

Supplementary Online Content

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This supplementary material has been provided by the authors to give readers additional information about their work.

eTable 1. Education Adjusted Logical Memory Thresholds for Defining EMCI and LMCI

≤ 7 years	Logical Memory ≤ 6	Logical Memory ≤ 2
8 to 15 years	Logical Memory ≤ 9	Logical Memory ≤ 4
≥ 16 years	Logical Memory ≤ 11	Logical Memory ≤ 8

Abbreviations: EMCI, Early Mild Cognitive Impairment; LMCI, Late Mild Cognitive Impairment.

eTable 2. Linear Mixed-Effects Model of PiB SUVR

Fixed effects					95% confidence limits			
	Coefficient	SE	DF	t-value	lower	upper	p-value	
(Intercept)	0.57	1.50	29	0.38	-2.50	3.64	0.707	
Years	0.04	0.01	29	2.65	0.01	0.06	0.013	*
Age [years]	0.01	0.02	15	0.59	-0.03	0.05	0.563	
<i>APOE</i> ε4	0.29	0.21	15	1.39	-0.16	0.74	0.185	
PACC	0.07	0.20	15	0.32	-0.37	0.50	0.754	
Number of observations: 49					Random effects			
Number of individuals: 19					SD			
					(Intercept)	0.40		
					Residual	0.08		

Abbreviations: PiB, Pittsburgh Compound B; SUVR, standardized uptake value ratio; SE, standard error; DF, degrees of freedom; SD, standard deviation; PACC, Preclinical Alzheimer Cognitive Composite; * < 0.05.

eTable 3. Linear Mixed-Effects Model of Florbetapir SUVR

Fixed effects				95% confidence limits			
	Coefficient	SE	DF	t-value	lower	upper	p-value
(Intercept)	0.71	0.13	371	5.60	0.46	0.96	<0.001 ***
Years	0.01	0.00	243	4.19	0.00	0.01	<0.001 ***
Age [years]	0.00	0.00	371	2.87	0.00	0.01	0.004 **
APOEε4	0.14	0.02	371	6.66	0.10	0.18	<0.001 ***
PACC	0.00	0.02	371	-0.29	-0.03	0.03	0.772
Number of observations: 619				Random effects			
Number of individuals: 375						SD	
				(Intercept)	0.18		
				Residual	0.05		

Abbreviations: SUVR, standardized uptake value ratio; SE, standard error; DF, degrees of freedom; SD, standard deviation; PACC, Preclinical Alzheimer Cognitive Composite; ** < 0.01; *** < 0.001.

eTable 4. Linear Mixed-Effects Model of Ventricular Volume (mm³)

Fixed effects				95% confidence limits			
	Coefficient	SE	DF	t-value	lower	upper	p-value
(Intercept)	-12028	9831.8	1399	-1.22	-31315	7258.74	0.221
Years	1612	65.8	1399	24.49	1483	1740.83	<0.001 ***
Age [years]	633	131.5	432	4.81	374	891.13	<0.001 ***
APOE4>0	-3264	1655.9	432	-1.97	-6519	-9.43	0.049 *
PACC	-1898	1178.1	432	-1.61	-4214	417.53	0.108
Number of observations: 1836				Random effects			
Number of individuals: 436					SD	Correlation	
				(Intercept)	17479		
				Years	1087	0.63	
				Residual	1109		

Abbreviations: SE, standard error; DF, degrees of freedom; SD, standard deviation; PACC, Preclinical Alzheimer Cognitive Composite; * < 0.05; *** < 0.001.

eTable 5. Summary Statistics for the Follow-up Time in Years

Variable	Group	N	Minimum	1 st Quartile	Median	Mean	3 rd Quartile	Maximum
PACC	Normal	243	0.00	2.01	3.90	4.16	5.55	10.10
	Elevated	202	0.00	2.01	3.00	3.65	4.04	10.30
	Overall	445	0.00	2.01	3.06	3.93	4.17	10.30
CDR	Normal	243	0.00	2.00	3.08	4.11	6.02	10.10
	Elevated	202	0.00	2.01	2.99	3.68	4.04	10.30
	Overall	445	0.00	2.00	3.01	3.91	4.14	10.30
Logical Memory	Normal	243	0.00	2.01	3.12	4.10	5.55	10.10
	Elevated	202	0.00	2.01	3.00	3.62	4.04	10.30
	Overall	445	0.00	2.01	3.03	3.88	4.17	10.30
Florbetapir PET	Normal	204	0.00	1.97	2.02	3.15	4.08	9.31
	Elevated	172	0.00	0.00	2.01	2.55	2.45	9.16
	Overall	376	0.00	1.96	2.01	2.88	4.02	9.31
FDG PET	Normal	228	0.00	0.00	1.98	2.35	4.01	8.03
	Elevated	191	0.00	0.00	1.98	1.98	2.61	7.99
	Overall	419	0.00	0.00	1.98	2.18	3.05	8.03
CSF A β ₄₂	Normal	195	0.00	0.00	0.00	1.20	1.99	6.69
	Elevated	180	0.00	0.00	0.00	1.12	1.99	6.97
	Overall	375	0.00	0.00	0.00	1.16	1.99	6.97
CSF Tau	Normal	192	0.00	0.00	0.00	1.17	1.98	6.69
	Elevated	180	0.00	0.00	0.00	1.11	1.99	6.97
	Overall	372	0.00	0.00	0.00	1.14	1.99	6.97

CSF pTau	Normal	194	0.00	0.00	0.00	1.09	1.99	6.69
	Elevated	180	0.00	0.00	0.00	1.03	1.99	6.97
	Overall	374	0.00	0.00	0.00	1.06	1.99	6.97
Hippocampal vol.	Normal	241	0.00	1.95	2.02	2.86	4.02	10.00
	Elevated	201	0.00	1.17	2.02	2.56	3.35	9.08
	Overall	442	0.00	1.57	2.02	2.73	3.98	10.00
Ventricular vol.	Normal	239	0.00	1.04	2.02	2.89	4.04	10.00
	Elevated	196	0.00	1.04	2.02	2.60	3.65	9.03
	Overall	435	0.00	1.04	2.02	2.76	4.00	10.00

Abbreviations: PACC, Preclinical Alzheimer's Cognitive Composite; CDR, Clinical Dementia Rating; PET, positron emission tomography; FDG, fluorodeoxyglucose; CSF, cerebrospinal fluid; vol., volume.

eTable 6. Participant Counts by Month and Last Known Participant Status

Month	Normal				Elevated				Overall			
	Active	Lost to follow-up	Death	Sum	Active	Lost to follow-up	Death	Sum	Active	Lost to follow-up	Death	Sum
0	0 (0)	5 (6)	0 (0)	5 (2)	0 (0)	2 (2)	0 (0)	2 (1)	0 (0)	7 (4)	0 (0)	7 (1)
6	0 (0)	6 (7)	0 (0)	6 (2)	0 (0)	10 (12)	0 (0)	10 (4)	0 (0)	16 (10)	0 (0)	16 (3)
12	2 (1)	6 (7)	0 (0)	8 (3)	1 (1)	2 (2)	0 (0)	3 (1)	3 (1)	8 (5)	0 (0)	11 (2)
18	0 (0)	3 (4)	0 (0)	3 (1)	0 (0)	2 (2)	0 (0)	2 (1)	0 (0)	5 (3)	0 (0)	5 (1)
24	48 (30)	16 (20)	0 (0)	64 (17)	42 (35)	19 (24)	0 (0)	61 (19)	90 (32)	35 (22)	0 (0)	125 (18)
30	1 (1)	5 (6)	2 (67)	8 (24)	0 (0)	11 (14)	1 (100)	12 (38)	1 (0)	16 (10)	3 (75)	20 (28)
36	15 (9)	12 (15)	0 (0)	27 (8)	8 (7)	14 (18)	0 (0)	22 (8)	23 (8)	26 (16)	0 (0)	49 (8)
42	0 (0)	4 (5)	0 (0)	4 (2)	0 (0)	2 (2)	0 (0)	2 (1)	0 (0)	6 (4)	0 (0)	6 (1)
48	49 (31)	1 (1)	0 (0)	50 (11)	44 (36)	2 (2)	0 (0)	46 (13)	93 (33)	3 (2)	0 (0)	96 (12)
54	0 (0)	3 (4)	1 (33)	4 (12)	0 (0)	2 (2)	0 (0)	2 (1)	0 (0)	5 (3)	1 (25)	6 (9)
60	0 (0)	0 (0)	0 (0)	0 (0)	1 (1)	0 (0)	0 (0)	1 (0)	1 (0)	0 (0)	0 (0)	1 (0)
66	0 (0)	1 (1)	0 (0)	1 (0)	0 (0)	1 (1)	0 (0)	1 (0)	0 (0)	2 (1)	0 (0)	2 (0)
72	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (2)	0 (0)	2 (1)	0 (0)	2 (1)	0 (0)	2 (0)
78	0 (0)	3 (4)	0 (0)	3 (1)	0 (0)	2 (2)	0 (0)	2 (1)	0 (0)	5 (3)	0 (0)	5 (1)
84	0 (0)	6 (7)	0 (0)	6 (2)	0 (0)	4 (5)	0 (0)	4 (2)	0 (0)	10 (6)	0 (0)	10 (2)
90	0 (0)	2 (2)	0 (0)	2 (1)	0 (0)	1 (1)	0 (0)	1 (0)	0 (0)	3 (2)	0 (0)	3 (1)
96	8 (5)	7 (9)	0 (0)	15 (5)	5 (4)	3 (4)	0 (0)	8 (3)	13 (5)	10 (6)	0 (0)	23 (4)
108	25 (16)	1 (1)	0 (0)	26 (6)	12 (10)	1 (1)	0 (0)	13 (4)	37 (13)	2 (1)	0 (0)	39 (5)
120	10 (6)	1 (1)	0 (0)	11 (3)	8 (7)	0 (0)	0 (0)	8 (2)	18 (6)	1 (1)	0 (0)	19 (2)
Sum	158 (100)	82 (100)	3 (100)	243 (100)	121 (100)	80 (100)	1 (100)	202 (100)	279 (100)	162 (100)	4 (100)	445 (100)

Numbers in parentheses are percentages.

