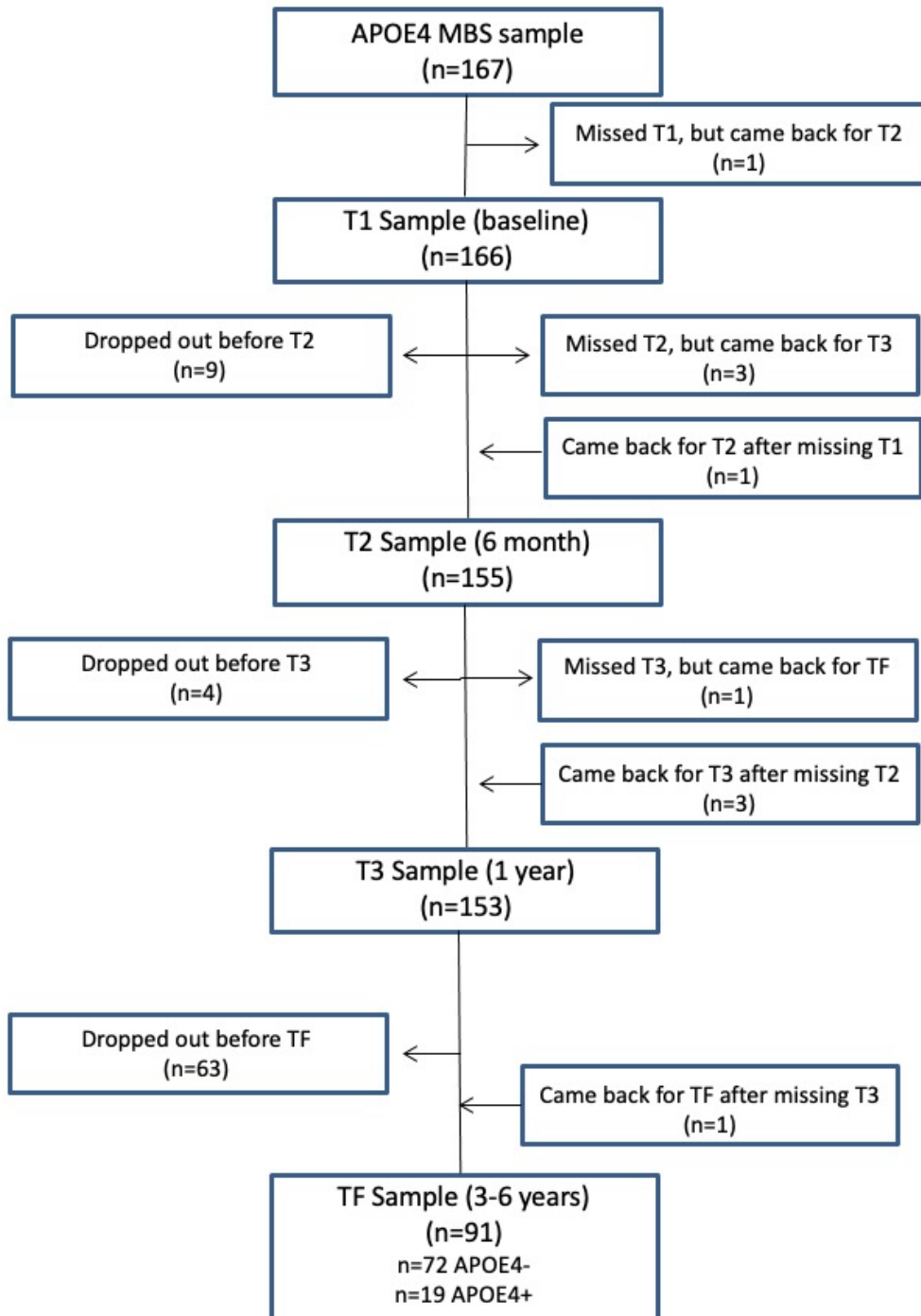


Supplementary Materials

Supplementary Figure 1: Recruitment Flow Diagram



Supplementary Table 1: Estimates and F-Tests of Fixed Effects in Mixed Effects Models of Cognitive Domains\*

