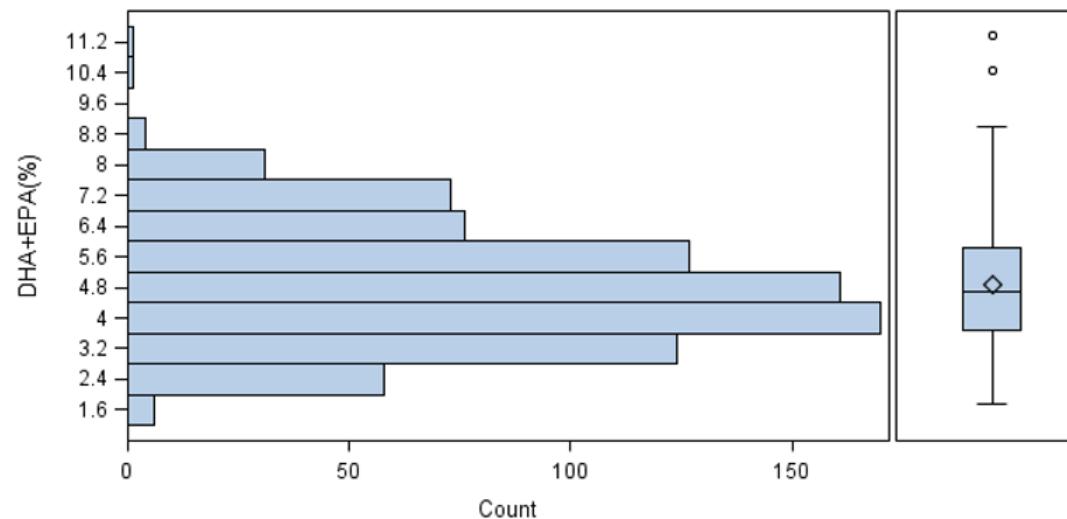


**Associations between erythrocyte omega-3 fatty acids, cognition, brain imaging and biomarkers in the Alzheimer's Disease**

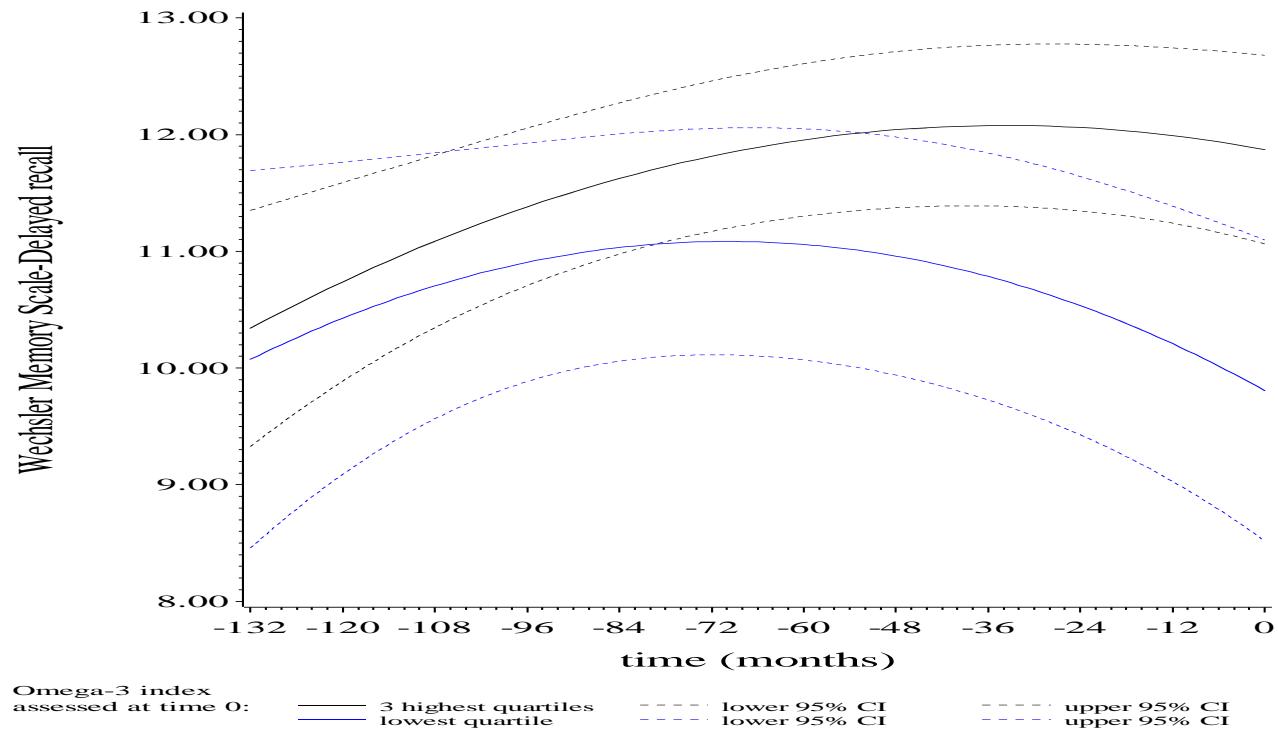
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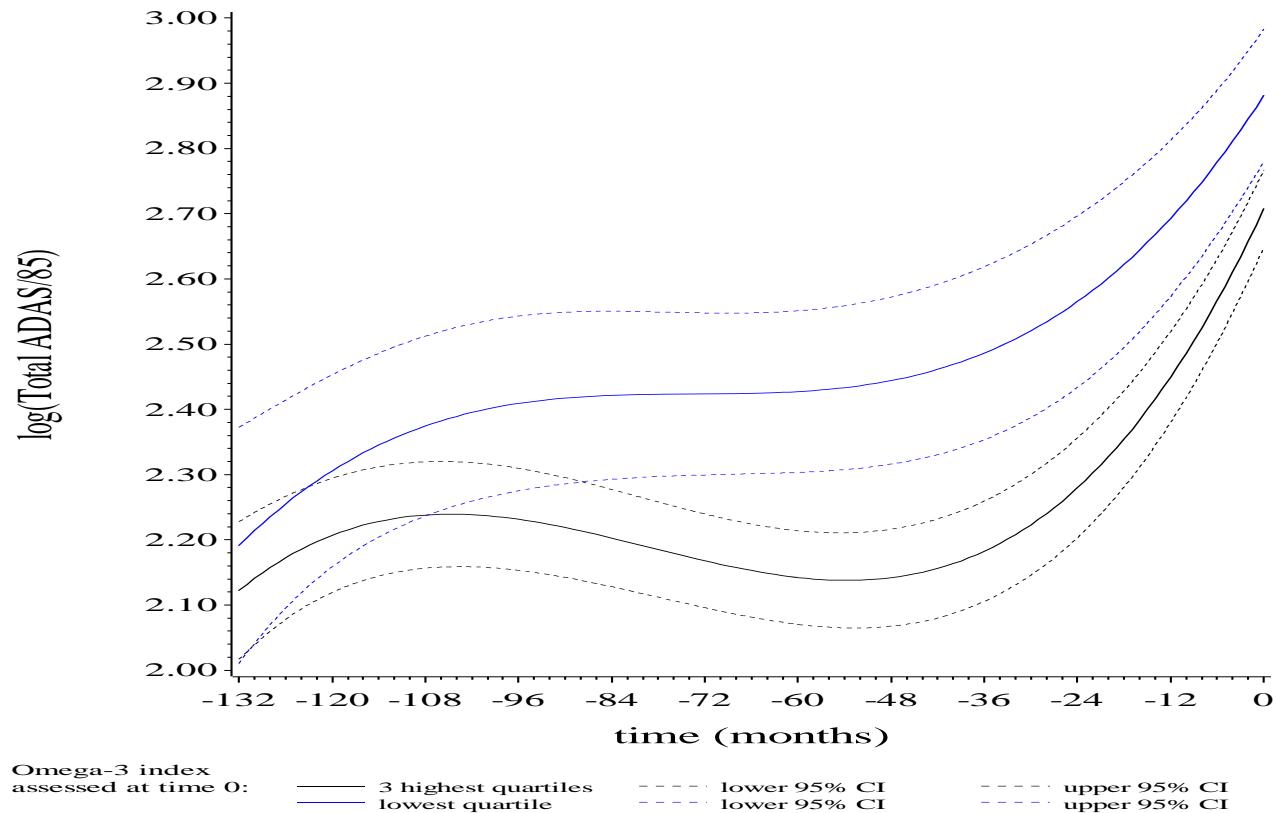
Online Supplementary Material