eTable 7. Characteristics by Last Known Follow-up Status

		Not Active at last follow-up (N=166)	Active at last follow-up (N=279)	Combined (N=445)	P-value
Baseline Characteristics					
Age [years]	445	75.15 (5.91)	73.26 (5.74)	74.0 (5.9)	0.001
Female	445	80 (48%)	153 (55%)	233 (52%)	0.12
Education [years]	445	16.37 (2.66)	16.41 (2.69)	16.4 (2.7)	0.86
Family history of dementia	445	62 (37%)	113 (41%)	175 (39%)	0.51
Ethnicity: Not Hispanic/Latino	445	162 (98%)	264 (95%)	426 (96%)	0.23
Hispanic/Latino		4 (2%)	12 (4%)	16 (4%)	
Unknown		0 (0%)	3 (1%)	3 (1%)	
Race: American Indian/Alaskan	445	0 (0%)	1 (0%)	1 (0.2%)	0.18
Asian		2 (1%)	4 (1%)	6 (1%)	
Black		14 (8%)	15 (5%)	29 (7%)	
White		146 (88%)	258 (92%)	404 (91%)	
More than one		4 (2%)	1 (0%)	5 (1%)	
Subjective memory concern	445	18 (11%)	86 (31%)	104 (23%)	<0.001
At least one APOEε4 allele	444	46 (28%)	79 (28%)	125 (28%)	0.89
PACC	445	-0.32 (2.5)	0.17 (2.6)	0.00 (0.65)	0.05
Mini-Mental State Exam	445	29.03 (1.08)	29.05 (1.23)	29.0 (1.2)	0.83
Logical Memory Delayed Recall	445	13.10 (3.39)	13.18 (3.18)	13.1 (3.3)	0.80
ADAS13	445	9.80 (4.29)	8.87 (4.31)	9.2 (4.3)	0.03
CDR-SB: 0	445	154 (93%)	259 (93%)	413 (93%)	0.42
0.5		11 (7%)	20 (7%)	31 (7%)	
1		1 (1%)	0 (0%)	1 (0.2%)	
Ventricular volume [% ICV]	435	2.337 (1.187)	2.121 (0.999)	2.2 (1.1)	0.05
CSF Tau [pg/ml]	369	68.1 (32.2)	67.6 (32.5)	67.8 (32.3)	0.89
CSF pTau [pg/ml]	371	30.9 (20.4)	32.7 (17.4)	32.1 (18.6)	0.39
CSF Aβ ₄₂ : < 192 pg/ml	372	65 (47%)	90 (38%)	155 (42%)	0.08
CSF Aβ ₄₂ [pg/ml]	372	197.5 (57.3)	201.4 (48.2)	200.0 (51.7)	0.50
Amyloid PET [SUVR]: > 1.1	385	41 (36%)	97 (36%)	138 (36%)	0.91
Amyloid PET [SUVR]	385	1.1 (0.16)	1.1 (0.19)	1.11 (0.18)	0.21
Elevated amyloid by PET or CSF	445	81 (49%)	121 (43%)	202 (45%)	0.27

eTable 7. *continued*

Counts (%) or mean (SD) are provided for each variable at baseline. Elevated brain amyloid is defined as baseline amyloid PET SUVR > 1.1 or CSF A β < 192 pg/ml. Status is defined as “Active” if the participant has not been reported lost to follow-up or deceased. P-values are based on two-sample t-tests or Pearson Chi-squared tests. The PACC is a sum of four baseline standardized Z-scores which decreases with worse performance.

The MMSE ranges from zero (worst) to 30 (best) points, Logical Memory Delayed Recall range from zero (worst) to 25 (best) story units, ADAS13 ranges from zero (best) to 85 (worst), and the CDRSB ranges from zero (best) to 18 (worst) points. Anti-dementia medications included donepezil, tacrine, rivastigmine, memantine, or galantamine.

Abbreviations: PACC, Preclinical Alzheimer’s Cognitive Composite; ADAS13, Alzheimer’s Disease Assessment Scale 13 item cognitive subscale; CDR-SB, Clinical Dementia Rating Sum of Boxes; ICV, intracranial volume; CSF, cerebrospinal fluid; pTau, phospho-tau; PET, positron emission tomography; SUVR, standard uptake value ratio.

eTable 8. Quadratic Time Linear Mixed-Effects Model of PACC

Fixed effects								
	Coefficient	SE	DF	t-statistic	p-value			
<i>APOEε4</i>	0.38	0.24	427	-1.58				
Age	-0.10	0.02	427	-5.32	<0.001	***		
Female	1.17	0.21	427	5.32	<0.001	***		
Education	0.27	0.04	427	6.88	<0.001	***		
Ventricular volume	-0.19	0.10	427	-2.07	0.039	*		
Family history	0.33	0.22	427	1.53	0.126			
Amyloid Group Contrasts			95% confidence limits					
Years	Contrast	SE	lower	upper	t-statistic	DF	P-value	
0	-0.39	0.22	-0.83	0.04	-1.77	2306	0.076	.
0.5	-0.41	0.22	-0.84	0.02	-1.85	2306	0.064	.
1	-0.46	0.22	-0.90	-0.03	-2.08	2306	0.038	*
2	-0.67	0.23	-1.12	-0.22	-2.93	2306	0.003	**
3	-1.02	0.25	-1.51	-0.53	-4.10	2306	<0.001	***
4	-1.51	0.29	-2.08	-0.94	-5.21	2306	<0.001	***
5	-2.14	0.36	-2.84	-1.44	-6.00	2306	<0.001	***
6	-2.92	0.45	-3.80	-2.03	-6.46	2306	<0.001	***
7	-3.83	0.57	-4.95	-2.71	-6.70	2306	<0.001	***
8	-4.88	0.71	-6.28	-3.48	-6.83	2306	<0.001	***
9	-6.07	0.88	-7.80	-4.34	-6.89	2306	<0.001	***
10	-7.40	1.07	-9.50	-5.30	-6.92	2306	<0.001	***
AIC	BIC	Log-likelihood		Random effects				
10371	10457	-5171			SD	Correlation		
					(Intercept)	1.79		
					Years	0.58	0.25	
					Residual	1.71		

Abbreviations: PACC, Preclinical Alzheimer's Cognitive Composite; SE, standard error; DF, degrees of freedom; SD, standard deviation; AIC, Akaike Information Criterion; BIC, Bayesian Information Criterion; * <0.05; ** < 0.01; *** < 0.001.

eTable 9. Quadratic Time Linear Mixed-Effects Model of MMSE

Fixed effects								
	Coefficient	SE	DF	t-statistic	p-value			
Age	-0.02	0.01	440	-3.37	<0.001	***		
Female	0.33	0.08	440	3.93	<0.001	***		
Education	0.07	0.02	440	4.23	<0.001	***		
Amyloid Group Contrasts			95% confidence limits					
Years	Contrast	SE	lower	upper	t-statistic	DF	P-value	
0	-0.05	0.08	-0.21	0.12	-0.54	2341	0.588	
0.5	-0.05	0.08	-0.22	0.11	-0.64	2341	0.522	
1	-0.08	0.08	-0.24	0.09	-0.93	2341	0.351	
2	-0.17	0.08	-0.34	-0.01	-2.06	2341	0.039	*
3	-0.34	0.09	-0.52	-0.15	-3.55	2341	<0.001	***
4	-0.56	0.12	-0.80	-0.32	-4.66	2341	<0.001	***
5	-0.85	0.16	-1.17	-0.53	-5.20	2341	<0.001	***
6	-1.21	0.22	-1.64	-0.77	-5.41	2341	<0.001	***
7	-1.62	0.30	-2.21	-1.04	-5.48	2341	<0.001	***
8	-2.11	0.38	-2.86	-1.36	-5.50	2341	<0.001	***
9	-2.66	0.48	-3.60	-1.71	-5.50	2341	<0.001	***
10	-3.27	0.60	-4.44	-2.10	-5.49	2341	<0.001	***
AIC	BIC	Log-likelihood		Random effects				
8054	8123	-4015			SD	Correlation		
				(Intercept)	0.64			
				Years	0.28	-0.23		
				Residual	1.14			

Abbreviations: MMSE, Mini-Mental State Exam; SE, standard error; DF, degrees of freedom; SD, standard deviation; AIC, Akaike Information Criterion; BIC, Bayesian Information Criterion; * <0.05; ** < 0.01; *** < 0.001.

eTable 10. Quadratic Time Linear Mixed-Effects Model of CDRSB

Fixed effects								
	Coefficient	SE	t-statistic	p-value				
Age	0.00	0.00	0.26	0.798				
Amyloid Group Contrasts			95% confidence limits					
Years	Contrast	SE	lower	upper	t-statistic	DF	P-value	
0	0.01	0.01	-0.02	0.03	0.47	2331	0.641	
0.5	-0.01	0.02	-0.05	0.03	-0.53	2331	0.596	
1	-0.02	0.03	-0.07	0.04	-0.51	2331	0.607	
2	0.02	0.05	-0.08	0.11	0.32	2331	0.749	
3	0.10	0.06	-0.02	0.22	1.61	2331	0.107	
4	0.23	0.08	0.08	0.38	3.07	2331	0.002	**
5	0.42	0.10	0.23	0.62	4.30	2331	<0.001	***
6	0.66	0.13	0.41	0.92	5.07	2331	<0.001	***
7	0.96	0.18	0.61	1.30	5.45	2331	<0.001	***
8	1.31	0.23	0.85	1.76	5.60	2331	<0.001	***
9	1.71	0.30	1.11	2.30	5.63	2331	<0.001	***
10	2.16	0.38	1.40	2.91	5.61	2331	<0.001	***
AIC	BIC	Log-likelihood			Compound symmetry correlation rho = 0.49			
2755	2870	-1357			Residual standard error 0.15			

Heterogeneous variance parameters per month:

0	6	12	24	36	48	60	72	84	96	108	120
1	2.18	3.14	3.94	5.68	5.31	5.56	7.49	15.94	16.46	24.09	20.99

Abbreviations: CDRSB, Clinical Dementia Rating Sum of Boxes; SE, standard error; DF, degrees of freedom; SD, standard deviation; AIC, Akaike Information Criterion; BIC, Bayesian Information Criterion; * <0.05; ** < 0.01; *** < 0.001.

eTable 11. Quadratic Time Linear Mixed-Effects Model of Logical Memory

Fixed effects							
	Coefficient	SE	DF	t-statistic	p-value		
<i>APOEε4</i>	-0.58	0.35	428	-1.66	0.097	.	
Age	-0.04	0.03	428	-1.57	0.117		
Female	1.16	0.31	428	3.71	<0.001	***	
Education	0.38	0.06	428	6.71	<0.001	***	
Ventricular volume	-0.25	0.15	428	-1.69	0.091	.	
Amyloid Group Contrasts			95% confidence limits				
Years	Contrast	SE	lower	upper	t-statistic	DF	P-value
0	-0.12	0.32	-0.75	0.51	-0.38	1879	0.704
1	-0.16	0.32	-0.79	0.47	-0.50	1879	0.619
2	-0.27	0.33	-0.92	0.37	-0.84	1879	0.402
3	-0.47	0.34	-1.14	0.21	-1.35	1879	0.177
4	-0.73	0.38	-1.48	0.02	-1.91	1879	0.056
5	-1.07	0.45	-1.96	-0.19	-2.39	1879	0.017
6	-1.49	0.55	-2.57	-0.41	-2.72	1879	0.007
7	-1.99	0.68	-3.33	-0.65	-2.91	1879	0.004
8	-2.56	0.85	-4.22	-0.90	-3.03	1879	0.002
9	-3.21	1.04	-5.24	-1.18	-3.10	1879	0.002
10	-3.93	1.25	-6.39	-1.47	-3.14	1879	0.002
AIC	BIC	Log-likelihood		Random effects			
9715	9793	-4844			SD	Correlation	
				(Intercept)	2.58		
				Years	0.55	0.24	
				Residual	2.38		