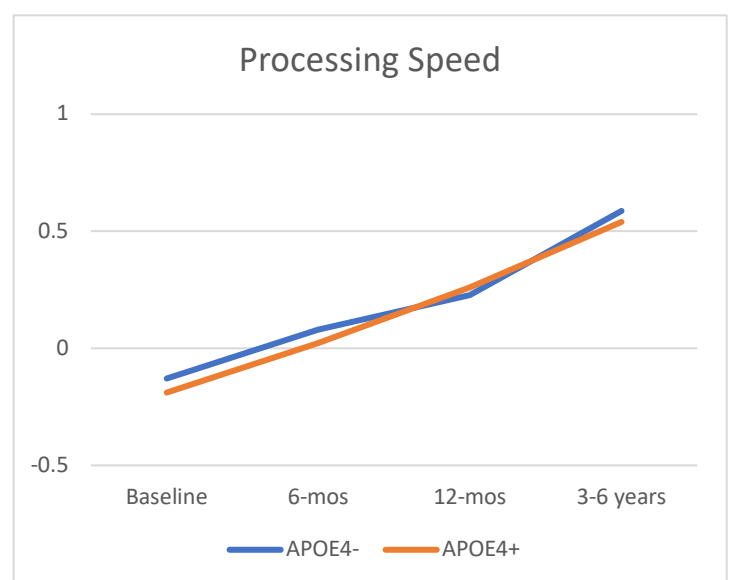
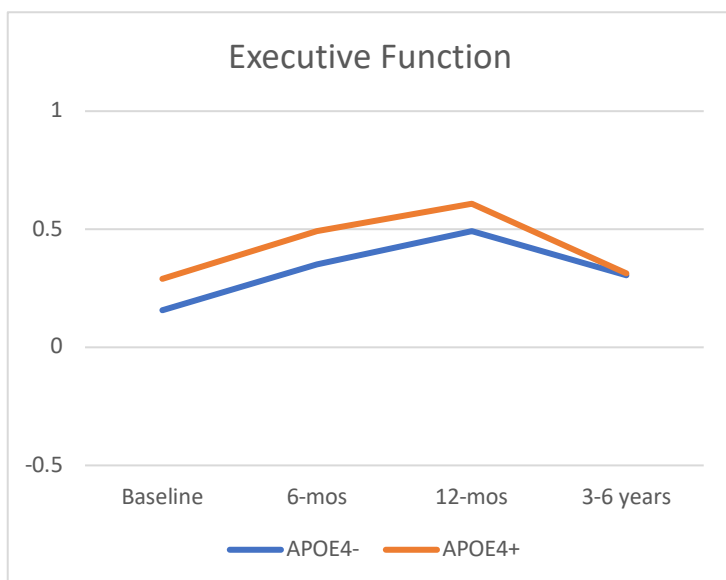
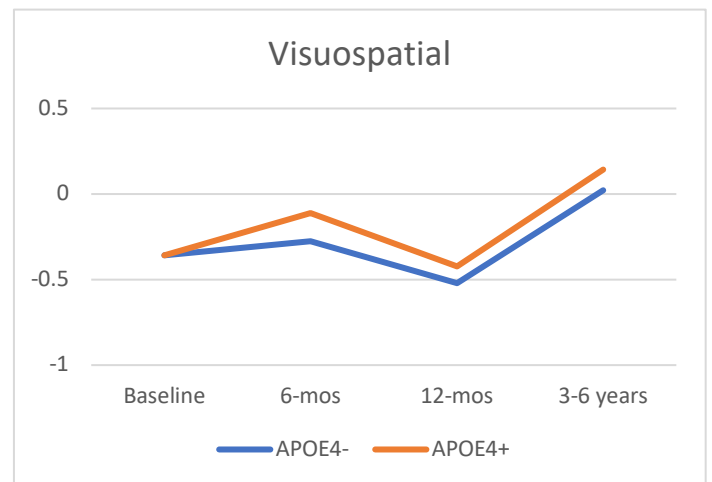
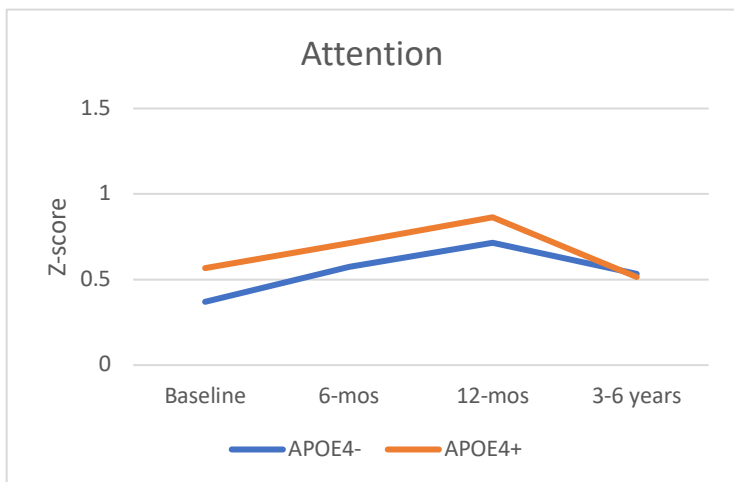
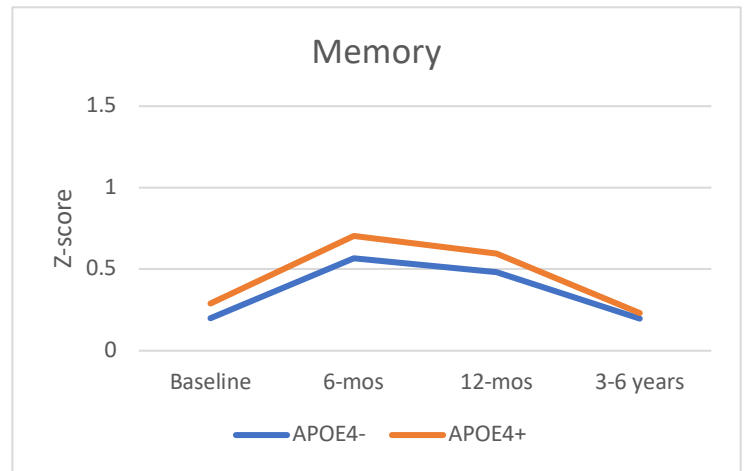
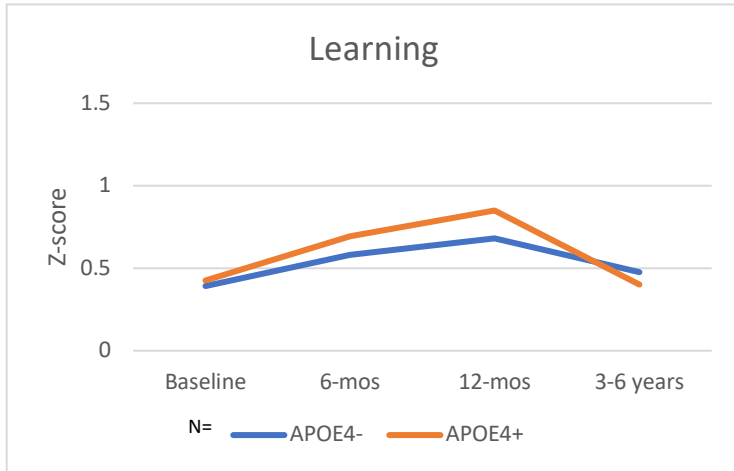
	Learning	Memory	Attention	Visuospatial	Executive Function	Processing Speed
APOE4 x Time	F(3, 186.78) = 1.66, p=.18	F(3, 187.06) = 0.29, p=.83	F(3, 184.41) = 0.1.20, p=.31	F(3, 208.28) = .75, p=.52	F(3, 145.09) = .16, p=.92	F(3, 159.64) = 0.56, p=.64
<i>APOE4 (ref=none) * Time at 3-6 yrs (ref=BL)</i>	0.11	0.06	0.21	-0.12	0.13	-0.01
<i>APOE4 (ref=none) * Time at 12 mos (ref=BL)</i>	-0.14	-0.03	0.05	-0.10	0.02	-0.09
<i>APOE4 (ref=none) * Time at 6 mos (ref=BL)</i>	-0.08	-0.05	0.06	-0.16	-0.01	0.001
Chemo x APOE4	-2.6 F(1, 157.34) = 1.23, p=.27	-2.7 F(1, 156.75) = 1.53, p=.22	-0.001 F(1, 149.29) = .00, p=.99	-2.5 F(1, 150.32) = 1.42, p=.23	0.23 F(1, 157.75) = 0.89, p=.35	0.21 F(1, 156.66) = 0.80, p=.37
Chemo x APOE4 x Time	F(2, 161.41) = 0.14, p=.87	F(2, 154.34) = .80, p=.45	F(3, 181.15) = 1.61, p=.19	F(3, 204.44) = 0.916, p=.43	F(3, 141.95) = 0.16, p=.93	F(3, 159.14) = 1.26, p=.29
<i>APOE4 (ref=none) * Chemo (ref=no) * Time at 3-6 yrs (ref=BL)</i>	-0.01	-0.04	0.31	-0.31	0.03	-0.17
<i>APOE4 (ref=none) * Chemo (ref=no) * Time at 12 mos (ref=BL)</i>	0.05	-0.15	-0.01	-0.13	0.08	-0.29
<i>APOE4 (ref=none) * Chemo (ref=no) * Time at 6 mos (ref=BL)</i>	-0.04	0.01	-0.05	-0.10	0.09	-0.33

