177 (14%)	199 (15%)	224 (17%)	
Cognitively normal	4,348 (85%)	1,087 (85%)	1,090 (86%)	1,107 (85%)	1,064 (83%)	
<b>Age (years)</b>	66.36 (9.90)	66.35 (10.17)	67.05 (9.77)	66.60 (9.73)	65.45 (9.88)	<b>&lt;0.001</b>
<b>Race</b>						<b>&lt;0.001</b>
Non-Hispanic Black	488 (9.5%)	88 (6.9%)	75 (5.9%)	133 (10%)	192 (15%)	
Hispanic	376 (7.3%)	71 (5.5%)	91 (7.2%)	107 (8.2%)	107 (8.3%)	
Non-Hispanic White	4,279 (83%)	1,123 (88%)	1,101 (87%)	1,066 (82%)	989 (77%)	
<b>Sex</b>						<b>&lt;0.001</b>
Female	3,189 (62%)	718 (56%)	719 (57%)	836 (64%)	916 (71%)	
Male	1,954 (38%)	564 (44%)	548 (43%)	470 (36%)	372 (29%)	
<b>Educational Category</b>						<b>&lt;0.001</b>
> College	602 (12%)	221 (17%)	148 (12%)	124 (9.5%)	109 (8.5%)	
College/Some	1,109 (22%)	297 (23%)	308 (24%)	261 (20%)	243 (19%)	
HS or <	3,432 (67%)	764 (60%)	811 (64%)	921 (71%)	936 (73%)	
<b>Alcohol (# drinks/day when drinks)</b>	0.74 (1.27)	0.83 (1.27)	0.81 (1.33)	0.71 (1.26)	0.60 (1.21)	<b>&lt;0.001</b>
<b>Smoking Status</b>						<b>&lt;0.001</b>
Current/Former	2,835 (55%)	631 (49%)	708 (56%)	743 (57%)	753 (58%)	
Never	2,308 (45%)	651 (51%)	559 (44%)	563 (43%)	535 (42%)	
<b>Body Mass Index (kg/m<sup>2</sup>)</b>	28.46 (5.75)	25.89 (4.30)	27.48 (4.66)	29.01 (5.34)	31.40 (6.84)	<b>&lt;0.001</b>
<b>Chronic Conditions</b>						<b>&lt;0.001</b>
At least 1	4,223 (82%)	972 (76%)	1,008 (80%)	1,114 (85%)	1,129 (88%)	

Characteristic	Overall N = 5,143 <sup>1</sup>	C-reactive protein (µg/mL) percentiles				p-value <sup>2</sup>
		25 <sup>th</sup> (<0.96) N = 1,282 <sup>1</sup>	25 <sup>th</sup> - 50 <sup>th</sup> (≥0.96 & <1.97) N = 1,267 <sup>1</sup>	50 <sup>th</sup> - 75 <sup>th</sup> (≥1.97 & <4.57) N = 1,306 <sup>1</sup>	75 <sup>th</sup> (≥4.57) N = 1,288 <sup>1</sup>	
		No	920 (18%)	310 (24%)	259 (20%)	159 (12%)
<b><i>APOE-ε4</i></b>						<b>&lt;0.001</b>
At least 1 copy	1,363 (27%)	447 (35%)	347 (27%)	301 (23%)	268 (21%)	
No copy	3,780 (73%)	835 (65%)	920 (73%)	1,005 (77%)	1,020 (79%)	
<b>Time (years)</b>						<b>0.009</b>
2	302 (5.9%)	58 (4.5%)	80 (6.3%)	68 (5.2%)	96 (7.5%)	
4	269 (5.2%)	71 (5.5%)	51 (4.0%)	80 (6.1%)	67 (5.2%)	
6	4,572 (89%)	1,153 (90%)	1,136 (90%)	1,158 (89%)	1,125 (87%)	
<b>Wave</b>						0.470
2006	2,597 (50%)	659 (51%)	640 (51%)	636 (49%)	662 (51%)	
2008	2,546 (50%)	623 (49%)	627 (49%)	670 (51%)	626 (49%)	

<sup>1</sup>n (%); Mean (SD)

<sup>2</sup>Pearson's Chi-squared test; One-way ANOVA

*APOE-ε4*: apolipoprotein E ε4 allele carrier status

**Supplemental Table 5:** Odds ratio of elevated levels of C-reactive protein ( $\geq 4.57\mu\text{g/mL}$  or  $\geq 75^{\text{th}}$  percentile) stratified by minoritized status and racialized social groups in the US Health and Retirement Study, waves 2006 & 2008