Abbreviations: SE, standard error; DF, degrees of freedom; SD, standard deviation; AIC, Akaike Information Criterion; BIC, Bayesian Information Criterion; * <0.05; ** < 0.01; *** < 0.001.

eTable 12. Quadratic Time Logistic Mixed-Effects Model of CDR-Global Progression to Scores Greater Than 0

Fixed effects								
	Coefficient	SE	z-statistic	p-value				
Age	0.01	0.03	0.35	0.724				
Ventricular volume	0.57	0.18	3.13	0.002	**			
Amyloid Group Profiles			95% confidence limits					
Year	Group	Rate	lower	upper				
0	Elevated	2.14	0.47	3.81				
	Normal	2.40	0.95	3.84		AIC	BIC	Log-likelihood
1	Elevated	6.43	3.78	9.09		1270	1321	-626
	Normal	4.80	2.84	6.76				
2	Elevated	13.45	9.51	17.39				
	Normal	8.01	5.39	10.63		Random effects		
3	Elevated	22.18	16.50	27.86			SD	
	Normal	11.63	8.21	15.06		(Intercept)	2.78	
4	Elevated	32.23	24.27	40.20				
	Normal	15.31	10.99	19.63				
5	Elevated	43.93	33.55	54.30				
	Normal	18.84	13.58	24.11				
6	Elevated	56.59	44.71	68.46				
	Normal	22.16	15.92	28.39				
7	Elevated	68.18	56.00	80.37				
	Normal	25.11	17.75	32.48				
8	Elevated	77.25	65.20	89.31				
	Normal	27.49	18.46	36.52				
9	Elevated	83.72	71.46	95.98				
	Normal	29.01	17.38	40.64				
10	Elevated	88.21	74.98	100.00				
	Normal	29.43	14.16	44.70				

Abbreviations: CDR, Clinical Dementia Rating; SE, standard error; DF, degrees of freedom; SD, standard deviation; AIC, Akaike Information Criterion; BIC, Bayesian Information Criterion; * <0.05; ** < 0.01; *** < 0.001.

eTable 13. Linear Time Logistic Mixed-Effects Model of CDR-Sum of Boxes Increase of More Than One Point

Fixed effects								
	Coefficient	SE	z-statistic	p-value				
Age	0.02	0.04	0.46	0.643				
Ventricular volume	0.69	0.22	3.16	0.002	**			
Amyloid Group Profiles			95% confidence limits					
Year	Group	Rate	lower	upper				
0	Elevated	0.89	0.00	2.21				
	Normal	1.62	0.52	2.72				
1	Elevated	2.40	0.42	4.38				
	Normal	2.50	1.13	3.87				
2	Elevated	5.23	2.46	8.00		AIC	BIC	Log-likelihood
	Normal	3.67	1.98	5.35		924	965	-455
3	Elevated	9.36	5.62	13.09				
	Normal	5.13	3.09	7.18				
4	Elevated	14.48	9.37	19.58		Random effects		
	Normal	6.87	4.39	9.35		(Intercept)	SD	
5	Elevated	20.96	13.41	28.51				
	Normal	8.85	5.81	11.89				
6	Elevated	30.60	18.73	42.47				
	Normal	11.07	7.23	14.91				
7	Elevated	45.52	28.35	62.68				
	Normal	13.65	8.58	18.71				
8	Elevated	64.13	44.63	83.62				
	Normal	16.85	9.83	23.88				
9	Elevated	80.28	63.41	97.15				
	Normal	21.15	11.10	31.19				
10	Elevated	90.43	78.57	100.00				
	Normal	27.14	12.84	41.43				

Abbreviations: CDR, Clinical Dementia Rating; SE, standard error; DF, degrees of freedom; SD, standard deviation; AIC, Akaike Information Criterion; BIC, Bayesian Information Criterion; * <0.05; ** < 0.01; *** < 0.001.

eTable 14. Linear Time Logistic Mixed-Effects Model of Progression to EMCI

Fixed effects							
	Coefficient	SE	z-statistic	p-value			
Age	0.15	0.06	2.35	0.019	*		
Ventricular volume	0.69	0.31	2.24	0.025	*		
Amyloid Group Profiles			95% confidence limits				
Year	Group	Rate	lower	upper			
0	Elevated	0.77	0.00	1.74			
	Normal	0.41	0.00	1.13			
1	Elevated	1.96	0.47	3.44			
	Normal	0.80	0.00	1.73		AIC	BIC
2	Elevated	3.87	1.81	5.94		602	641
	Normal	1.39	0.23	2.54			Log-likelihood
3	Elevated	6.32	3.62	9.02			-294
	Normal	2.12	0.72	3.53		Random effects	
4	Elevated	9.18	5.71	12.66			SD
	Normal	2.95	1.27	4.62		(Intercept)	3.83
5	Elevated	12.50	7.72	17.28			
	Normal	3.81	1.84	5.78			
6	Elevated	16.94	9.16	24.73			
	Normal	4.70	2.35	7.05			
7	Elevated	24.84	10.58	39.11			
	Normal	5.69	2.78	8.60			
8	Elevated	39.87	16.84	62.90			
	Normal	6.89	3.02	10.76			
9	Elevated	61.62	34.49	88.76			
	Normal	8.46	2.80	14.11			
10	Elevated	80.84	57.44	100.00			
	Normal	10.59	1.59	19.58			

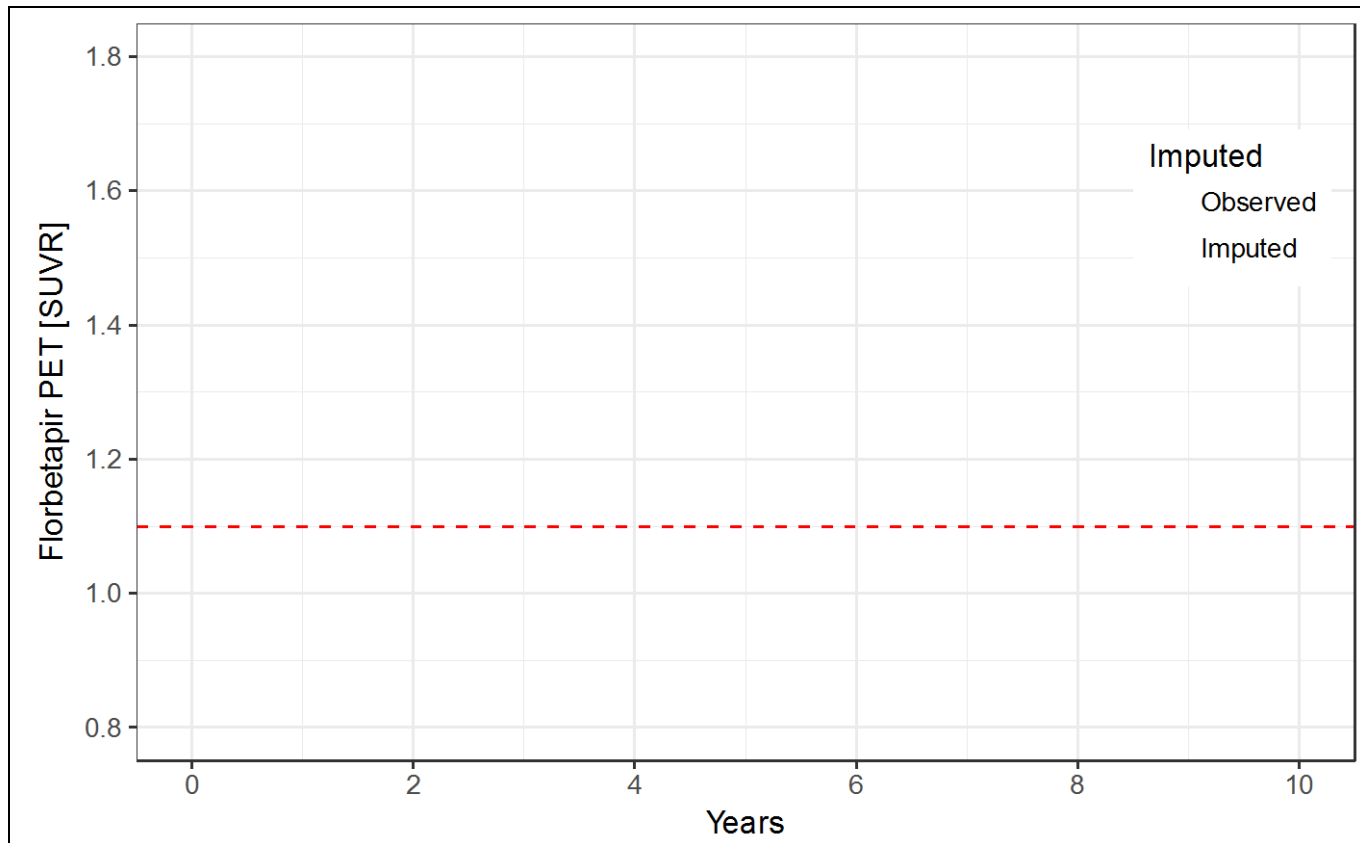
Abbreviations: EMCI, Early Mild Cognitive Impairment; SE, standard error; DF, degrees of freedom; SD, standard deviation; AIC, Akaike Information Criterion; BIC, Bayesian Information Criterion; * <0.05; ** < 0.01; *** < 0.001.

eTable 15. Linear Time Logistic Mixed-Effects Model of Progression to LMCI

Fixed effects							
	Coefficient	SE	z-statistic	p-value			
Age	0.21	0.10	2.15	0.031	*		
Education	0.28	0.19	1.43	0.152			
Amyloid Group Profiles			95% confidence limits				
Year	Group	Rate	lower	upper			
0	Elevated	0.00	0.00	0.50			
	Normal	0.16	0.00	0.66		AIC	BIC
1	Elevated	0.10	0.00	1.09		358	397
	Normal	0.37	0.00	1.02			Log-likelihood
2	Elevated	0.86	0.00	2.30			
	Normal	0.70	0.00	1.51		Random effects	
3	Elevated	2.20	0.30	4.11			SD
	Normal	1.11	0.13	2.10		(Intercept)	4.82
4	Elevated	3.88	1.48	6.28			
	Normal	1.56	0.39	2.73			
5	Elevated	5.83	2.87	8.79			
	Normal	2.00	0.64	3.36			
6	Elevated	7.58	3.63	11.54			
	Normal	2.45	0.90	4.00			
7	Elevated	9.11	2.34	15.88			
	Normal	2.93	1.17	4.68			
8	Elevated	12.06	0.00	26.77			
	Normal	3.43	1.42	5.44			
9	Elevated	21.55	0.00	50.13			
	Normal	3.89	1.50	6.28			
10	Elevated	46.57	7.78	85.36			
	Normal	4.23	1.11	7.36			

Abbreviations: LMCI, Late Mild Cognitive Impairment; SE, standard error; DF, degrees of freedom; SD, standard deviation; AIC, Akaike Information Criterion; BIC, Bayesian Information Criterion; * <0.05; ** < 0.01; *** < 0.001.