ET x APOE4	-0.56	F(1, 158.71) = 4.17, p=.04	-0.48	F(1, 158.67) = 3.22, p=.07	-0.41	F(1, 150.62) = 3.13, p=.08	-0.46	F(1, 155.01) = 3.56, p=.06	-0.37	F(1, 158.69) = 1.56, p=.21	-0.42	F(1, 158.39) = 2.42, p=.12
ET x APOE4 x Time		F(3, 191.36) = 0.59, p=.62		F(3, 175.55) = 1.41, p=.24		F(3, 175.92) = 1.23, p=.30		F(3, 202.89) = 0.61, p=.61		F(2, 143.71) = 1.43, p=.24		F(3, 160.49) = .83, p=.48
<i>APOE4 (ref=none)</i>												
<i>* ET (ref=no) * Time at 3-6 yrs (ref=BL)</i>	-0.37		-0.34		-0.34		0.07		-0.85		0.02	
<i>APOE4 (ref=none)</i>												
<i>* ET (ref=no) * Time at 12 mos (ref=BL)</i>	-0.02		0.14		0.14		-0.18		-0.21		-0.08	
<i>APOE4 (ref=none)</i>												
<i>* ET (ref=no) * Time at 6 mos (ref=BL)</i>	0.02		0.15		0.15		-0.16		-0.16		0.07	