**Supplementary Figure 1.** Distribution of erythrocyte omega-3 index in the ADNI study population (cross-sectional analysis)



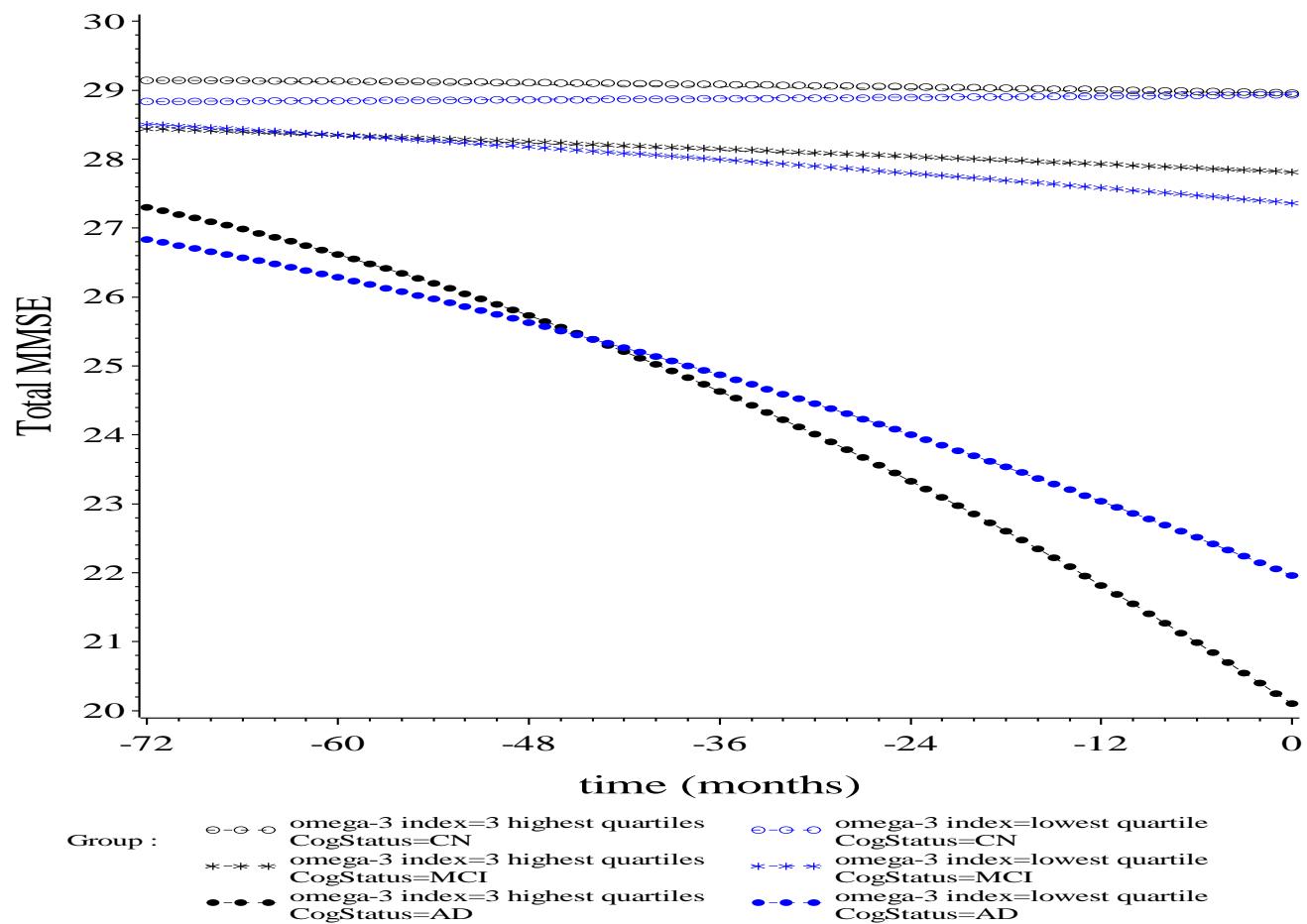
**Supplementary Figure 2.** WMS-Delayed recall and Total ADAS-Cog cognitive trajectories over time according to the lowest vs. highest  $\omega$ -3 index quartiles (retrospective longitudinal analysis - whole population)

