From: **Association of African Ancestry–Specific APOE Missense Variant R145C With Risk of Alzheimer Disease**

JAMA. 2023;329(7):551-560. doi:10.1001/jama.2023.0268

Table 3. R145C Association With Alzheimer Disease Risk and Age at Onset[a]

	Regression analysis							
	Case-control				Age at onset			
Study stage	No. of individuals	Minor allele count	Odds ratio (95% CI)	P value	No. of individuals	Minor allele count	β (95% CI)[b]	P value
APOE ε2/ε3 genotype								
Discovery (stage 1)[c,d]	934	22	0.73 (0.26-2.04)	.55	222	4	−6.96 (−15.56 to 1.64)	.11
Replication (stage 2)[c,d]	453	12	0.78 (0.11-5.35)	.80	53	1	−18.42 (−39.23 to 2.38)	.08
Meta-analysis (stages 1 and 2)	1387	34	0.74 (0.3-1.84)	.52	275	5	−8.63 (−16.58 to −0.69)	.03
APOE ε3/ε3 genotype								
Discovery (stage 1)[c,d]	3767	196	1.06 (0.78-1.46)	.71	1108	58	−1.68 (−3.87 to 0.5)	.13
Replication (stage 2)[c,d]	1748	100	0.85 (0.48-1.53)	.60	347	8	−1.36 (−8.29 to 5.58)	.70
Meta-analysis (stages 1 and 2)	5515	296	1.01 (0.77-1.34)	.94	1455	66	−1.65 (−3.74 to 0.43)	.12
APOE ε3/ε4 genotype								
Discovery (stage 1)[c,d]	2381	71	3.01 (1.87-4.85)	6.0×10^{-6}	1063	51	−5.87 (−8.35 to −3.4)	3.4×10^{-6}
Replication (stage 2)[c,d]	1277	44	2.20 (1.04-4.65)	.04	421	21	−5.23 (−9.58 to −0.87)	.02
Meta-analysis (stages 1 and 2)	3658	115	2.75 (1.84-4.11)	8.3×10^{-7}	1484	72	−5.72 (−7.87 to −3.58)	2.0×10^{-7}
MVP replication (stage 3)[c,e]	5703	160	1.90 (0.99-3.64)	.051	289	11	−10.15 (−15.66 to −4.64)	4.0×10^{-4}

[a] Because R145C is in phase with APOE ε3, stratified analyses were limited to ε2/ε3, ε3/ε3, and ε3/ε4 genotypes. The discovery sample is composed of next-generation sequencing data, while the replication sample included imputed microarray data. Individuals with ε3[R145C]/ε4 have significantly higher Alzheimer disease risk, younger onset, and higher risk of conversion from healthy aging to Alzheimer disease than individuals with ε3/ε4.

[b] The β is the parameter estimate in the regression.

[c] Adjusted for sex and 3 genetic principal components.

[d] Stage 1 and stage 2 analyses were additionally covaried by a sparse genetic relationship matrix.

[e] Stage 3 case-control primary analysis was additionally covaried by age at last visit in the electronic health record of the Million Veteran Program.

Table Title:

R145C Association With Alzheimer Disease Risk and Age at Onset[aa] Because R145C is in phase with APOE ε3, stratified analyses were limited to ε2/ε3, ε3/ε3, and ε3/ε4 genotypes. The discovery sample is composed of next-generation sequencing data, while the replication sample included imputed microarray data. Individuals with ε3[R145C]/ε4 have significantly higher Alzheimer disease risk, younger onset, and higher risk of conversion from healthy aging to Alzheimer disease than individuals with ε3/ε4.

[b] The β is the parameter estimate in the regression.

[c] Adjusted for sex and 3 genetic principal components.

[d] Stage 1 and stage 2 analyses were additionally covaried by a sparse genetic relationship matrix.