\*Main effects and two-way interactions were examined separately in iterative models; models with three-way interactions included all subordinate terms. Data are assumed to be missing at random.

ET=endocrine therapy (no/yes); time, BL=baseline, 6-month, 12-month, and 3-year to 6-year visits (categorical). The fixed effects included in the models were age, intelligence quotient, chemotherapy exposure, and race, and all models included a random intercept.

Supplementary Figure 2: Cognitive Domain Scores by APOE4 status over time. Models adjusted for age, IQ, chemotherapy, and race.

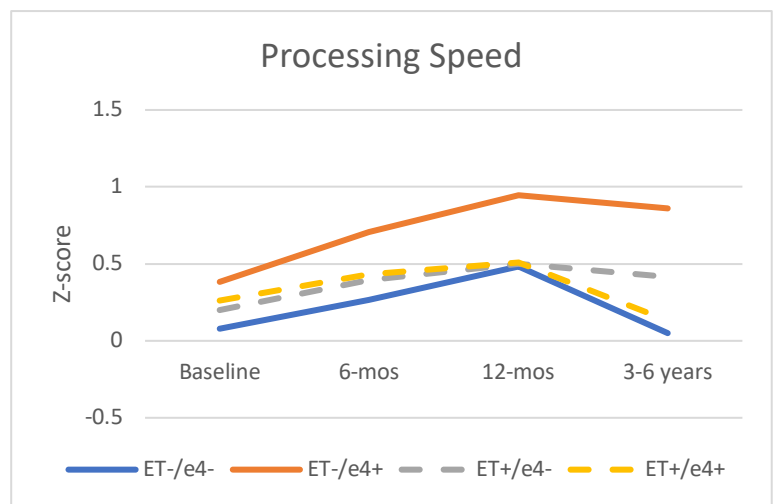
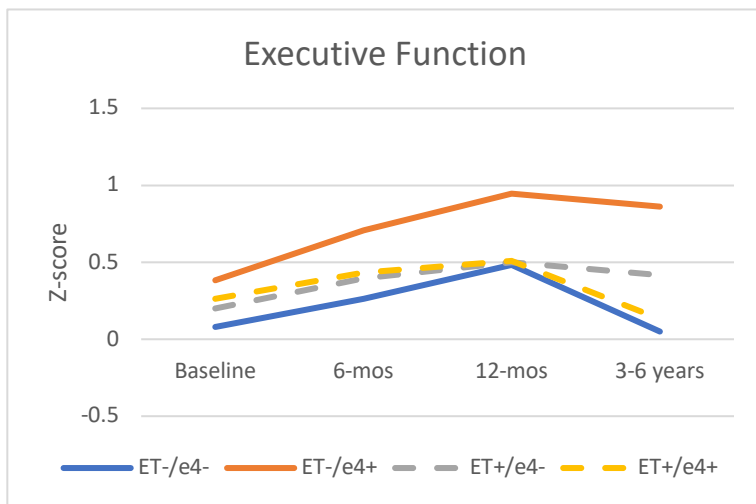
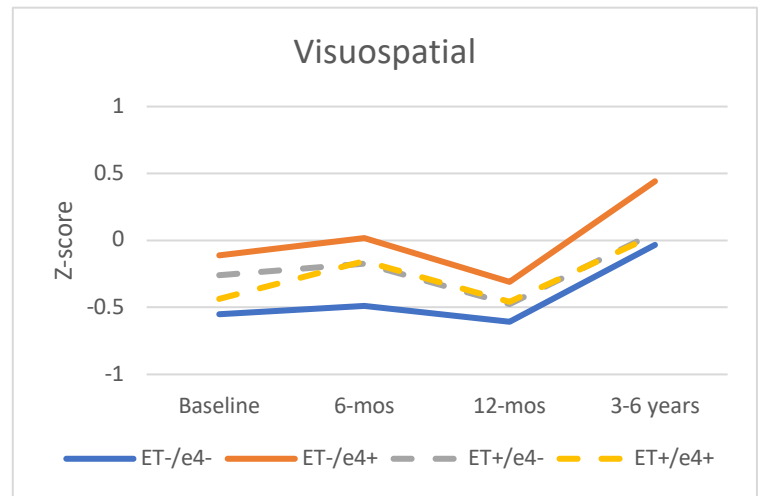
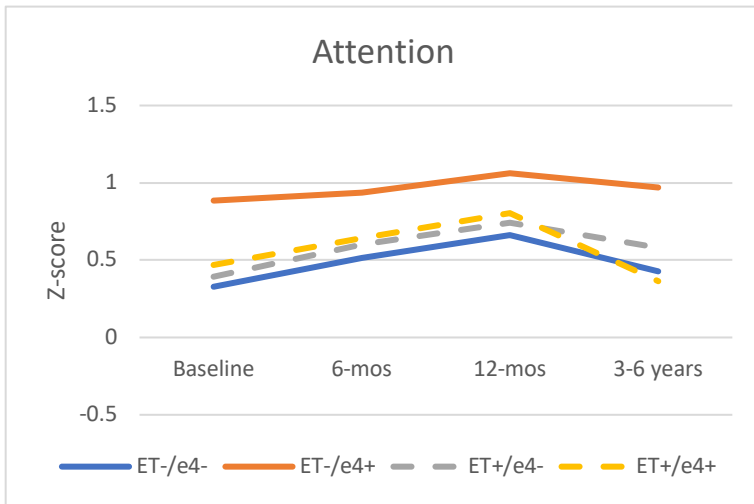
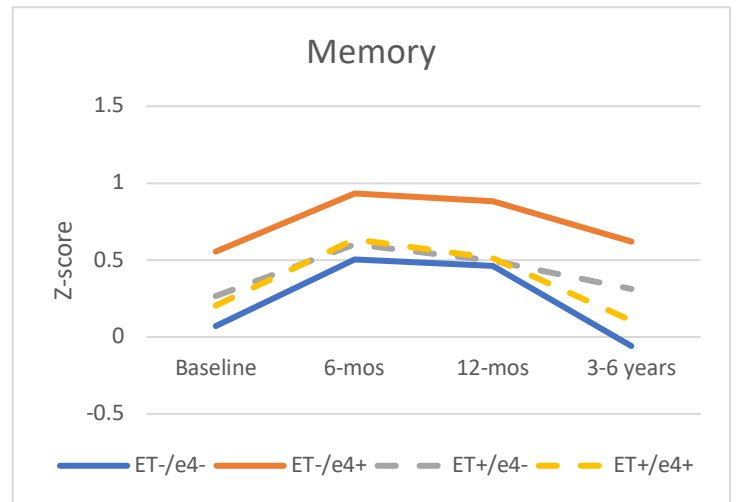
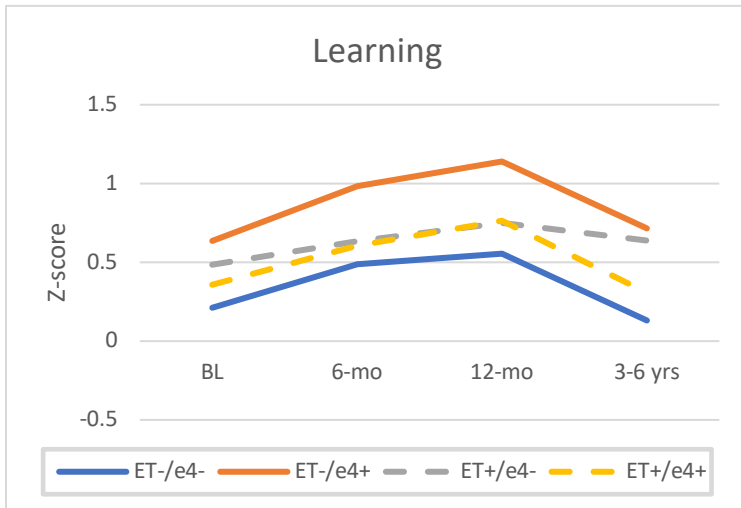