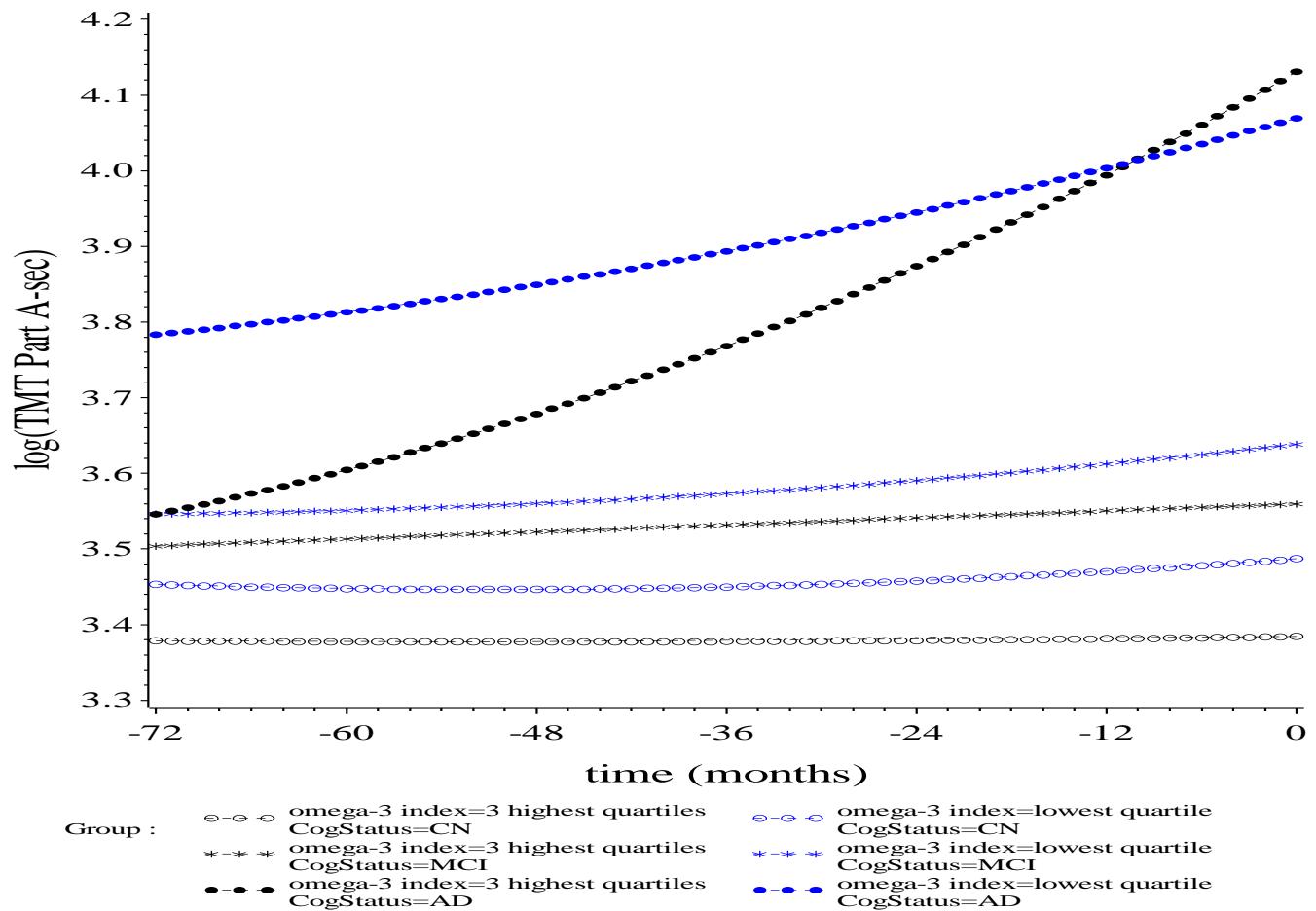


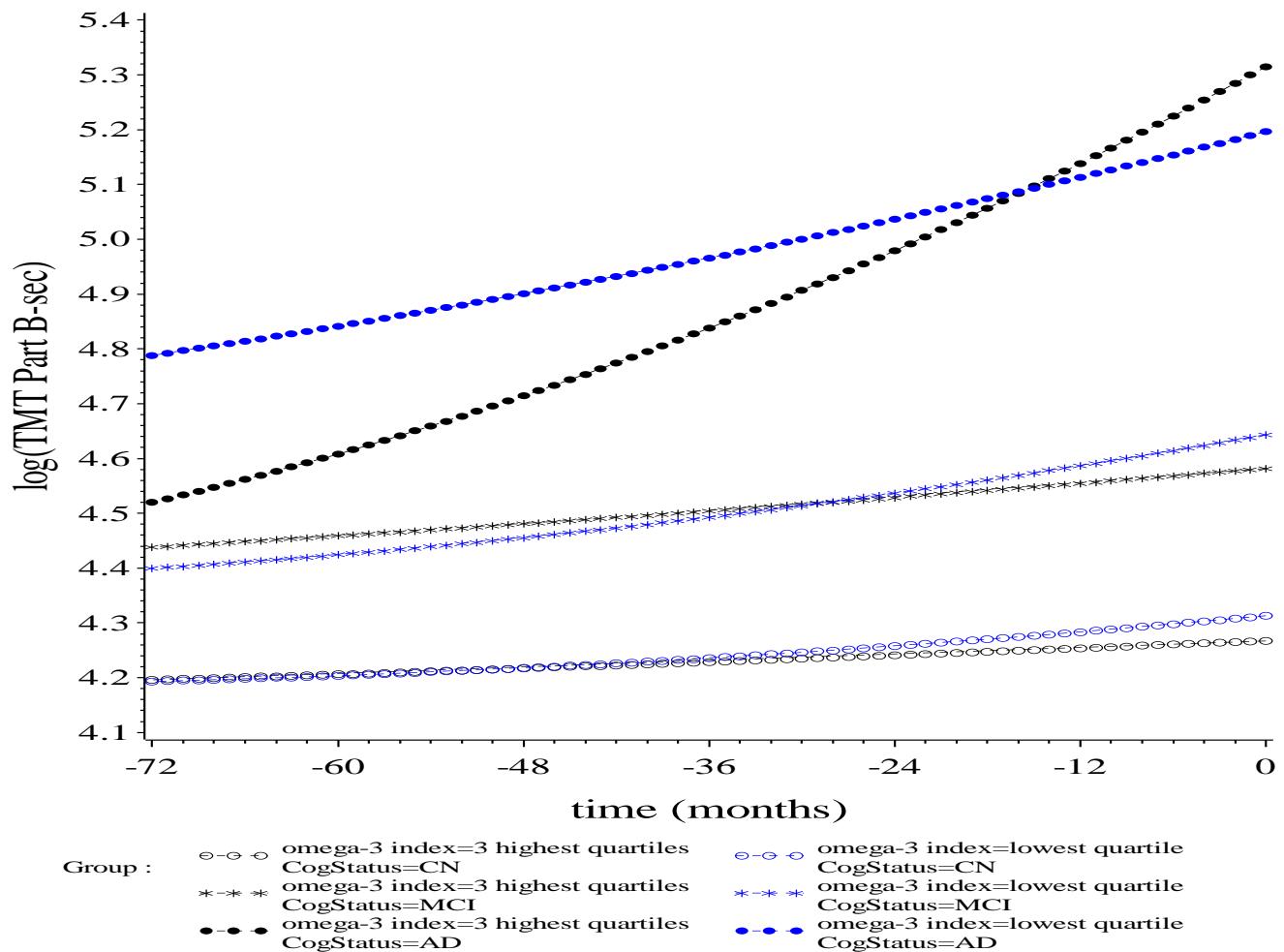


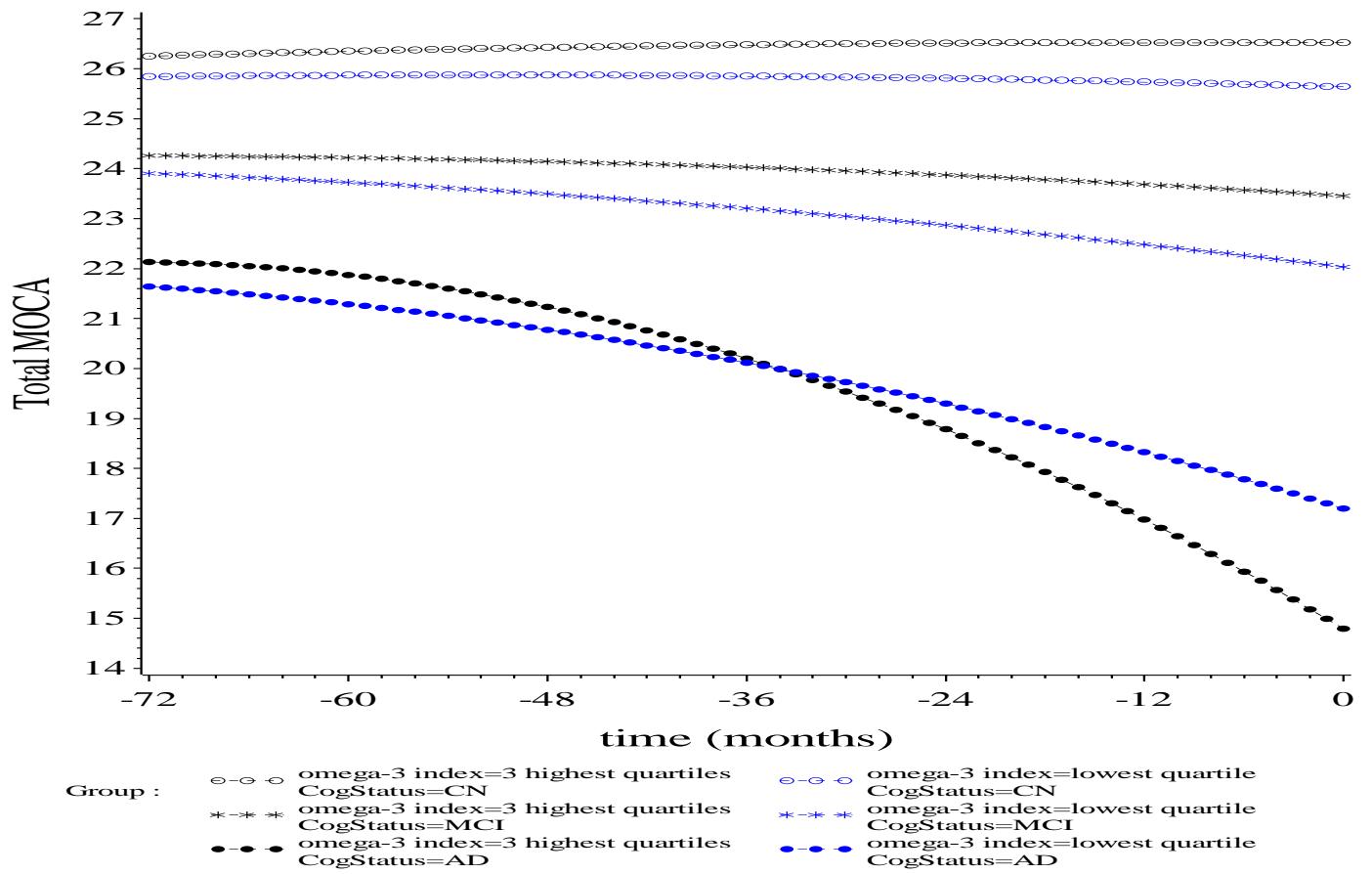
ADAS, Alzheimer's disease assessment scale; results from mixed linear regression models (mean estimate and 95% CI)

**Supplementary Figure 3.** Cognitive trajectories over time of participants in the lowest vs. the 3 highest ω-3 index quartiles according to cognitive status (retrospective longitudinal analysis).









