

Table S1. Demographic Characteristics of Participants at Initial Visit.

AD Cohort (N=11,871)								
	All (N=11871)	£3£3 (n=6454, 54.37%)	£3£4 (n=3239, 27.28%)	£2£3 (n=1308, 11.02%)	£4£4 (n=526, 4.43%)	£2£4 (n=294, 2.48%)	£2£2 (n=50, 0.42%)	P-Value
Age (year) (Mean±SD)	72.1±10.4	72.8±10.4	70.8±9.8	73.1±11.6	68.2±8.7	71.5±11.2	73.9±10.1	<0.0001
Age (n, %)								<0.0001
<65	2407 ( 20.3)	1212 ( 18.8)	717 ( 22.1)	249 ( 19.0)	160 ( 30.4)	62 ( 21.1)	7 ( 14.0)	
65-74	4475 ( 37.7)	2313 ( 35.8)	1355 ( 41.8)	429 ( 32.8)	249 ( 47.3)	110 ( 37.4)	19 ( 38.0)	
75-84	3750 ( 31.6)	2144 ( 33.2)	950 ( 29.3)	442 ( 33.8)	103 ( 19.6)	94 ( 32.0)	17 ( 34.0)	
>85	1239 ( 10.4)	785 ( 12.2)	217 ( 6.7)	188 ( 14.4)	14 ( 2.7)	28 ( 9.5)	7 ( 14.0)	
Sex (n, %)								0.08
Male	5243 ( 44.2)	2828 ( 43.8)	1459 ( 45.0)	550 ( 42.0)	252 ( 47.9)	126 ( 42.9)	28 ( 56.0)	
Female	6628 ( 55.8)	3626 ( 56.2)	1780 ( 55.0)	758 ( 58.0)	274 ( 52.1)	168 ( 57.1)	22 ( 44.0)	
Education (Year) (Mean±SD)	16.0± 2.8	16.0± 2.8	16.1± 2.7	16.0±2.8	16.1±2.9	16.2±2.7	16.2±2.4	0.725
Diagnosis of MCI (n, %)	3566 ( 30.0)	1674 ( 25.9)	1179 ( 36.4)	322 ( 24.6)	287 ( 54.6)	94 ( 32.0)	10 ( 20.0)	<0.0001
Year of Initial Visit (n, %)								0.0006
2005-2007	5336 ( 44.9)	2984 ( 46.2)	1373 ( 42.4)	624 ( 47.7)	207 ( 39.4)	127 ( 43.2)	21 ( 42.0)	
2008-2012	4219 ( 35.5)	2261 ( 35.0)	1215 ( 37.5)	422 ( 32.3)	191 ( 36.3)	111 ( 37.8)	19 ( 38.0)	
2013-2017	2316 ( 19.5)	1209 ( 18.7)	651 ( 20.1)	262 ( 20.0)	128 ( 24.3)	56 ( 19.0)	10 ( 20.0)	