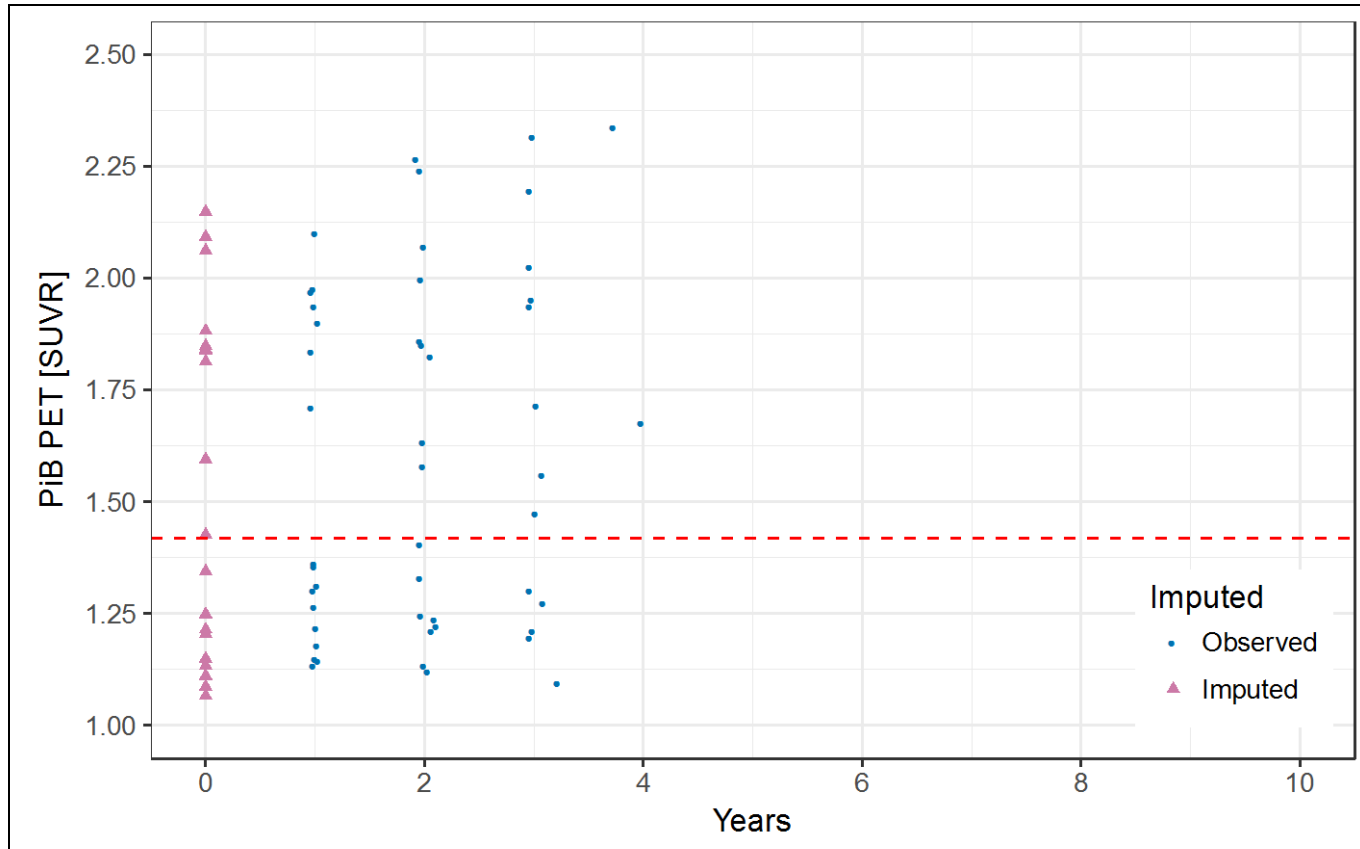
eFigure 1. Imputed Baseline Florbetapir SUVR



For individuals with follow-up florbetapir SUVR observations, but missing baseline florbetapir SUVR, values were imputed based on a linear mixed-effects model. The model was fit to all individuals with florbetapir data (n=375), but only those with missing baseline data are shown. The imputation is similar to the intercepts individual-specific ordinary least square regression, but with some shrinkage to the mean. A few individuals who are above the threshold for elevated amyloid (horizontal dashed line) at follow-up visits are classified as normal amyloid.

Abbreviations: SUVR, standardized uptake value ratio.

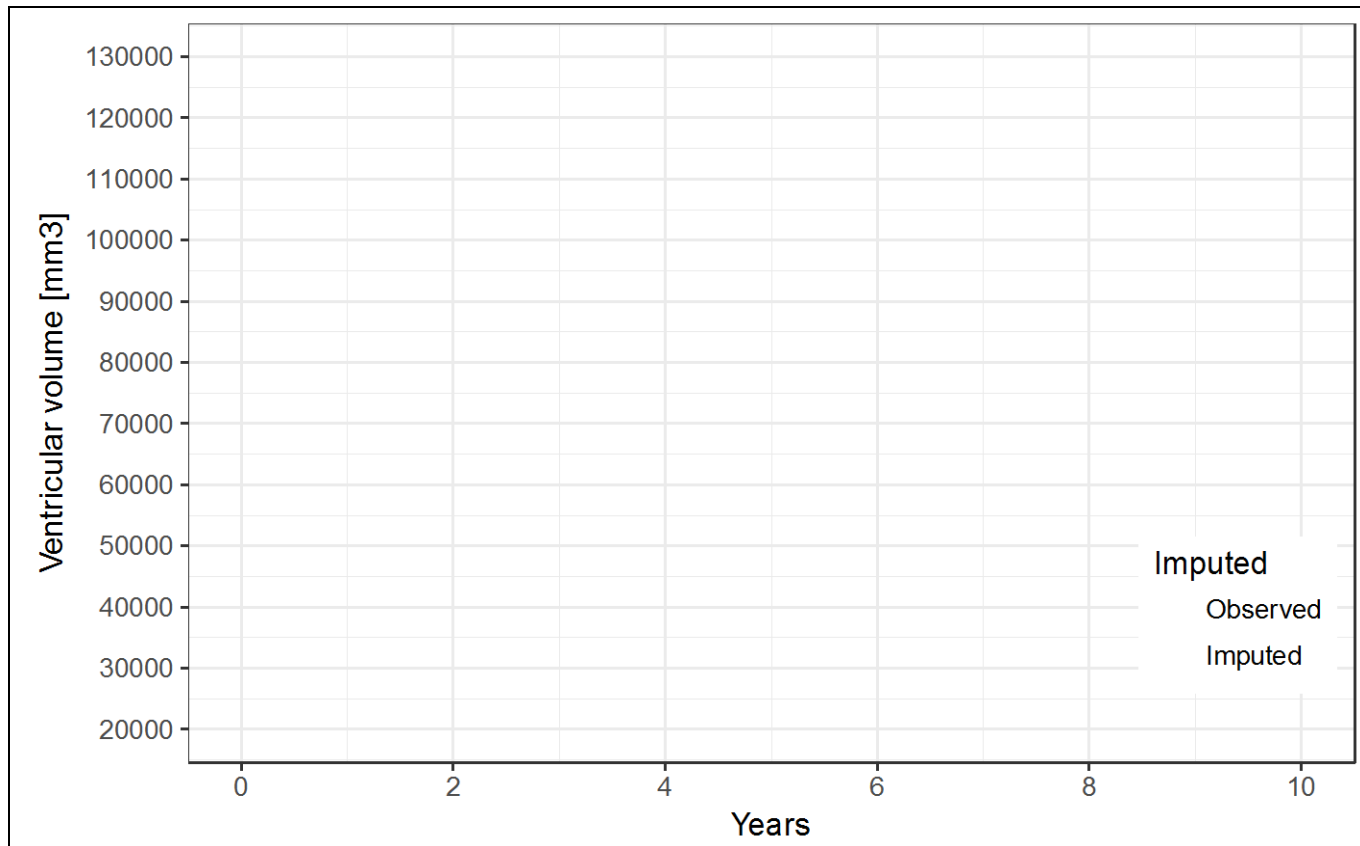
eFigure 2. Imputed Baseline PiB SUVR



For individuals with follow-up PiB SUVR observations, but missing baseline PiB SUVR, values were imputed based on a linear mixed-effects model. The model was fit to all individuals with PiB data (n=19). No individuals with baseline subjective memory concerns received PiB PET imaging. The imputation is similar to the intercepts of individual-specific ordinary least square regression, but with some shrinkage to the mean. One individual who is above the threshold for abnormal amyloid (horizontal dashed line) at follow-up visits is classified as normal.

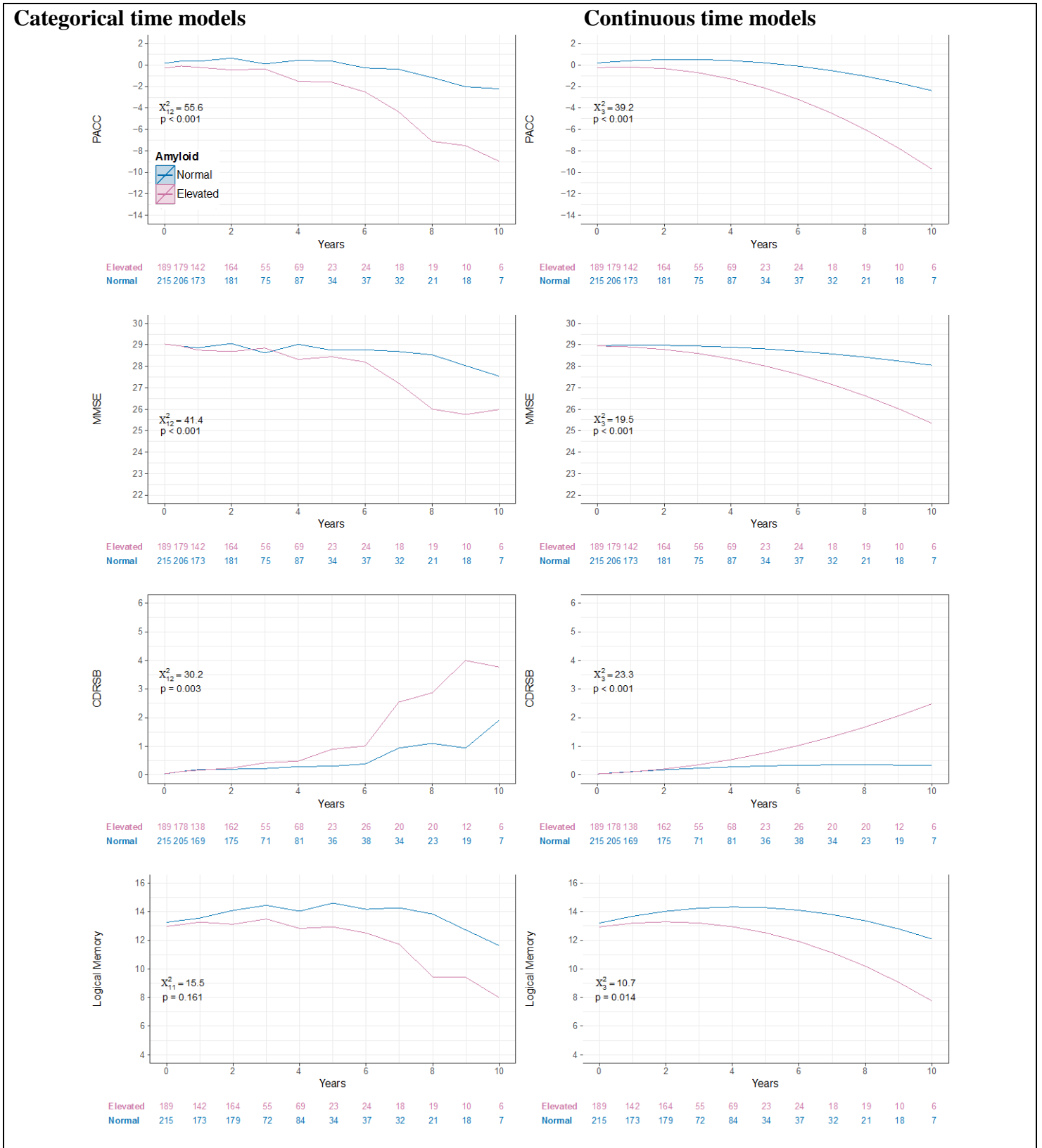
Abbreviation: PiB, Pittsburgh Compound B; SUVR, standardized uptake value ratio.