	Non-Hispanic Black vs non-Hispanic White <sup>1</sup> N = 4,767	Hispanic vs non-Hispanic White <sup>1</sup> N = 4,655	Minoritized Racial Group vs non-Hispanic White <sup>2</sup> N = 5,143
<b>Models</b>			+
<b>Unadjusted</b>	2.16*** [1.78,2.62]	1.32* [1.05,1.67]	1.76*** [1.50,2.06]
<b>Demographic<sup>+</sup></b>	2.11*** [1.72,2.58]	1.17 [0.92,1.49]	1.66*** [1.41,1.95]
<b>Risk Factors<sup>\$</sup></b>	1.67*** [1.34,2.08]	1.13 [0.87,1.46]	1.42*** [1.20,1.70]
<b>Chronic Conditions<sup>§</sup></b>	1.66*** [1.33,2.07]	1.14 [0.88,1.47]	1.42*** [1.20,1.70]

Demographic model: adjusted for age, sex, education categories, *APOE-ε4* allele status, and wave

<sup>\$</sup> Risk factors model: adjusted for age, sex, education categories, *APOE-ε4* allele status, wave, smoking status, alcohol consumption, body mass index

<sup>§</sup> Chronic conditions model: adjusted for age, sex, education categories, *APOE-ε4* allele status, wave, smoking status, alcohol consumption, body mass index, and chronic conditions

<sup>1</sup> Odds ratios, CI: confidence interval in brackets

<sup>2</sup> Odds ratios, CI: confidence intervals in brackets. Minoritized racial group: (non-Hispanic Black and Hispanic participants)

\*  $p < 0.05$ , \*\*  $p < 0.01$ , \*\*\*  $p < 0.001$

**Supplemental Table 6:** Randomized analogue mediation models for racial disparities in incident dementia using elevated levels of C-reactive protein (CRP  $>4.57\mu\text{g/mL}$ ) as mediator. Models are stratified by minoritized status and racialized social groups in a sample of United States adults in the Health and Retirement Study

Mediator (CRP) Excess Risk	Minoritized Racial Group vs non-Hispanic White N = 5,143				Randomized Analogue Model <sup>+</sup> (Outcome: Incident Dementia) non-Hispanic Black vs non-Hispanic White N = 4,767				Hispanic vs non-Hispanic White N = 4,655			
	Estimate	[95%CI]	[95%CI]	p-value	Estimate	[95%CI]	[95%CI]	p-value	Estimate	[95%CI]	[95%CI]	p-value
	RERI Controlled Direct Effect	1.94	1.58	2.44	<0.00	2.57	1.90	3.32	<0.00	1.40	0.94	2.00
RERI Interaction Reference	0.26	0.04	0.52	0.02	0.18	-0.11	0.53	0.22	0.39	0.03	0.87	0.03
RERI Interaction Mediation	0.06	-0.01	0.13	0.08	0.05	-0.03	0.21	0.23	0.01	-0.09	0.14	0.68
RERI Pure Indirect Effect	0.01	0.00	0.02	0.12	0.01	0.00	0.04	0.07	0.00	-0.01	0.02	0.71
<b>% Attributable</b>												
% Controlled Direct Effect	0.85	0.75	0.97	<0.00	0.91	0.76	1.05	<0.00	0.78	0.57	0.98	<0.00
% Interaction Reference	0.11	0.02	0.22	0.02	0.06	-0.04	0.18	0.22	0.22	0.02	0.42	0.03
% Interaction Mediation	0.03	0.00	0.05	0.08	0.02	-0.01	0.07	0.23	0.00	-0.05	0.07	0.68
% Pure Indirect Effect	0.01	0.00	0.01	0.12	0.00	0.00	0.01	0.07	0.00	-0.01	0.01	0.71
Percent Mediated	0.03	0.00	0.06	0.07	0.02	-0.01	0.08	0.13	0.01	-0.05	0.07	0.68
Percent due to Interaction	0.14	0.02	0.25	0.02	0.08	-0.05	0.24	0.22	0.22	0.02	0.43	0.03
Percent Eliminated	0.15	0.03	0.25	0.01	0.09	-0.05	0.24	0.21	0.22	0.02	0.43	0.03

<sup>+</sup>Model: outcome 6-year incident dementia, model adjusting for age, sex, education categories, wave, smoking status, alcohol consumption, body mass index, alcohol consumption, and chronic conditions, using *APOE-ε4* as variable affected by the race/ethnicity through ancestry. Minoritized racial group: (non-Hispanic Black and Hispanic participants)

**Supplemental Table 7A:** Mediational E-values for regression-based models; estimates are presented in the rate ratio scale. Models are stratified by racialized social groups in a sample of the United States adults in the Health and Retirement Study.

