

Supplementary Table. Parameter estimates for primary analyses. The top panel shows the results for models that examined total WMH volume. Model 1 is adjusted for age and *APOE-ε4* status. Model 2 is adjusted for age, *APOE-ε4*, and CSF ptau181 levels. Model 3 is adjusted for CSF Aβ₄₂ levels. The bottom 3 panels show the results from the regional WMH analyses and from the analyses that examined CSF tau and CSF Aβ₄₂ levels as outcomes. For all models, overall model fits were significant (LRT test, p's <0.0001).

Parameter	Total WMH									
	Beta	95% CI		Beta	95% CI		Beta	95% CI		
Intercept	0.404 **	0.198	0.610	0.511 **	0.237	0.784	0.754 ***	0.4	1.1	
EYO	0.003	-0.007	0.012	0.096	-0.193	0.385	0.081	-0.1	0.3	
Mutation status (carrier=1)	0.144	-0.037	0.325	0.001	-0.011	0.014	0.001	0.0	0.0	
EYO x Mutation status	0.028 *	0.002	0.054	0.022 *	0.002	0.041	0.011	0.0	0.0	
Inflection point	-6.6	-0.1	22.8	-19.0	12.9	27.6	-3.0	-21.0	30.0	
LRT test (p-value)	0.03			0.03			0.48			
CSF ptau181				-0.004 *	-0.007	0.000				
CSF Aβ42							-0.001 *	-0.001	0.000	
Frontal Lobe WMH				Temporal Lobe WMH				Parietal Lobe WMH		
Intercept	0.168 **	0.056	0.279	0.047	-0.017	0.110	0.087	-0.032	0.206	
EYO	0.001	-0.004	0.006	0.002	-0.001	0.005	0.003	-0.003	0.009	
Mutation status (carrier=1)	0.027	-0.069	0.123	0.052 .	-0.004	0.108	0.051	-0.060	0.163	
EYO x Mutation status	0.021 *	0.003	0.039	0.015 *	0.002	0.027	0.018 *	0.002	0.033	
Inflection point	-3.0	-0.2	14.2	-1.3	-1.5	6.0	-7.0	-0.1	26.1	
LRT test (p-value)	0.02			0.02			0.03			
Occipital Lobe WMH				CSF pTAU181				CSF Aβ42		
Intercept	0.090	-0.018	0.197	34.707 ***	25.578	43.835	439.490 ***	395.260	483.720	
EYO	0.002	-0.004	0.007	0.078	-0.384	0.540	1.354	-0.898	3.606	
Mutation status (carrier=1)	0.056	-0.085	0.196	-2.942	-16.123	10.239	100.050 **	25.506	174.594	
EYO x Mutation status	0.008 .	0.000	0.016	1.945 ***	1.327	2.562	-9.619 ***	-12.608	-6.630	
Inflection point	-22.0	-21.0	30.0	-26.0	-21.0	30.0	-30.1	-21.0	30.0	
LRT test (p-value)	0.05			<0.001			<0.001			
CSF Aβ42/tau ratio										
Intercept	9.127 ***	7.508	10.745							
EYO	-0.037	-0.099	0.026							
Mutation status (carrier=1)	-0.239	-2.142	1.665							
EYO x Mutation status	-0.176 ***	-0.256	-0.096							

Inflection point	-28.5	-21.0	-30.0	
LRT test (p-value)	<0.001			

. <0.1, * <0.05, ** <0.01, *** <0.0001. [#]Likelihood ratio test (LRT) compared to the model without an inflection point.