MMSE, Mini Mental State Examination; TMT-A and TMT-B, Trail Making Test A and B; MoCA, Montreal Cognitive Assessment

Results from mixed linear regression models (mean estimate)

**Supplementary Table 1.** Interactions between  $\omega$ -3 index (lowest vs. 3 highest  $\omega$ -3 index quartiles) and cognitive status (cognitively normal, MCI, AD) on cognitive, brain imaging and biomarkers variables among community-dwelling older adults (cross-sectional analysis)

	n	Cognitively normal	$\omega$ -3 index x			$\omega$ -3 index x			$\omega$ -3
			Mild cognitive impairment			Alzheimer's disease			index x
			$\beta$	SE	p-value	$\beta$	SE	p-value	cognitive status
									p-value
<b>Model 1 (unadjusted)</b>									
Composite cognitive score	801	Ref.	-0.12	0.37	0.748	0.78	0.55	0.159	0.294
MMSE score	828	Ref.	-0.55	0.37	0.142	<b>1.54</b>	<b>0.53</b>	<b>0.004</b>	<b>0.001</b>
Total ADAS-Cog <sup>1</sup>	823	Ref.	-0.01	0.06	0.828	-0.04	0.08	0.623	0.882
ADAS-Cog delayed recall	831	Ref.	-0.09	0.34	0.790	-0.11	0.49	0.823	0.953
Wechsler Memory Scale-Delayed recall	826	Ref.	-0.23	0.70	0.738	0.82	1.00	0.414	0.613
Wechsler Memory Scale-Immediate recall	828	Ref.	-0.24	0.69	0.727	1.40	0.98	0.157	0.281
Category Fluency test (words)	829	Ref.	1.05	0.92	0.251	1.94	1.30	0.137	0.241
TMT-A (seconds) <sup>1</sup>	825	Ref.	-0.10	0.06	0.125	-0.09	0.09	0.320	0.253

TMT-B (seconds) <sup>1</sup>	808	Ref.	-0.03	0.08	0.665	0.00	0.12	0.989	0.906
MoCA total score	810	Ref.	-0.47	0.57	0.414	<b>1.72</b>	<b>0.81</b>	<b>0.033</b>	<b>0.039</b>
CDR sum of boxes	829	Ref.	-0.09	0.21	0.663	-0.04	0.30	0.902	0.910
Total hippocampal volume (mm <sup>3</sup> )	651	Ref.	276.55	190.33	0.147	<b>940.28</b>	<b>293.46</b>	<b>0.001</b>	<b>0.005</b>
Left hippocampal subcortical volume (mm <sup>3</sup> )	651	Ref.	167.83	94.58	0.077	<b>443.29</b>	<b>145.83</b>	<b>0.003</b>	<b>0.006</b>
Right hippocampal subcortical volume (mm <sup>3</sup> )	651	Ref.	108.72	101.71	0.286	<b>496.99</b>	<b>156.82</b>	<b>0.002</b>	<b>0.007</b>
White matter hyperintensities volume (cm <sup>3</sup> ) <sup>1</sup>	773	Ref.	0.11	0.28	0.685	0.36	0.41	0.370	0.657
Cortical SUVr <sup>1</sup>	472	Ref.	0.02	0.04	0.686	-0.01	0.06	0.899	0.898
Tau <sup>18</sup> F-AV1451 meta-temporal region <sup>1</sup>	693	Ref.	0.01	0.04	0.795	-0.04	0.05	0.515	0.736
Tau <sup>18</sup> F-AV1451 Braak stage 1 <sup>1</sup>	693	Ref.	0.02	0.05	0.661	-0.08	0.07	0.227	0.361
Tau <sup>18</sup> F-AV1451 Braak stage 2	693	Ref.	0.04	0.05	0.478	<b>-0.14</b>	<b>0.07</b>	<b>0.041</b>	<b>0.056</b>
Tau <sup>18</sup> F-AV1451 Braak stages 3 and 4 <sup>1</sup>	693	Ref.	0.02	0.03	0.578	-0.02	0.05	0.609	0.684
Tau <sup>18</sup> F-AV1451 Braak stages 5 and 6	693	Ref.	0.08	0.07	0.230	0.14	0.09	0.153	0.247

### Model 2 (adjusted)

Composite cognitive score	745	Ref.	-0.17	0.38	0.659	0.90	0.55	0.104	0.188
MMSE score	769	Ref.	-0.46	0.39	0.244	<b>1.55</b>	<b>0.55</b>	<b>0.005</b>	<b>0.003</b>
Total ADAS-Cog <sup>1</sup>	765	Ref.	-0.01	0.06	0.827	-0.05	0.08	0.582	0.856

ADAS-Cog delayed recall	773	Ref.	-0.13	0.36	0.722	-0.13	0.50	0.787	0.922
Wechsler Memory Scale-Delayed recall	769	Ref.	-0.66	0.72	0.359	0.72	1.01	0.478	0.416
Wechsler Memory Scale-Immediate recall	771	Ref.	-0.26	0.71	0.710	1.41	0.99	0.155	0.278
Category Fluency test (words)	771	Ref.	1.15	0.93	0.217	2.14	1.30	0.100	0.177
TMT-A (seconds) <sup>1</sup>	767	Ref.	-0.08	0.06	0.206	-0.10	0.09	0.253	0.309
TMT-B (seconds) <sup>1</sup>	751	Ref.	-0.02	0.08	0.787	-0.03	0.12	0.815	0.949
MoCA total score	754	Ref.	-0.16	0.58	0.787	<b>1.85</b>	<b>0.81</b>	<b>0.023</b>	<b>0.054</b>
CDR sum of boxes	770	Ref.	-0.01	0.22	0.960	0.01	0.31	0.975	0.998
Total hippocampal volume (mm <sup>3</sup> )	608	Ref.	170.78	168.98	0.313	<b>1289.58</b>	<b>262.38</b>	<0.0001	<0.0001
Left hippocampal subcortical volume (mm <sup>3</sup> )	608	Ref.	123.34	85.69	0.151	<b>605.28</b>	<b>133.05</b>	<0.0001	<0.0001
Right hippocampal subcortical volume (mm <sup>3</sup> )	608	Ref.	47.45	90.60	0.601	<b>684.30</b>	<b>140.68</b>	<0.0001	<0.0001
White matter hyperintensities (cm <sup>3</sup> ) <sup>1</sup>	718	Ref.	0.18	0.27	0.508	0.49	0.38	0.204	0.414
Cortical SUVR <sup>1</sup>	454	Ref.	0.02	0.04	0.548	-0.03	0.06	0.623	0.680
Tau <sup>18</sup> F-AV1451 meta-temporal region <sup>1</sup>	648	Ref.	0.01	0.04	0.801	-0.07	0.05	0.162	0.315
Tau <sup>18</sup> F-AV1451 Braak stage 1 <sup>1</sup>	648	Ref.	0.02	0.05	0.615	-0.10	0.07	0.123	0.205
Tau <sup>18</sup> F-AV1451 Braak stage 2	648	Ref.	0.05	0.05	0.299	<b>-0.19</b>	<b>0.07</b>	<b>0.004</b>	<b>0.003</b>
Tau <sup>18</sup> F-AV1451 Braak stages 3 and 4 <sup>1</sup>	648	Ref.	0.02	0.03	0.578	-0.06	0.05	0.231	0.337
Tau <sup>18</sup> F-AV1451 Braak stages 5 and 6	648	Ref.	0.06	0.07	0.347	0.06	0.10	0.517	0.583