Data for Supplementary Figure 2

		Mean	Std. Error	95% Confidence Interval	
				Lower Bound	Upper Bound
<b>Learning</b>					
e4-	Baseline	0.392	0.057		
	6-mos	0.58	0.057	0.468	0.693
	12-mos	0.681	0.058	0.568	0.795
	3-6 years	0.477	0.079	0.322	0.632
e4+	Baseline	0.424	0.111	0.205	0.644
	6-mos	0.692	0.112	0.471	0.913
	12-mos	0.85	0.114	0.625	1.074
	3-6 years	0.401	0.151	0.104	0.699
<b>Memory</b>					
e4-	Baseline	0.198	0.055	0.089	0.306
	6-mos	0.567	0.054	0.461	0.673
	12-mos	0.48	0.052	0.378	0.582
	3-6 years	0.197	0.069	0.06	0.334
e4+	Baseline	0.288	0.108	0.076	0.501
	6-mos	0.704	0.105	0.497	0.912
	12-mos	0.597	0.102	0.395	0.799
	3-6 years	0.231	0.133	-0.031	0.493
<b>Attention</b>					
e4-	Baseline	0.37	0.049	0.273	0.467
	6-mos	0.574	0.047	0.482	0.666
	12-mos	0.715	0.045	0.627	0.803
	3-6 years	0.533	0.062	0.41	0.656
e4+	Baseline	0.566	0.097	0.375	0.756
	6-mos	0.713	0.09	0.534	0.891
	12-mos	0.864	0.088	0.691	1.038
	3-6 years	0.515	0.119	0.279	0.751
<b>Visuospatial</b>					
e4-	Baseline	-0.359	0.057	-0.471	-0.246
	6-mos	-0.275	0.057	-0.387	-0.164
	12-mos	-0.521	0.055	-0.63	-0.412
	3-6 years	0.022	0.081	-0.138	0.182
e4+	Baseline	-0.359	0.112	-0.58	-0.139
	6-mos	-0.112	0.11	-0.329	0.104

	12-mos	-0.423	0.109	-0.639	-0.207
	3-6 years	0.143	0.156	-0.165	0.451
Executive Function					
e4-	Baseline	0.157	0.058	0.042	0.272
	6-mos	0.351	0.06	0.233	0.468
	12-mos	0.492	0.059	0.376	0.609
	3-6 years	0.306	0.106	0.096	0.516
e4+	Baseline	0.29	0.114	0.065	0.516
	6-mos	0.493	0.117	0.263	0.723
	12-mos	0.608	0.117	0.377	0.839
	3-6 years	0.314	0.205	-0.091	0.719
Processing Speed					
e4-	Baseline	-0.129	0.06	-0.248	-0.01
	6-mos	0.081	0.056	-0.03	0.192
	12-mos	0.226	0.057	0.113	0.339
	3-6 years	0.587	0.104	0.382	0.792
e4+	Baseline	-0.189	0.119	-0.423	0.046
	6-mos	0.023	0.11	-0.195	0.241
	12-mos	0.261	0.113	0.037	0.484
	3-6 years	0.54	0.2	0.144	0.937

Supplementary Figure 3: Cognitive Domain scores by APOE4 status and endocrine therapy over time. Models adjusted for age, IQ, chemotherapy, and race.