eFigure 3. Imputed Baseline Ventricular Volumes



For individuals with follow-up volumetric magnetic resonance imaging, missing baseline values were imputed based on a linear mixed-effects model. The model was fit to all individuals with magnetic resonance imaging data (n=436), but only those with missing baseline data are shown. The imputation is similar to the intercepts of individual-specific ordinary least square regression, but with some shrinkage to the mean. These imputed baseline values are used as covariates in regression models of other outcomes.

eFigure 4. Mean Cognitive Profiles Without Imputing Baseline Amyloid Status

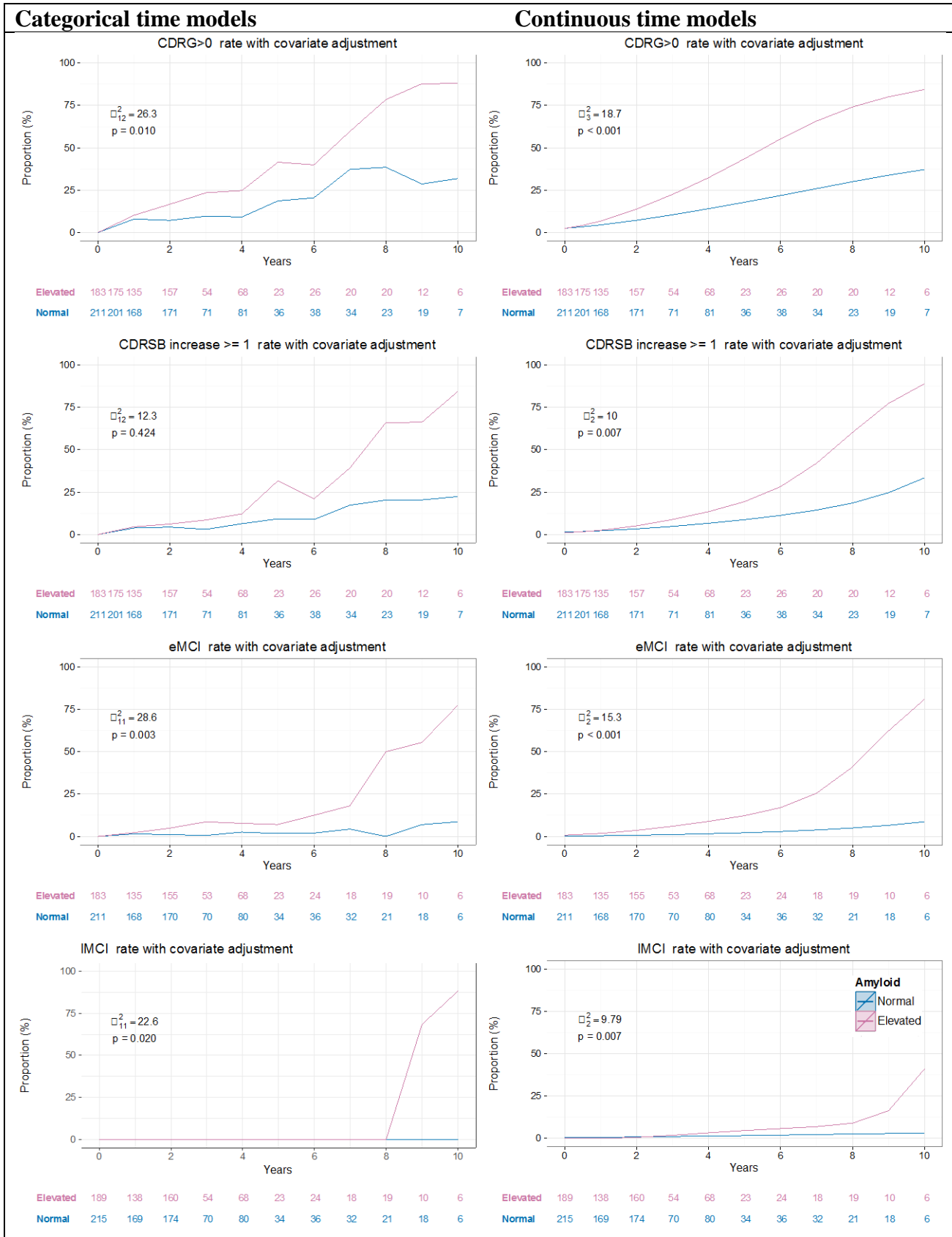


eFigure 4. continued

Only individuals with baseline Amyloid data are included in these analyses. Profiles are from linear mixed-effects models controlling for age at baseline (conditional on mean age, 74 years). The models depicted on the left treat time as a categorical variable, while those on the right treat time as continuous and include a quadratic term. P-values are from likelihood ratio tests comparing models with versus without Amyloid group. Shaded regions represent 95% confidence intervals. Dot sizes are proportional to the number of observations. The PACC is a sum of four baseline standardized Z-scores which decreases with worse performance. The MMSE ranges from zero (worst) to 30 (best) points, Logical Memory Delayed Recall range from zero (worst) to 25 (best) story units, and the CDRSB ranges from zero (best) to 18 (worst) points.

Abbreviations: PACC, Preclinical Alzheimer's Cognitive Composite; MMSE, Mini-Mental State Exam; CDRSB, Clinical Dementia Rating Sum of Boxes.

eFigure 5. Progression Event Rates Without Imputing Amyloid Group

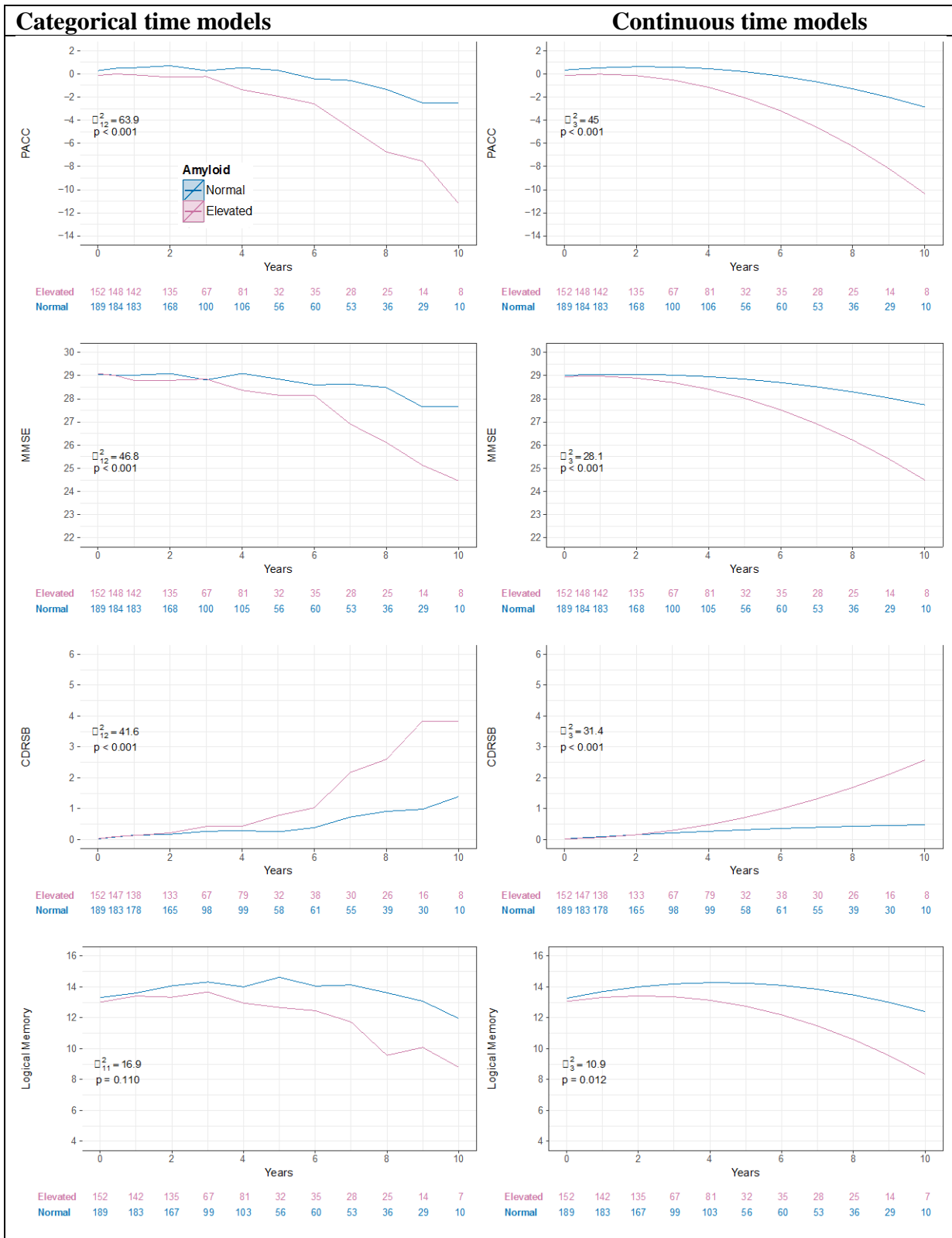


eFigure 5. *continued*

Only individuals with baseline Amyloid data are included in these analyses. Profiles are from logistic mixed-effects models controlling for baseline age (conditional on mean age, 74 years) and other covariates selected by AIC. P-values are from likelihood ratio tests comparing models with versus without Amyloid group. Shaded regions represent 95% confidence intervals. Dot sizes are proportional to the number of observations.