ADAS, Alzheimer's disease assessment scale; CDR, Clinical Dementia Rating; MoCA, Montreal Cognitive Assessment; MMSE, Mini Mental State Examination; TMT, Trail Making Test; SE, standard error; SUVR, standard uptake value ratio normalized by whole cerebellum. The modified composite score included the delayed word recall from the Alzheimer's Disease Assessment Scale - Cognitive Subscale (ADAS-Cog), the Trail Making Test B (TMT-B), the MMSE total score and the Wechsler Memory Scale delayed recall; ω-3 index defined as erythrocyte % docosahexaenoic acid (DHA) + % eicosapentaenoic acid (EPA). Model 2 was adjusted for age, education, ApoE ε4 genotype, history of cardiovascular disease, body mass index and total intracranial volume (this last only for white matter hyperintensities and hippocampal volume); <sup>1</sup>Variable with log transformation; Significant p-values are presented in bold, and marginally significant p-values are presented in italics. Results from linear regression models.

**Supplementary Table 2.** Associations between ω-3 index (lowest vs. 3 highest ω-3 index quartiles) and cognitive, brain imaging and biomarkers variables among community-dwelling older adults with different cognitive status (within-group estimates according to the interaction between ω-3 index and cognitive status presented in Supplementary Table 3) (cross-sectional analysis)

	Cognitively normal			Mild cognitive impairment			Alzheimer's disease		
	β	SE	p-value	β	SE	p-value	β	SE	p-value
<b>Model 1 (unadjusted)</b>									
MMSE score	0.12	0.22	0.577	-0.42	0.30	0.156	<b>1.66</b>	<b>0.48</b>	<b>&lt;0.001</b>
MoCA total score	-0.10	0.34	0.779	-0.56	0.46	0.218	<b>1.63</b>	<b>0.73</b>	<b>0.026</b>
Total hippocampal volume (mm <sup>3</sup> )	-170.84	113.59	0.133	105.72	152.72	0.489	<b>769.44</b>	<b>270.58</b>	<b>0.005</b>
Left hippocampal subcortical volume (mm <sup>3</sup> )	-86.61	56.45	0.125	81.22	75.89	0.285	<b>356.68</b>	<b>134.46</b>	<b>0.008</b>
Right hippocampal subcortical volume (mm <sup>3</sup> )	-84.23	60.70	0.166	24.50	81.61	0.764	<b>412.76</b>	<b>144.59</b>	<b>0.004</b>
Tau 18F-AV1451 Braak stage 2	0.00	0.03	0.881	0.03	0.04	0.440	<b>-0.15</b>	<b>0.06</b>	<b>0.020</b>
<b>Model 2 (adjusted)</b>									
MMSE score	0.23	0.23	0.312	-0.23	0.32	0.486	<b>1.78</b>	<b>0.50</b>	<b>&lt;0.001</b>
MoCA total score	0.01	0.34	0.979	-0.15	0.48	0.757	<b>1.86</b>	<b>0.74</b>	<b>0.013</b>

Total hippocampal volume (mm <sup>3</sup> )	<b>-187.71</b>	97.78	0.055	-16.93	139.78	0.904	<b>1101.88</b>	<b>245.07</b>	<b>&lt;0.001</b>
Left hippocampal subcortical volume (mm <sup>3</sup> )	<b>-89.80</b>	49.59	0.071	33.53	70.88	0.636	<b>515.48</b>	<b>124.27</b>	<b>&lt;0.001</b>
Right hippocampal subcortical volume (mm <sup>3</sup> )	<b>-97.90</b>	52.43	0.062	-50.46	74.94	0.501	<b>586.40</b>	<b>131.40</b>	<b>&lt;0.001</b>
Tau 18F-AV1451 Braak stage 2	0.02	0.03	0.553	0.07	0.04	0.096	<b>-0.18</b>	<b>0.06</b>	<b>0.004</b>

MoCA, Montreal Cognitive Assessment; MMSE, Mini Mental State Examination; SE, standard error; ω-3 index defined as erythrocyte % docosahexaenoic acid (DHA) + % eicosapentaenoic acid (EPA). Model 2 was adjusted for age, education, ApoE ε4 genotype, history of cardiovascular disease, body mass index and total intracranial volume (this last only for hippocampal volume); Significant p-values are presented in bold.