Data for Supplementary Figure 3

Learning		Mean	Std. Error	95% Confidence Interval		
				Lower Bound	Upper Bound	
ET-/e4-	Baseline	0.21	0.10	0.03	0.40	
	6-mos	0.49	0.10	0.29	0.68	
	12-mos	0.56	0.10	0.36	0.75	
	3-6 years	0.13	0.14	-0.14	0.40	
ET+/e4-	Baseline	0.49	0.07	0.35	0.62	
	6-mos	0.64	0.07	0.50	0.77	
	12-mos	0.75	0.07	0.61	0.89	
	3-6 years	0.64	0.09	0.46	0.82	
ET-/e4+	Baseline	0.64	0.23	0.19	1.08	
	6-mos	0.99	0.23	0.53	1.44	
	12-mos	1.14	0.23	0.68	1.60	
	3-6 years	0.72	0.29	0.14	1.29	
ET+/e4+	Baseline	0.36	0.13	0.11	0.61	
	6-mos	0.61	0.13	0.36	0.86	
	12-mos	0.76	0.13	0.51	1.02	
	3-6 years	0.31	0.17	-0.03	0.64	
Memory	ET-/e4-	Baseline	0.07	0.09	-0.11	0.25
		6-mos	0.50	0.10	0.32	0.69
		12-mos	0.46	0.09	0.29	0.64
		3-6 years	-0.06	0.12	-0.29	0.18
ET+/e4-	Baseline	0.27	0.07	0.13	0.40	
	6-mos	0.60	0.07	0.47	0.73	
	12-mos	0.50	0.06	0.37	0.62	
	3-6 years	0.31	0.08	0.15	0.48	
ET-/e4+	Baseline	0.56	0.22	0.12	0.99	
	6-mos	0.93	0.22	0.50	1.37	
	12-mos	0.88	0.21	0.47	1.30	
	3-6 years	0.62	0.26	0.11	1.13	
ET+/e4+	Baseline	0.21	0.12	-0.04	0.45	
	6-mos	0.64	0.12	0.40	0.87	
	12-mos	0.51	0.12	0.28	0.74	



	3-6 years	0.11	0.15	-0.19	0.40
Attention					
ET-/e4-	Baseline	0.33	0.08	0.16	0.49
	6-mos	0.52	0.08	0.36	0.68
	12-mos	0.66	0.08	0.51	0.82
	3-6 years	0.43	0.11	0.21	0.64
ET+/e4-	Baseline	0.39	0.06	0.27	0.51
	6-mos	0.60	0.06	0.49	0.72
	12-mos	0.74	0.05	0.63	0.85
	3-6 years	0.58	0.07	0.44	0.73
ET-/e4+	Baseline	0.89	0.20	0.50	1.27
	6-mos	0.94	0.19	0.56	1.31
	12-mos	1.06	0.18	0.70	1.42
	3-6 years	0.97	0.24	0.50	1.43
ET+/e4+	Baseline	0.47	0.11	0.25	0.68
	6-mos	0.64	0.10	0.44	0.85
	12-mos	0.80	0.10	0.61	1.00
	3-6 years	0.36	0.14	0.09	0.63
Visuospatial					
ET-/e4-	Baseline	-0.55	0.10	-0.74	-0.36
	6-mos	-0.49	0.10	-0.69	-0.29
	12-mos	-0.61	0.10	-0.80	-0.42
	3-6 years	-0.03	0.15	-0.32	0.26
ET+/e4-	Baseline	-0.26	0.07	-0.40	-0.12
	6-mos	-0.17	0.07	-0.31	-0.04
	12-mos	-0.48	0.07	-0.61	-0.34
	3-6 years	0.06	0.10	-0.13	0.25
ET-/e4+	Baseline	-0.11	0.23	-0.56	0.34
	6-mos	0.02	0.23	-0.44	0.47
	12-mos	-0.31	0.23	-0.76	0.14
	3-6 years	0.44	0.31	-0.16	1.05
ET+/e4+	Baseline	-0.44	0.13	-0.69	-0.19
	6-mos	-0.15	0.12	-0.40	0.09
	12-mos	-0.46	0.12	-0.70	-0.21
	3-6 years	0.04	0.18	-0.32	0.40

Executive Function

ET-/e4-	Baseline	0.08	0.10	-0.12	0.27
	6-mos	0.26	0.11	0.06	0.47
	12-mos	0.48	0.10	0.28	0.69
	3-6 years	0.05	0.19	-0.32	0.43

ET+/e4-	Baseline	0.20	0.07	0.06	0.34
	6-mos	0.39	0.07	0.25	0.54
	12-mos	0.50	0.07	0.36	0.64
	3-6 years	0.42	0.13	0.17	0.67

ET-/e4+	Baseline	0.38	0.23	-0.08	0.85
	6-mos	0.71	0.24	0.23	1.19
	12-mos	0.95	0.24	0.47	1.42
	3-6 years	0.86	0.40	0.07	1.65