Rate Ratio Scale	Minoritized vs non-Hispanic White*					
	Estimate	LB 95%CI	UB 95%CI	E-value	E-value LB	E-value UB
Controlled direct effect (Rcde)	2.99	2.58	3.50	5.43	4.61	NA
Pure natural direct effect (Rpnde)	3.13	2.75	3.58	5.71	4.95	NA
Total natural direct effect (Rtnde)	3.15	2.78	3.62	5.76	5.00	NA
Pure natural indirect effect (Rpnie)	1.01	1.00	1.02	1.09	1.00	NA
Total natural indirect effect (Rtnie)	1.02	1.00	1.04	1.14	1.05	NA
Total effect (Rte)	3.17	2.79	3.66	5.80	5.03	NA
non-Hispanic Black vs non-Hispanic White*						
	Estimate	LB 95%CI	UB 95%CI	E-value	E-value LB	E-value UB
Controlled direct effect (Rcde)	3.48	2.84	4.26	6.42	5.12	NA
Pure natural direct effect (Rpnde)	3.53	2.96	4.23	6.51	5.36	NA
Total natural direct effect (Rtnde)	3.54	2.98	4.25	6.54	5.41	NA
Pure natural indirect effect (Rpnie)	1.01	1.00	1.04	1.13	1.00	NA
Total natural indirect effect (Rtnie)	1.02	0.99	1.06	1.15	1.00	NA
Total effect (Rte)	3.59	3.04	4.30	6.64	5.53	NA
Hispanic vs non-Hispanic White*						
	Estimate	LB 95%CI	UB 95%CI	E-value	E-value LB	E-value UB
Controlled direct effect (Rcde)	2.53	2.02	3.19	4.50	3.45	NA
Pure natural direct effect (Rpnde)	2.82	2.33	3.45	5.08	4.09	NA
Total natural direct effect (Rtnde)	2.81	2.35	3.46	5.06	4.13	NA
Pure natural indirect effect (Rpnie)	1.00	0.99	1.02	1.04	NA	1.00
Total natural indirect effect (Rtnie)	0.99	0.97	1.04	1.08	NA	1.00
Total effect (Rte)	2.80	2.35	3.47	5.05	4.14	NA

\* These E-values are on the rate ratio scale and correspond to the decomposition presented on Table 3

LB: Lower bound; UB: Upper bound

95%CI: 95% Confidence interval

NA: not applicable

**Supplemental Table 7B:** Mediational E-values for randomized analogue models; estimates are presented in the rate ratio scale. Models are stratified by racialized social groups in a sample of the United States adults in the Health and Retirement Study.

Rate Ratio Scale	Minoritized vs non-Hispanic White*					
	Estimate	LB 95%CI	UB 95%CI	E-value	E-value LB	E-value UB
Controlled direct effect (Rcde)	3.03	2.65	3.58	5.51	4.74	NA
Pure natural direct effect (rRpnde) <sup>+</sup>	3.20	2.83	3.71	5.85	5.10	NA
Total natural direct effect (rRtnde) <sup>+</sup>	3.23	2.86	3.77	5.92	5.16	NA
Pure natural indirect effect (rRpnie) <sup>+</sup>	1.01	1.00	1.02	1.12	1.00	NA
Total natural indirect effect (rRtnie) <sup>+</sup>	1.02	1.00	1.04	1.18	1.00	NA
Total effect (Rte)	3.27	2.88	3.80	6.00	5.21	NA
non-Hispanic Black vs non-Hispanic White*						
	Estimate	LB 95%CI	UB 95%CI	E-value	E-value LB	E-value UB
Controlled direct effect (Rcde)	3.69	2.99	4.50	6.85	5.43	NA
Pure natural direct effect (rRpnde) <sup>+</sup>	3.75	3.15	4.46	6.95	5.76	NA
Total natural direct effect (rRtnde) <sup>+</sup>	3.76	3.17	4.51	6.98	5.78	NA
Pure natural indirect effect (rRpnie) <sup>+</sup>	1.01	1.00	1.04	1.13	1.00	NA
Total natural indirect effect (rRtnie) <sup>+</sup>	1.02	0.99	1.06	1.15	1.00	NA
Total effect (Rte)	3.81	3.22	4.56	7.09	5.90	NA
Hispanic vs non-Hispanic White*						
	Estimate	LB 95%CI	UB 95%CI	E-value	E-value LB	E-value UB
Controlled direct effect (Rcde)	2.47	1.97	3.12	4.38	3.36	NA
Pure natural direct effect (rRpnde) <sup>+</sup>	2.79	2.32	3.48	5.03	4.08	NA
Total natural direct effect (rRtnde) <sup>+</sup>	2.80	2.33	3.50	5.04	4.09	NA
Pure natural indirect effect (rRpnie) <sup>+</sup>	1.00	0.99	1.02	1.01	1.00	NA
Total natural indirect effect (rRtnie) <sup>+</sup>	1.00	0.97	1.05	1.06	1.00	NA
Total effect (Rte)	2.80	2.35	3.52	5.04	4.12	NA