**Supplementary Table 3.** Differences in retrospective change of cognitive, brain imaging and biomarkers variables between the lowest and the 3 highest ω-3 index quartiles according to ApoE ε4 genotype (longitudinal analysis)

Outcome	Time	ApoE ε4 non-carrier			ApoE ε4 carrier			ApoE ε4 carrier vs non-carrier	
		Lowest vs highest ω-3 index quartiles		3 highest ω-3 index quartiles	Lowest vs highest ω-3 index quartiles		3 highest ω-3 index quartiles	Lowest vs highest ω-3 index quartiles	
		unadjusted	unadjusted		adjusted <sup>1</sup>	unadjusted		adjusted <sup>1</sup>	adjusted <sup>1</sup>
		β [95% CI]	β [95% CI]		β [95% CI] p-value	β [95% CI]		β [95% CI] p-value	β [95% CI] p-value
Composite cognitive score	M0 - M-24	-0.55 [-0.83, -0.26]	-0.63 [-1.12, -0.14]	-0.02 [-0.59, 0.56] p=0.9549	-0.96 [-1.37, -0.55]	-1.50 [-2.23, -0.77]	-0.60 [-1.41, 0.22] p=0.1507	-0.58 [-1.56, 0.40] p=0.2457	
	M0 - M-36	-0.76 [-1.16, -0.36]	-0.91 [-1.60, -0.23]	-0.03 [-0.83, 0.76] p=0.9319	-1.35 [-1.92, -0.78]	-2.07 [-3.08, -1.06]	-0.80 [-1.93, 0.33] p=0.1632	-0.77 [-2.13, 0.60] p=0.2691	
	M0 - M-60	-1.09 [-1.67, -0.52]	-1.41 [-2.39, -0.42]	-0.09 [-1.23, 1.05] p=0.8752	-1.94 [-2.76, -1.12]	-2.87 [-4.31, -1.44]	-1.02 [-2.62, 0.57] p=0.2084	-0.93 [-2.87, 1.00] p=0.3443	
	Whatever time			p=0.8525			p=0.2974		p=0.3445
Total MMSE	M0 - M-24	-0.32 [-0.52, -0.11]	-0.32 [-0.67, 0.03]	0.12 [-0.21, 0.45] p=0.4605	-0.64 [-0.93, -0.35]	-0.82 [-1.34, -0.31]	-0.38 [-0.86, 0.10] p=0.1186	-0.51 [-1.08, 0.07] p=0.0841	
	M0 - M-36	-0.45 [-0.74, -0.17]	-0.47 [-0.96, 0.02]	0.14 [-0.32, 0.61] p=0.5431	-0.90 [-1.31, -0.50]	-1.16 [-1.88, -0.44]	-0.47 [-1.13, 0.20] p=0.1671	-0.61 [-1.41, 0.19] p=0.1336	
	M0 - M-60	-0.67 [-1.08, -0.27]	-0.76 [-1.45, -0.07]	0.10 [-0.59, 0.78] p=0.7810	-1.33 [-1.90, -0.76]	-1.67 [-2.68, -0.66]	-0.43 [-1.39, 0.54] p=0.3857	-0.52 [-1.69, 0.65] p=0.3801	
	Whatever time			p=0.2491			p=0.0784		p=0.0183
Total ADAS-Cog <sup>2</sup>	M0 - M-24	0.43 [0.38, 0.48]	0.33 [0.25, 0.41]	-0.08 [-0.19, 0.02] p=0.1156	0.42 [0.36, 0.49]	0.29 [0.17, 0.41]	-0.16 [-0.31, -0.01] p=0.0387	-0.08 [-0.25, 0.10] p=0.4108	
	M0 - M-36	0.53 [0.48, 0.58]	0.41 [0.32, 0.50]	-0.10 [-0.21, 0.02] p=0.1099	0.52 [0.45, 0.59]	0.36 [0.23, 0.49]	-0.17 [-0.34, 0.00] p=0.0506	-0.07 [-0.27, 0.13] p=0.4882	

Outcome	Time	ApoE ε4 non-carrier			ApoE ε4 carrier			ApoE ε4 carrier vs non-carrier	
		Lowest vs highest ω-3 index quartiles			Lowest vs highest ω-3 index quartiles			Lowest vs highest ω-3 index quartiles	
		3 highest ω-3 index quartiles	Lowest ω-3 index quartile	adjusted <sup>1</sup>	3 highest ω-3 index quartiles	Lowest ω-3 index quartile	adjusted <sup>1</sup>	3 highest ω-3 index quartiles	Lowest ω-3 index quartile
		unadjusted	unadjusted	β [95% CI]	unadjusted	unadjusted	adjusted <sup>1</sup>	unadjusted	adjusted <sup>1</sup>
		β [95% CI]	β [95% CI]	p-value	β [95% CI]	β [95% CI]	β [95% CI]	β [95% CI]	p-value
	M0 - M-60	0.57 [0.51, 0.62]	0.47 [0.37, 0.56]	-0.08 [-0.20, 0.04] p=0.1832	0.56 [0.49, 0.64]	0.43 [0.30, 0.57]	-0.11 [-0.28, 0.06] p=0.2065	-0.03 [-0.23, 0.18] p=0.8026	
	Whatever time			p=0.3230				p=0.2139	p=0.6843
<b>ADAS-Cog delayed recall</b>	M0 - M-24	0.27 [0.13, 0.41]	0.09 [-0.16, 0.33]	-0.15 [-0.45, 0.14] p=0.3004	0.35 [0.14, 0.56]	0.28 [-0.09, 0.66]	-0.02 [-0.45, 0.41] p=0.9404	0.14 [-0.37, 0.65] p=0.5964	
	M0 - M-36	0.38 [0.19, 0.58]	0.14 [-0.19, 0.47]	-0.21 [-0.61, 0.19] p=0.2933	0.49 [0.21, 0.77]	0.41 [-0.09, 0.91]	-0.01 [-0.59, 0.57] p=0.9726	0.20 [-0.49, 0.90] p=0.5628	
	M0 - M-60	0.55 [0.28, 0.82]	0.28 [-0.18, 0.74]	-0.30 [-0.84, 0.25] p=0.2900	0.70 [0.32, 1.07]	0.64 [-0.03, 1.31]	0.03 [-0.74, 0.80] p=0.9359	0.33 [-0.61, 1.26] p=0.4916	
	Whatever time			p=0.5694				p=0.9186	p=0.7450
<b>Wechsler Memory Scale- Delayed recall</b>	M0 - M-24	-0.11 [-0.42, 0.21]	-0.42 [-0.96, 0.13]	-0.28 [-0.90, 0.35] p=0.3850	-0.38 [-0.85, 0.08]	-1.54 [-2.38, -0.71]	-1.36 [-2.28, -0.45] p=0.0036	-1.09 [-2.18, 0.01] p=0.0513	
	M0 - M-36	-0.09 [-0.52, 0.35]	-0.55 [-1.29, 0.19]	-0.39 [-1.25, 0.46] p=0.3647	-0.47 [-1.10, 0.16]	-2.05 [-3.17, -0.93]	-1.84 [-3.07, -0.61] p=0.0035	-1.44 [-2.92, 0.04] p=0.0559	
	M0 - M-60	0.09 [-0.52, 0.71]	-0.67 [-1.71, 0.37]	-0.59 [-1.78, 0.60] p=0.3297	-0.44 [-1.30, 0.43]	-2.54 [-4.07, -1.01]	-2.37 [-4.05, -0.70] p=0.0055	-1.78 [-3.81, 0.25] p=0.0847	
	Whatever time			p=0.6095				p=0.0146	p=0.1443
<b>Wechsler Memory Scale- Immediate recall</b>	M0 - M-24	-0.10 [-0.39, 0.19]	-0.36 [-0.85, 0.14]	-0.15 [-0.72, 0.43] p=0.6203	-0.17 [-0.58, 0.25]	-1.11 [-1.86, -0.36]	-1.09 [-1.93, -0.26] p=0.0105	-0.95 [-1.95, 0.05] p=0.0636	
	M0 - M-36	-0.10 [-0.50, 0.30]	-0.51 [-1.19, 0.18]	-0.23 [-1.03, 0.56] p=0.5653	-0.18 [-0.76, 0.39]	-1.49 [-2.51, -0.47]	-1.50 [-2.64, -0.36] p=0.0099	-1.27 [-2.64, 0.10] p=0.0699	
	M0 - M-60	0.01	-0.75	-0.44	-0.09	-1.89	-2.03	-1.59	