MCI Cohort (N=8,305)								
	All (N=8305)	Ε3Ε3 (n=4780, 57.56%)	Ε3Ε4 (n=2060, 24.8%)	Ε2Ε3 (n=986, 11.87%)	Ε4Ε4 (n=239, 2.88%)	Ε2Ε4 (n=200, 2.41%)	Ε2Ε2 (n=40, 0.48%)	P-Value
Age (year) (Mean±SD)	71.5 ( 10.8)	72.3 ( 10.5)	69.8 ( 10.5)	72.7 ( 11.8)	65.9 ( 9.8)	70.6 ( 12.0)	73.6 ( 10.7)	<0.0001
Age (n, %)	<0.0001							
<65	1834 ( 22.1)	945 ( 19.8)	535 ( 26.0)	203 ( 20.6)	97 ( 40.6)	48 ( 24.0)	6 ( 15.0)	
65-74	3152 ( 38.0)	1782 ( 37.3)	863 ( 41.9)	321 ( 32.6)	99 ( 41.4)	71 ( 35.5)	16 ( 40.0)	
75-84	2447 ( 29.5)	1499 ( 31.4)	512 ( 24.9)	324 ( 32.9)	37 ( 15.5)	64 ( 32.0)	11 ( 27.5)	
>85	872 ( 10.5)	554 ( 11.6)	150 ( 7.3)	138 ( 14.0)	6 ( 2.5)	17 ( 8.5)	7 ( 17.5)	
Sex (n, %)	0.124							
Male	3239 ( 39.0)	1866 ( 39.0)	818 ( 39.7)	360 ( 36.5)	100 ( 41.8)	73 ( 36.5)	22 ( 55.0)	
Female	5066 ( 61.0)	2914 ( 61.0)	1242 ( 60.3)	626 ( 63.5)	139 ( 58.2)	127 ( 63.5)	18 ( 45.0)	
Education (Year) (Mean±SD)	16.1 ( 2.7)	16.1 ( 2.7)	16.2 ( 2.6)	16.0 ( 2.6)	16.1 ( 2.9)	16.2 ( 2.5)	16.5 ( 2.3)	0.429
Year of Initial Visit (n, %)	0.032							
2005-2007	3796 ( 45.7)	2225 ( 46.5)	890 ( 43.2)	484 ( 49.1)	91 ( 38.1)	86 ( 43.0)	20 ( 50.0)	
2008-2012	2869 ( 34.5)	1642 ( 34.4)	742 ( 36.0)	310 ( 31.4)	89 ( 37.2)	73 ( 36.5)	13 ( 32.5)	
2013-2017	1640 ( 19.7)	913 ( 19.1)	428 ( 20.8)	192 ( 19.5)	59 ( 24.7)	41 ( 20.5)	7 ( 17.5)	

Table S2. The Hazard Ratio of APOE Genotype from Discrete-time Proportional Hazards Model.

	AD Cohort (N=11,871)				MCI Cohort (N=8,305)			
	Unadjusted Model		Adjusted Model*		Unadjusted Model		Adjusted Model*	
	HR (95% CI)	P-value	HR (95% CI)	P-value	HR (95% CI)	P-value	HR (95% CI)	P-value
ε3ε3 (Reference group)								
ε3ε4	1.99 (1.80, 2.21)	<.0001	1.93 (1.74, 2.15)	<.0001	1.17 (1.05, 1.31)	0.005	1.31 (1.17, 1.46)	<.0001
ε2ε3	0.79 (0.65, 0.96)	0.019	0.85 (0.70, 1.04)	0.111	0.97 (0.83, 1.14)	0.753	0.94 (0.80, 1.10)	0.436
ε4ε4	3.26 (2.77, 3.84)	<.0001	2.79 (2.35, 3.31)	<.0001	1.66 (1.31, 2.09)	<.0001	2.30 (1.82, 2.92)	<.0001
ε2ε4	1.49 (1.12, 1.99)	0.006	1.66 (1.24, 2.21)	0.001	1.32 (1.00, 1.74)	0.049	1.42 (1.07, 1.88)	0.014
ε2ε2	0.47 (0.15, 1.47)	0.196	0.43 (0.14, 1.35)	0.151	1.08 (0.56, 2.08)	0.824	1.07 (0.55, 2.07)	0.840
ε2ε4 comparing to other genotype as reference group								
ε2ε4 vs. ε3ε4	0.75 (0.56, 1.00)	0.049	0.86 (0.64, 1.14)	0.298	1.13 (0.85, 1.50)	0.402	1.09 (0.81, 1.44)	0.581
ε2ε4 vs. ε4ε4	0.46 (0.34, 0.63)	<.0001	0.59 (0.43, 0.82)	0.001	0.80 (0.56, 1.13)	0.205	0.62 (0.43, 0.88)	0.007
ε2ε4 vs. ε2ε3	1.89 (1.36, 2.64)	<.0001	1.94 (1.40, 2.72)	<.0001	1.36 (1.00, 1.84)	0.051	1.51 (1.11, 2.06)	0.009
ε2ε4 vs. ε2ε2	3.16 (0.98, 10.1)	0.053	3.81 (1.19, 12.2)	0.025	1.23 (0.60, 2.49)	0.572	1.33 (0.65, 2.69)	0.436

Note. \*Models were adjusted for age, sex, education, baseline cognitive status and year of initial visit.