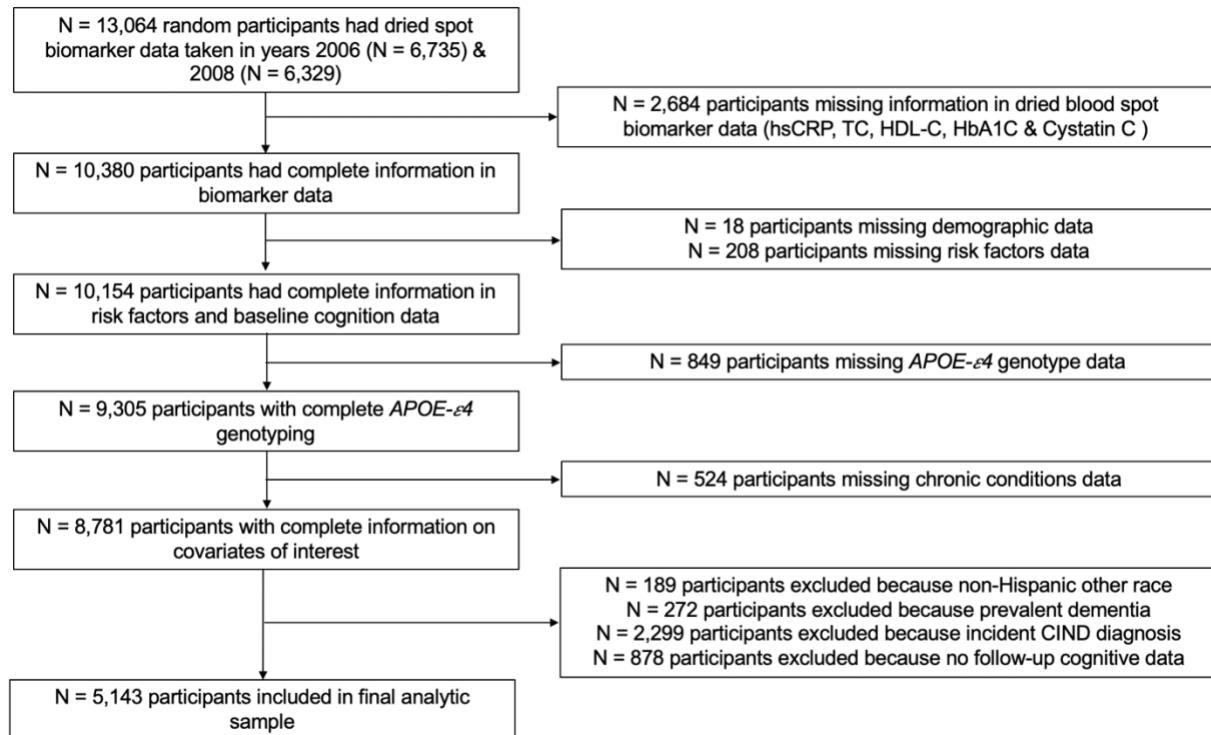
\* These E-values are on the rate ratio scale and correspond to the decomposition presented on Supplemental Table 6