Abbreviations: CDRSB, Clinical Dementia Rating Global; CDRSB, Clinical Dementia Rating Sum of Boxes; EMCI, Early Mild Cognitive Impairment; LMCI, Late Mild Cognitive Impairment.

eFigure 6. Mean Cognitive Profiles Excluding Individuals With Subjective Memory Concerns at Baseline

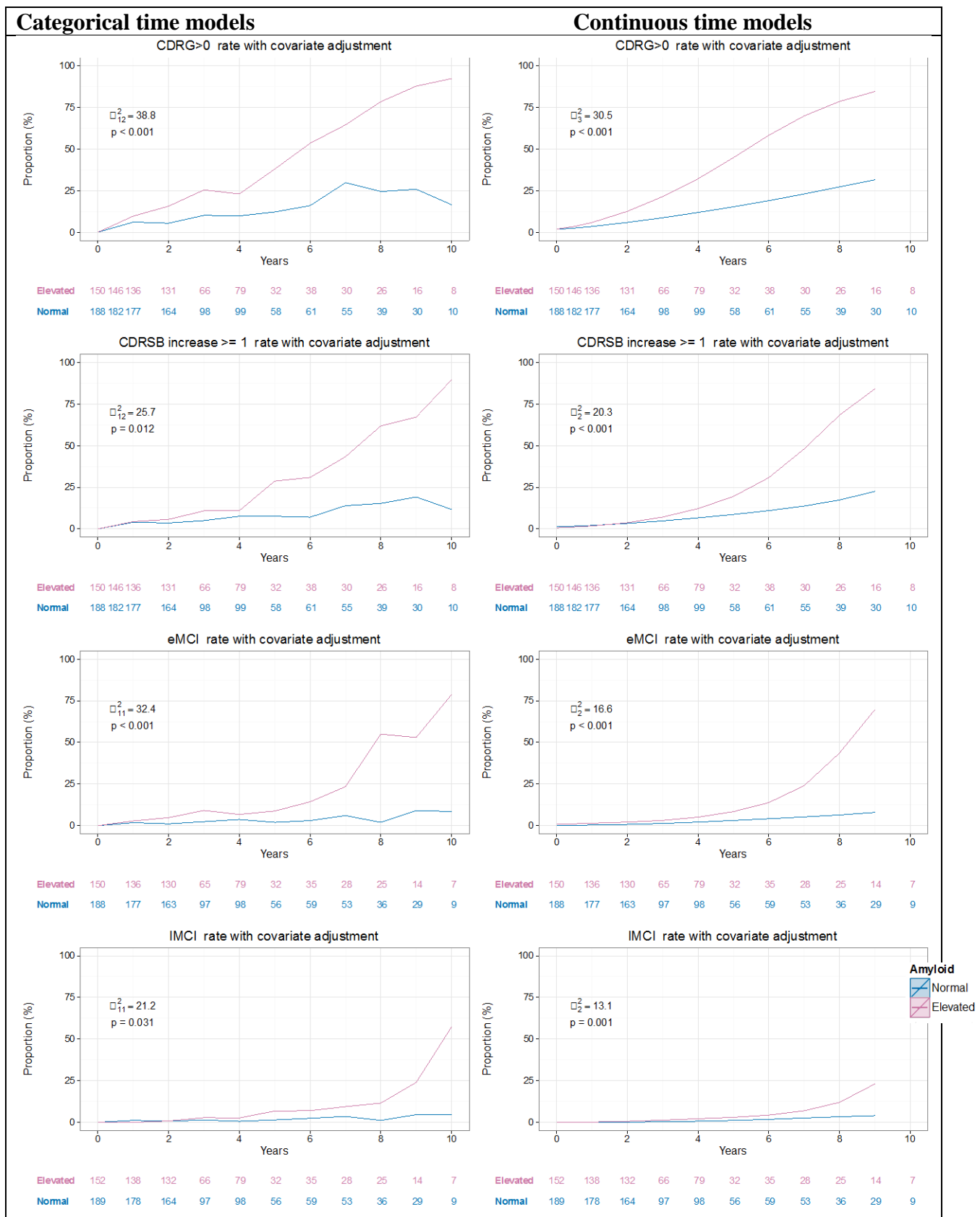


eFigure 6. *continued*

Profiles are from linear mixed-effects models controlling for age at baseline (conditional on mean age). The models depicted on the left treat time as a categorical variable, while those on the right treat time as continuous and include a quadratic term. P-values are from likelihood ratio tests comparing models with versus without Amyloid group. Shaded regions represent 95% confidence intervals. Dot sizes are proportional to the number of observations. The PACC is a sum of four baseline standardized Z-scores which decreases with worse performance. The MMSE ranges from zero (worst) to 30 (best) points, Logical Memory Delayed Recall range from zero (worst) to 25 (best) story units, and the CDRSB ranges from zero (best) to 18 (worst) points.

Abbreviations: PACC, Preclinical Alzheimer's Cognitive Composite; MMSE, Mini-Mental State Exam; CDRSB, Clinical Dementia Rating Sum of Boxes.

eFigure 7. Progression Event Rates Excluding Individuals With Subjective Memory Concerns at Baseline

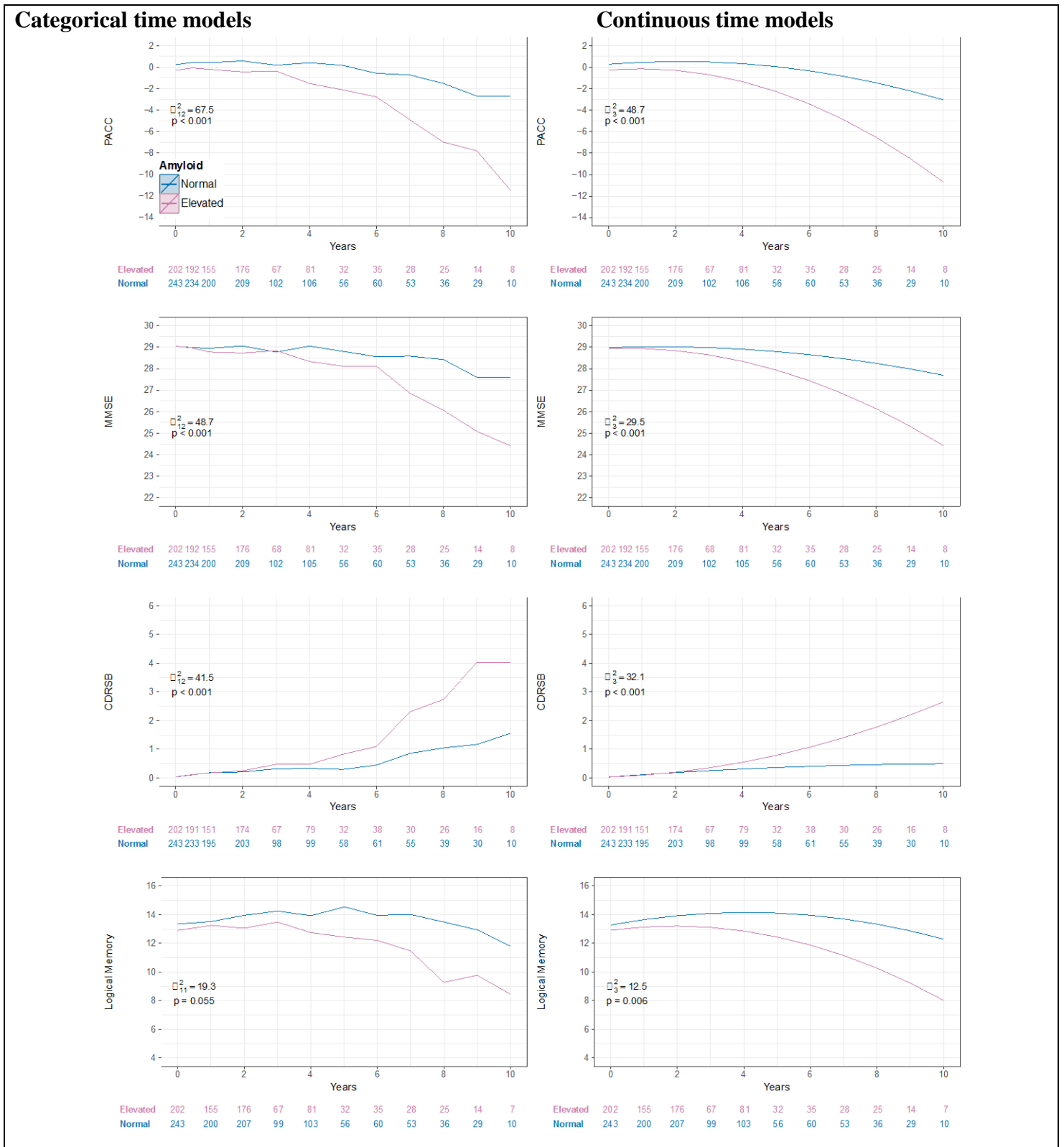


eFigure 7. continued

Profiles are from logistic mixed-effects models controlling for baseline age (conditional on mean age). P-values are from likelihood ratio tests comparing models with versus without Amyloid group. Shaded regions represent 95% confidence intervals. Dot sizes are proportional to the number of observations.