ET+/e4+	Baseline	0.26	0.13	0.00	0.52
	6-mos	0.43	0.13	0.17	0.70
	12-mos	0.51	0.13	0.25	0.77
	3-6 years	0.13	0.24	-0.34	0.60

Processing Speed

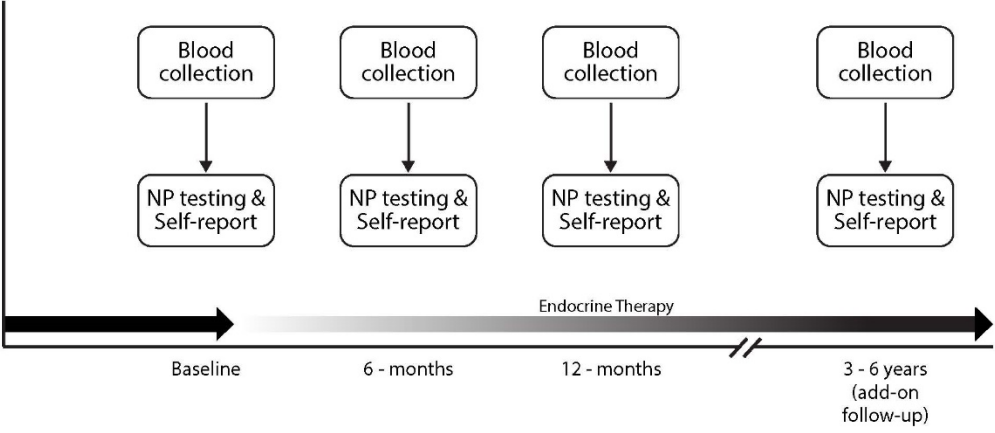
ET-/e4-	Baseline	-0.12	0.10	-0.32	0.09
	6-mos	0.02	0.10	-0.17	0.22
	12-mos	0.23	0.10	0.03	0.43
	3-6 years	0.59	0.19	0.21	0.96

ET+/e4-	Baseline	-0.13	0.08	-0.28	0.01
	6-mos	0.11	0.07	-0.03	0.24
	12-mos	0.22	0.07	0.08	0.36
	3-6 years	0.58	0.13	0.34	0.83

ET-/e4+	Baseline	0.04	0.24	-0.44	0.52
	6-mos	0.41	0.23	-0.05	0.86
	12-mos	0.54	0.24	0.07	1.01
	3-6 years	0.86	0.40	0.08	1.65

ET+/e4+	Baseline	-0.26	0.14	-0.53	0.01
	6-mos	-0.09	0.13	-0.33	0.16
	12-mos	0.18	0.13	-0.08	0.43
	3-6 years	0.44	0.23	-0.02	0.90

Supplementary Figure 4: Diagram of the study



**Supplementary Table 2: Neuropsychological Tests by Domain**

Domain	Test/Measure
Learning	CVLT-II List A Total Trials 1-5
	WMS-III LM I
	BVMT-R Total Trials 1-3
Memory	CVLT-II List A Long Delay Free Recall
	WMS-III LM II
	BVMT-R Delayed Recall
	ROCFT 3-minute Delayed Recall
Attention	WAIS-III Digit Span, Coding, Letter-Number Sequencing
	TMT A completion time
	PASAT Trial 2 total errors
Visuospatial	ROCFT copy
	WAIS-III Block Design
Executive Functioning	TMT B
	Stroop Color Word Interference <sup>1</sup>
	Verbal Fluency (FAS)
Processing Speed	Grooved Pegboard <sup>2</sup>
	Stroop Word Reading & Color Naming

BVMT-R=Brief Visuospatial Memory Test-Revised<sup>3</sup>; CVLT-II=California Verbal Learning Test-II<sup>4</sup>;TMT=Trail Making Test<sup>5</sup>; ROCFT=Rey-Osterreith Complex Figure Test<sup>6,7</sup>; Paced Auditory Serial Attention Test<sup>8</sup>; WAIS-III=Wechsler Adult Intelligence Scale-3rd Edition<sup>9</sup>; WMS-III=Wechsler Memory Scale-3<sup>rd</sup> Edition<sup>10</sup>

Note: WAIS and WMS tests at BL, 6-, and 12-month visits are the 3<sup>rd</sup> edition; 4<sup>th</sup> edition tests were used at the 3-6 year visit, which are highly correlated to the 3<sup>rd</sup> edition tests. The Stroop test was not administered at the 3-6 year visit. Also of note, 20 participants were missing WAIS-III Digit Span data at BL.

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