+ Randomized analogue estimate

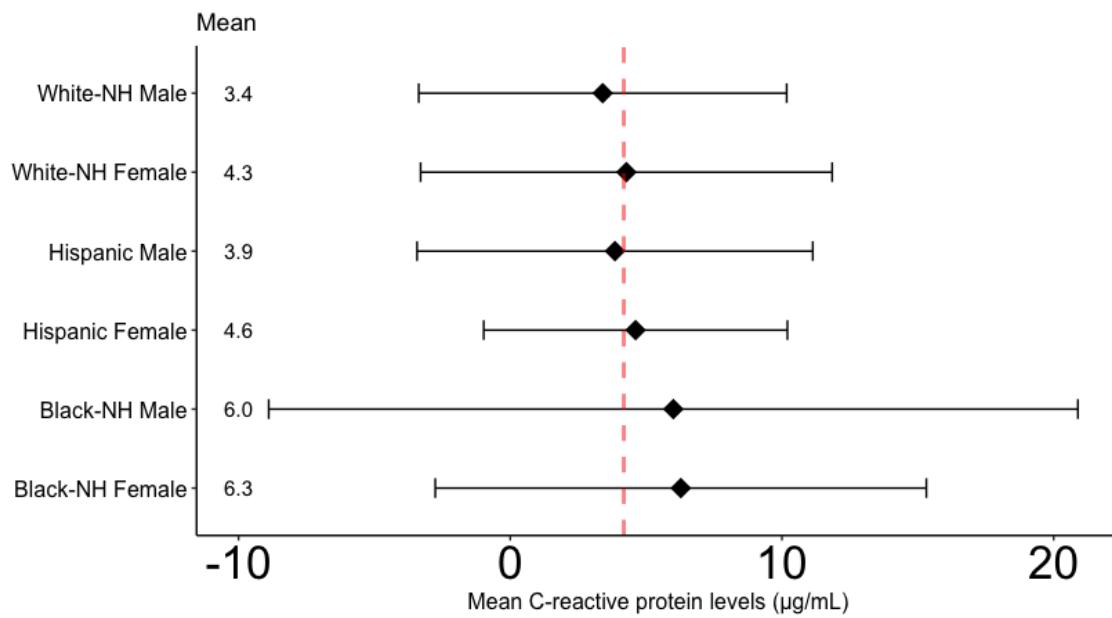
LB: Lower bound; UB: Upper bound

95%CI: 95% Confidence interval

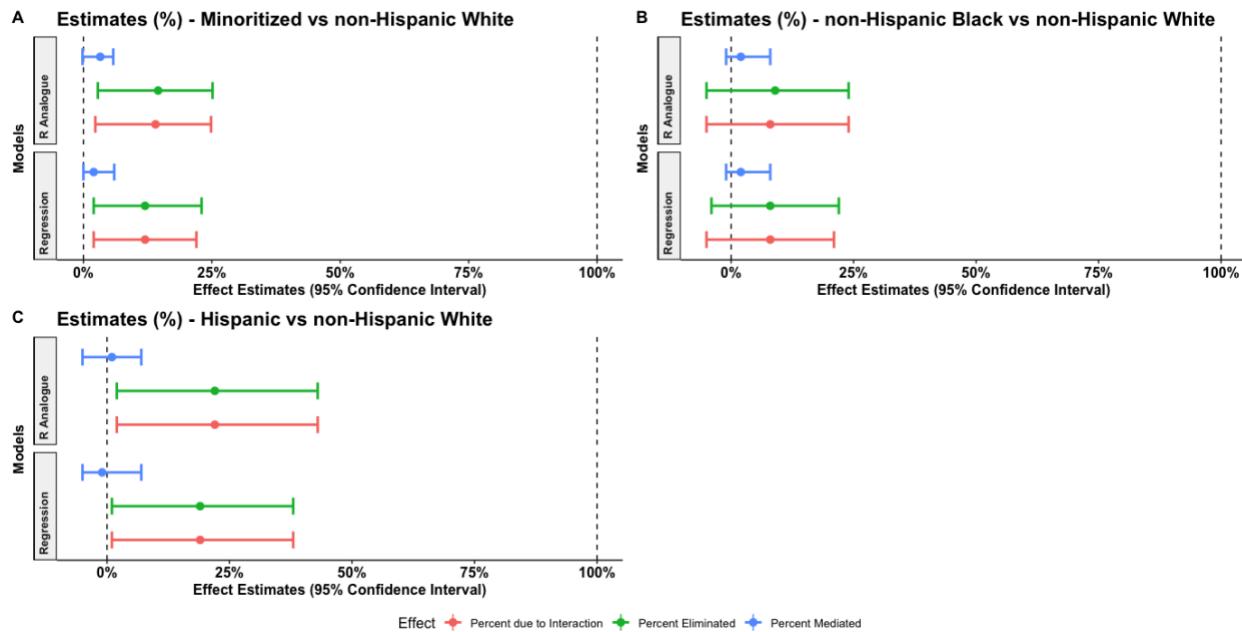
NA: not applicable



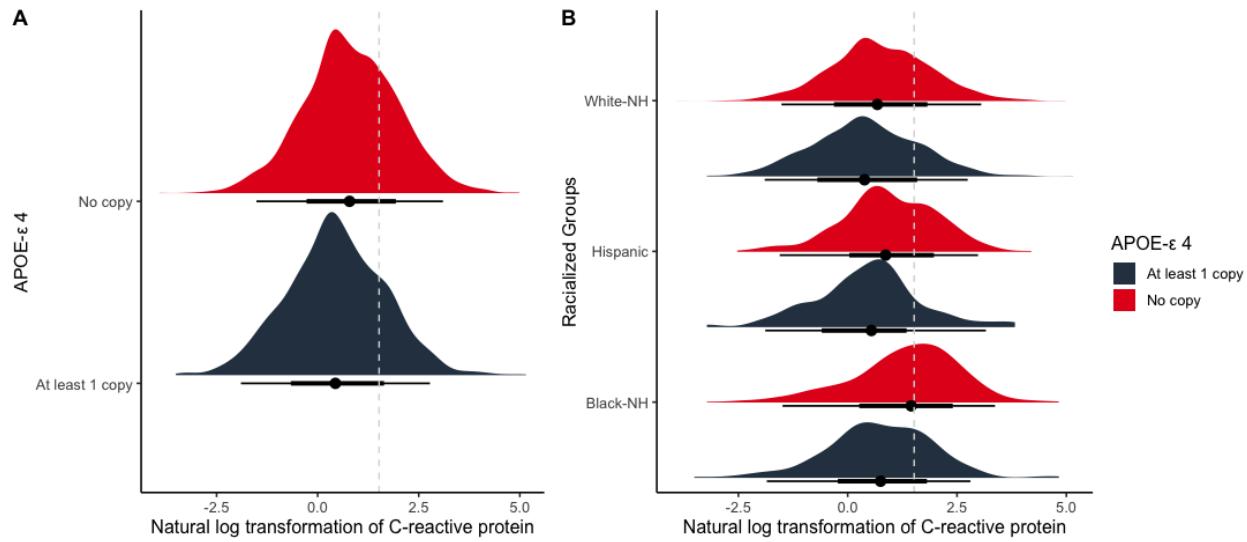
**Supplemental Figure 1:** Flow diagram of analytic sample study in the Health and Retirement Study. CRP: C-reactive protein, TC: total cholesterol; HDL-C: high density lipoprotein; HbA1C: glycosylated hemoglobin, *APOE-ε4*: apolipoprotein E  $\epsilon 4$  allele carrier status, CIND: cognitive impairment non-dementia.



**Supplemental Figure 2:** Baseline C-reactive protein levels ( $\mu\text{g/mL}$ ) by racialized social groups and sex in the United States Health and Retirement Study, waves 2006 & 2008. Dotted red line denotes the average levels of C-reactive protein in the overall sample ( $4.18\mu\text{g/mL}$ ). White-NH: non-Hispanic White, Black-NH: non-Hispanic Black.



**Supplemental Figure 3:** Plot of mediation analysis estimates from regression-based and randomized analogue models denoting percent of the racial disparity in incident dementia that is due to the mediating effect of C-reactive protein, the percent due to the interaction between exposure and mediator, and the proportion eliminated. **A.** Mediation estimates from the racial disparity between the minoritized racial group (non-Hispanic Black and Hispanic) vs the non-Hispanic White group. **B.** Mediation estimates from the racial disparity between the non-Hispanic Black vs the non-Hispanic White group. **C.** Mediation estimates from the racial disparity between the Hispanic group vs the non-Hispanic White group.



**Supplemental Figure 4:** Density plot of natural logarithmic transformation of C-reactive protein (CRP) in a selected sample of United States adults in the Health and Retirement Study.

**A.** Distribution of the natural logarithmic transformation of C-reactive protein (CRP) by *APOE-ε4* allele carrier status in our selected sample from the Health and Retirement Study (HRS). Dotted line denotes the cut off point for elevated levels of CRP at the 75th percentile ( $\geq 4.57\mu\text{g/mL}$ ).

**B.** Distribution of CRP by racialized groups and *APOE-ε4* allele carrier status. White-NH: non-Hispanic White, Black-NH: non-Hispanic Black.