Abbreviations: CDRSB, Clinical Dementia Rating Global; CDRSB, Clinical Dementia Rating Sum of Boxes; EMCI, Early Mild Cognitive Impairment; LMCI, Late Mild Cognitive Impairment.

eFigure 8. Mean Cognitive Profiles Controlling for Age Only

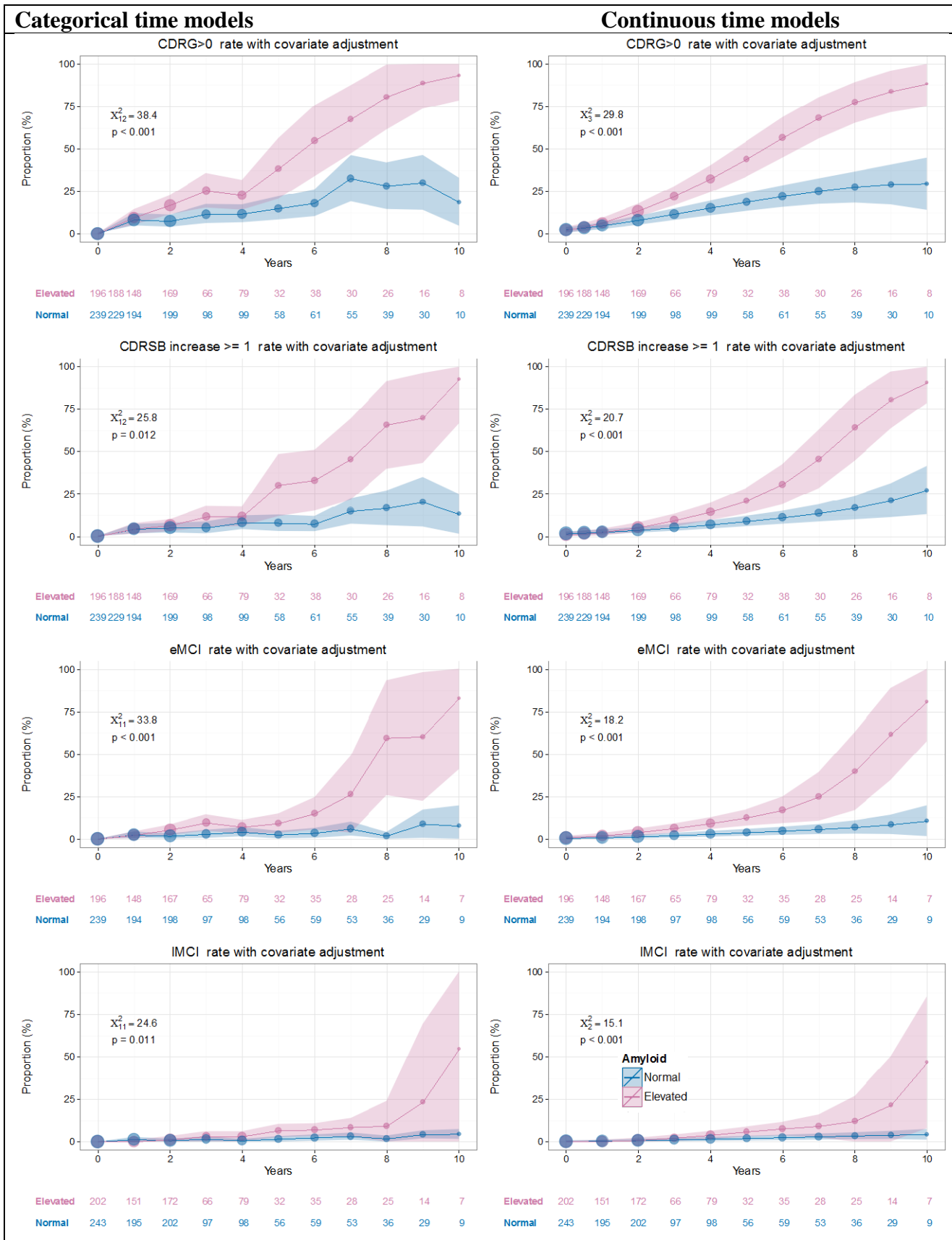


eFigure 8. *continued*

Profiles are from linear mixed-effects models controlling for age at baseline (conditional on mean age). The models depicted on the left treat time as a categorical variable, while those on the right treat time as continuous and include a quadratic term. P-values are from likelihood ratio tests comparing models with versus without Amyloid group. Shaded regions represent 95% confidence intervals. Dot sizes are proportional to the number of observations. The PACC is a sum of four baseline standardized Z-scores which decreases with worse performance. The MMSE ranges from zero (worst) to 30 (best) points, Logical Memory Delayed Recall range from zero (worst) to 25 (best) story units, and the CDRSB ranges from zero (best) to 18 (worst) points.

Abbreviations: PACC, Preclinical Alzheimer's Cognitive Composite; MMSE, Mini-Mental State Exam; CDRSB, Clinical Dementia Rating Sum of Boxes.

eFigure 9. Progression Event Rates Controlling for Age Only

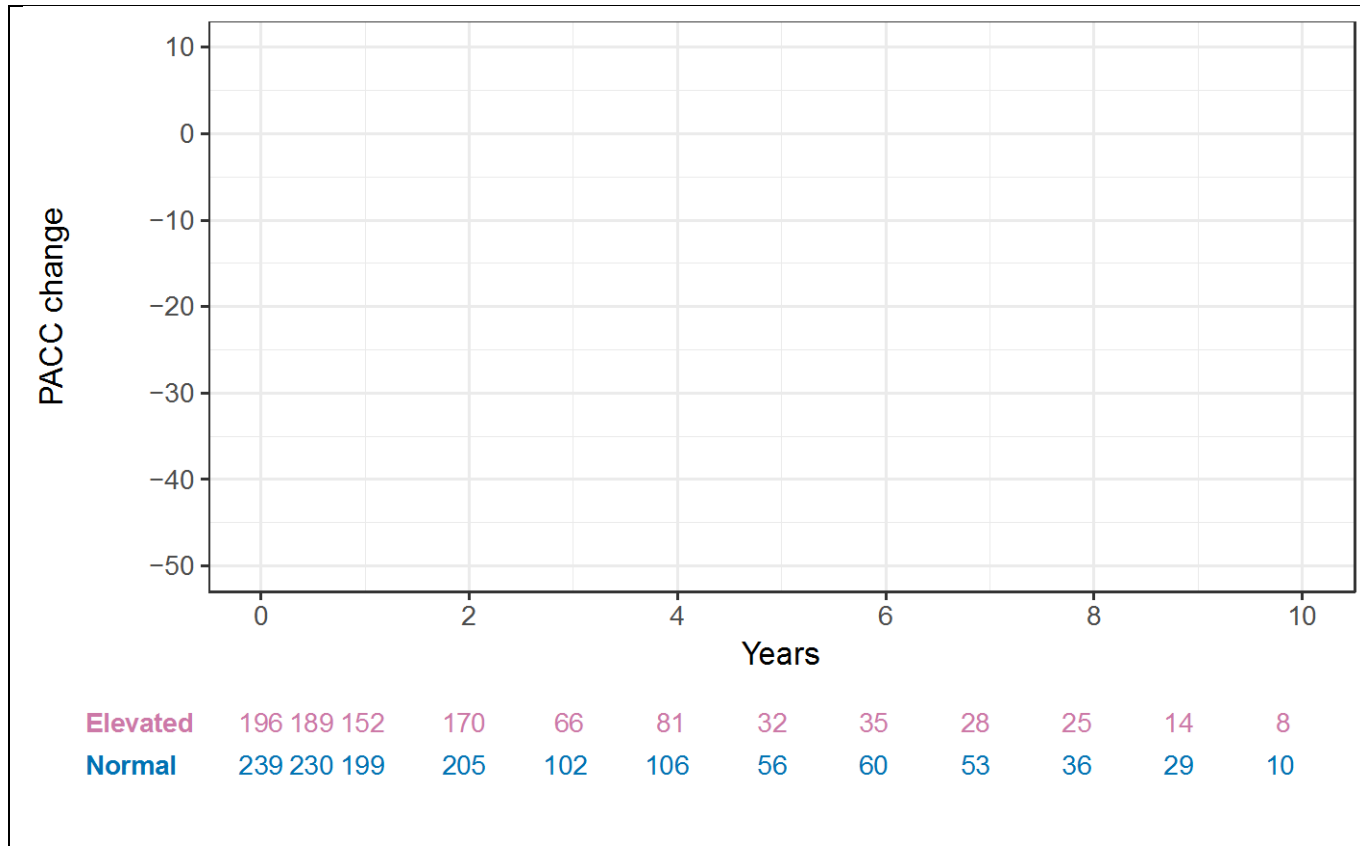


eFigure 9. *continued*

Profiles are from logistic mixed-effects models controlling for baseline age (conditional on mean age). P-values are from likelihood ratio tests comparing models with versus without Amyloid group. Shaded regions represent 95% confidence intervals. Dot sizes are proportional to the number of observations.

Abbreviations: CDRSB, Clinical Dementia Rating Global; CDRSB, Clinical Dementia Rating Sum of Boxes; EMCI, Early Mild Cognitive Impairment; LMCI, Late Mild Cognitive Impairment.

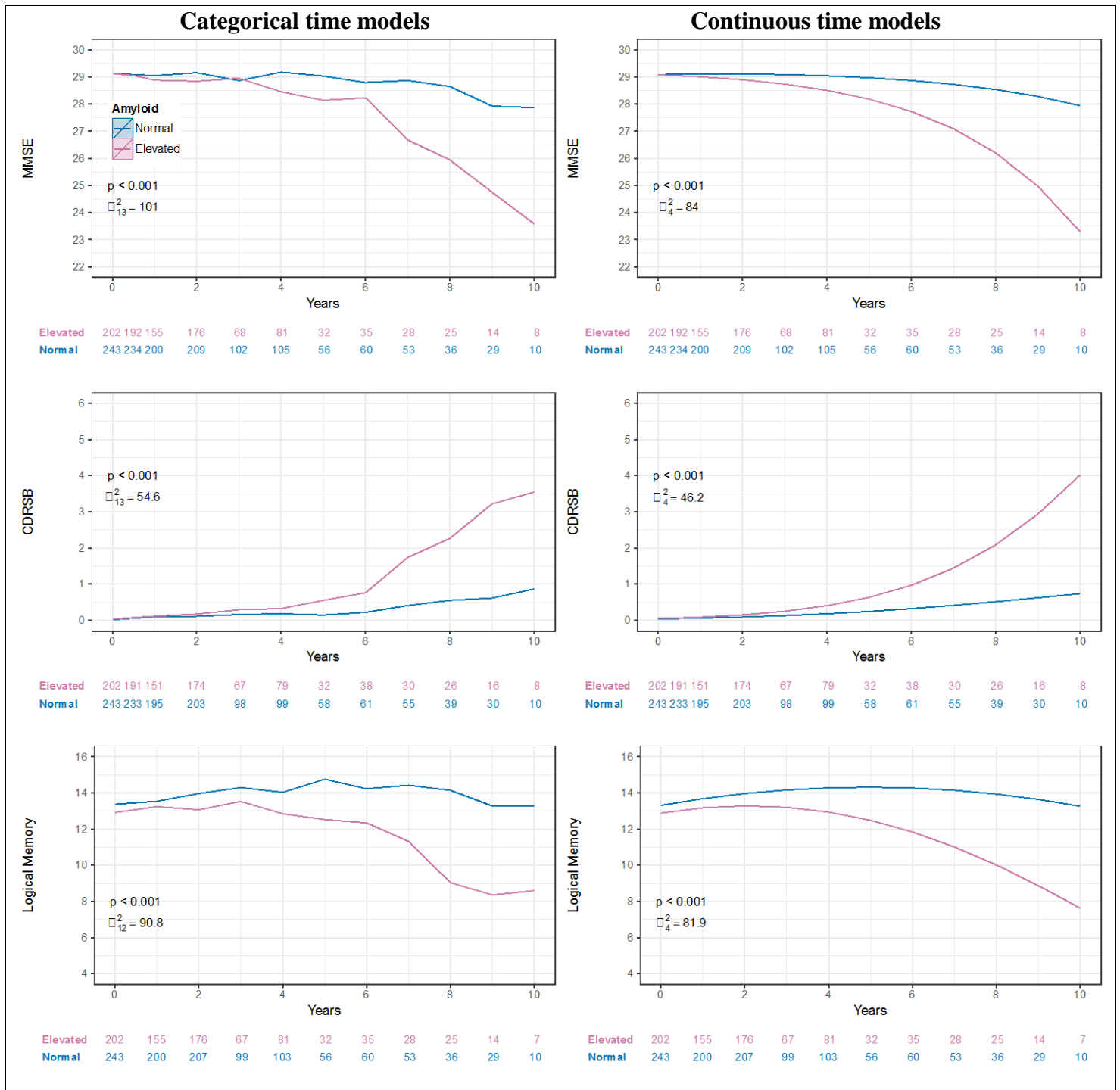
eFigure 10. PACC Change



Raw observations of PACC change plotted by Amyloid group. Numbers along the bottom are observation counts for each study visit. The PACC is a sum of four baseline standardized Z-scores which decreases with worse performance.

Abbreviation: PACC, Preclinical Alzheimer's Cognitive Composite.

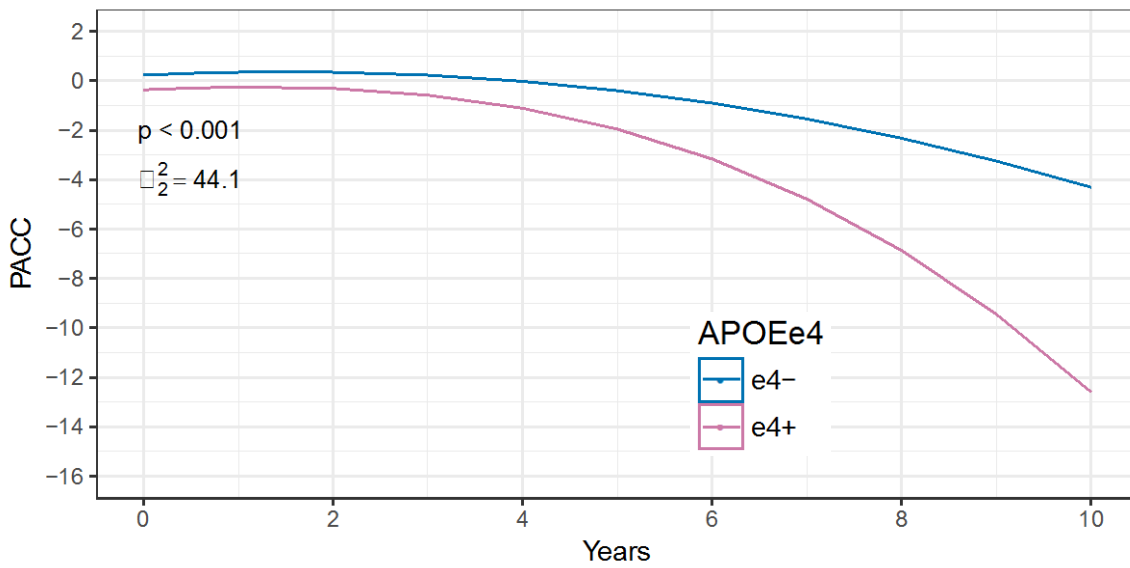
eFigure 11. Logistic Mixed-Effects Models Controlling for Age



Profiles are from logistic mixed-effects models controlling for baseline age (conditional on mean age). The models depicted on the left treat time as a categorical variable, while those on the right treat time as continuous and include a quadratic term. P-values are from likelihood ratio tests comparing models with versus without Amyloid group. Shaded regions represent 95% confidence intervals. The MMSE ranges from zero (worst) to 30 (best) points, Logical Memory Delayed Recall range from zero (worst) to 25 (best) story units, and the CDRSB ranges from zero (best) to 18 (worst) points.

Abbreviations: MMSE, Mini-Mental State Exam; CDRSB, Clinical Dementia Rating Sum of Boxes.

eFigure 12. Apolipoprotein E ε4 Allele Group Mean PACC Profiles for Those With Elevated Amyloid

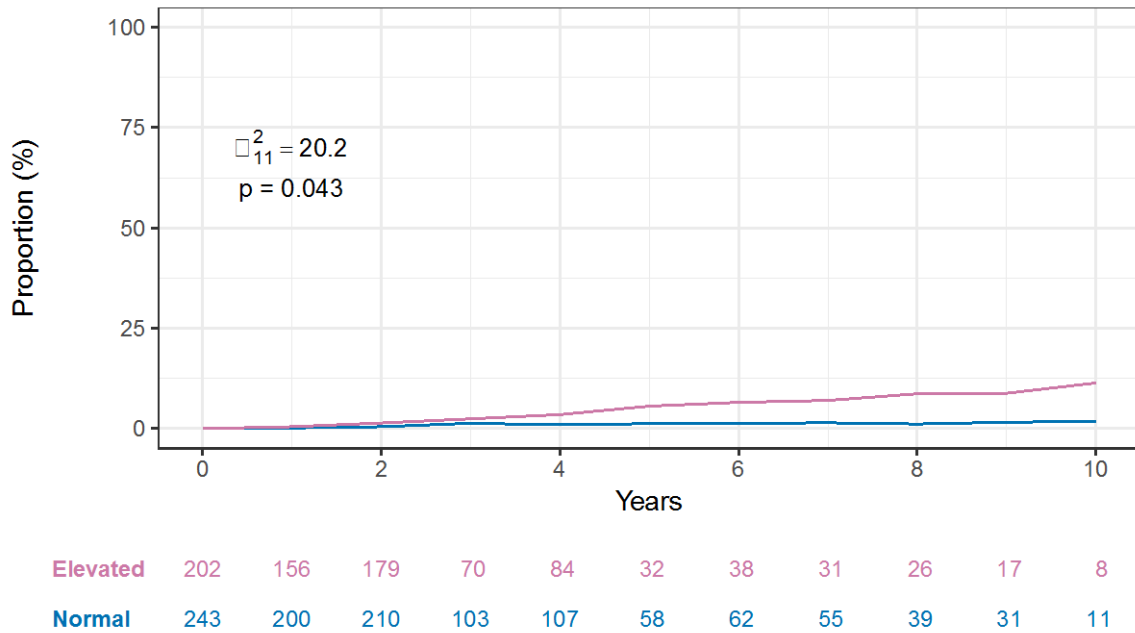


	0	1	2	3	4	5	6	7	8	9	10	
e4+	123	118	94	105	41	49	21	23	19	16	8	2
e4-	312	301	257	270	127	138	67	72	62	45	35	16

The profiles are from linear mixed-effects models, with time as a continuous measure, controlling for age and additional baseline covariates (education, ventricular volume, and sex) selected by Akaike Information Criterion. Shaded regions represent 95% confidence intervals. Dot sizes are proportional to the number of observations. The PACC is a sum of four baseline standardized Z-scores which decreases with worse performance.

Abbreviation: PACC, Preclinical Alzheimer’s Cognitive Composite.

eFigure 13. Logistic Mixed-Effects Model of Anti-Dementia Medication Use Controlling for Age



Anti-dementia medications included donepezil, tacrine, rivastigmine, memantine, or galantamine. Profiles are from logistic mixed-effects models controlling for baseline age (conditional on mean age). The model treats time as a categorical variable. P-value is from a likelihood ratio test comparing a model with versus without Amyloid group. Shaded regions represent 95% confidence intervals. Dot sizes are proportional to the number of observations

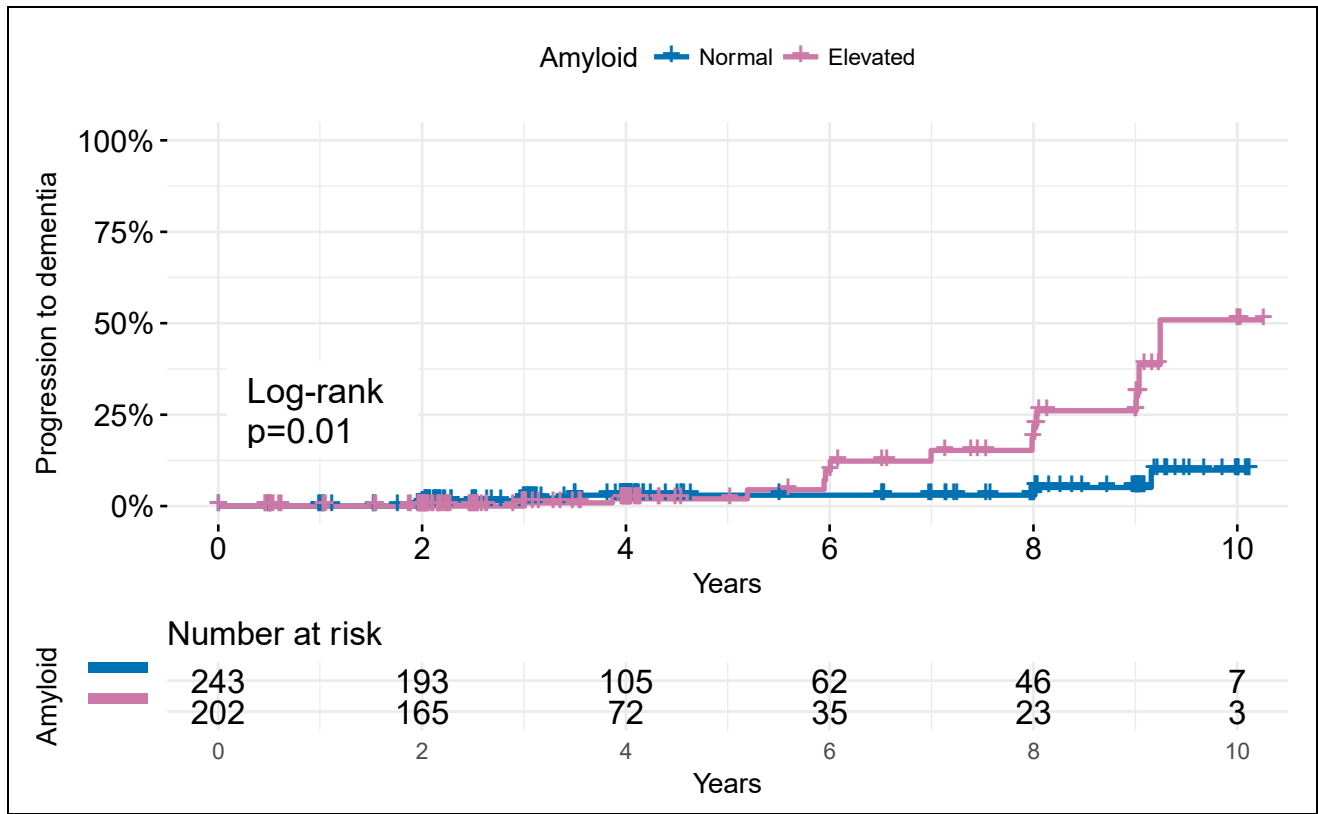


Figure 14. Kaplan-Meier plot of cumulative rate of progression to dementia. The log-rank test ($p=0.01$) indicates a significant difference between amyloid groups in the time to dementia. Shaded regions represent the 95% confidence intervals. Marks (+) indicate censored observations.