Outcome	Time	ApoE ε4 non-carrier			ApoE ε4 carrier			ApoE ε4 carrier vs non-carrier	
		Lowest vs highest ω-3 index quartiles			Lowest vs highest ω-3 index quartiles			Lowest vs highest ω-3 index quartiles	
		3 highest ω-3 index quartiles	Lowest ω-3 index quartile	adjusted <sup>1</sup>	3 highest ω-3 index quartiles	Lowest ω-3 index quartile	adjusted <sup>1</sup>	3 highest ω-3 index quartiles	Lowest ω-3 index quartile
		unadjusted	unadjusted	β [95% CI]	unadjusted	unadjusted	adjusted <sup>1</sup>	β [95% CI]	β [95% CI]
		β [95% CI]	β [95% CI]	p-value	β [95% CI]	β [95% CI]	p-value	β [95% CI]	p-value
<b>MoCA total score</b>	Whatever time			p=0.4172				p=0.9024	p=0.7068
				p=0.1325				p=0.9385	p=0.7768
	M0 - M-24	-0.34 [-0.64, -0.04]	-0.64 [-1.16, -0.12]	-0.36 [-0.93, 0.21] p=0.2116	-0.84 [-1.27, -0.41]	-0.93 [-1.69, -0.17]	-0.33 [-1.13, 0.47] p=0.4136	0.03 [-0.94, 1.00] p=0.9551	
	M0 - M-36	-0.45 [-0.84, -0.06]	-0.89 [-1.56, -0.22]	-0.48 [-1.21, 0.25] p=0.1998	-1.12 [-1.67, -0.57]	-1.29 [-2.27, -0.31]	-0.46 [-1.48, 0.56] p=0.3801	0.02 [-1.22, 1.26] p=0.9751	
	M0 - M-60	-0.55 [-1.04, -0.06]	-1.22 [-2.05, -0.38]	-0.58 [-1.51, 0.35] p=0.2220	-1.42 [-2.10, -0.74]	-1.82 [-3.03, -0.62]	-0.62 [-1.92, 0.67] p=0.3467	-0.04 [-1.62, 1.54] p=0.9603	
<b>CDR sum of boxes</b>	Whatever time			p=0.4347				p=0.6397	p=0.9841
	M0 - M-24	0.24 [0.09, 0.39]	0.39 [0.13, 0.65]	0.18 [-0.13, 0.49] p=0.2584	0.66 [0.45, 0.88]	0.83 [0.45, 1.22]	0.23 [-0.21, 0.67] p=0.2991	0.05 [-0.48, 0.59] p=0.8405	
	M0 - M-36	0.31 [0.10, 0.51]	0.50 [0.16, 0.85]	0.21 [-0.20, 0.62] p=0.3191	0.87 [0.58, 1.15]	1.07 [0.56, 1.58]	0.28 [-0.30, 0.87] p=0.3392	0.07 [-0.63, 0.78] p=0.8371	
	M0 - M-60	0.38 [0.10, 0.66]	0.62 [0.14, 1.09]	0.19 [-0.38, 0.76] p=0.5065	1.10 [0.70, 1.49]	1.30 [0.60, 1.99]	0.29 [-0.51, 1.08] p=0.4798	0.09 [-0.87, 1.06] p=0.8479	
	Whatever time			p=0.1781				p=0.3083	p=0.9698
<b>White matter hyperintensities (cm3)<sup>2</sup></b>	M0 - M-24	-0.30 [-0.45, -0.15]	-0.31 [-0.57, -0.05]	-0.03 [-0.31, 0.25] p=0.8374	-0.40 [-0.61, -0.19]	-0.36 [-0.73, 0.02]	0.06 [-0.34, 0.46] p=0.7632	0.09 [-0.39, 0.57] p=0.7117	
		-0.29 [-0.44, -0.13]	-0.22 [-0.48, 0.03]	0.05 [-0.23, 0.33] p=0.7209	-0.33 [-0.54, -0.12]	-0.29 [-0.67, 0.08]	0.07 [-0.33, 0.46] p=0.7445	0.01 [-0.46, 0.49] p=0.9513	
		-0.16 [-0.29, -0.02]	-0.03 [-0.26, 0.20]	0.14 [-0.11, 0.39] p=0.2871	-0.09 [-0.28, 0.09]	-0.03 [-0.36, 0.29]	0.09 [-0.26, 0.44] p=0.6286	-0.05 [-0.47, 0.38] p=0.8185	

Outcome	Time	ApoE ε4 non-carrier			ApoE ε4 carrier			ApoE ε4 carrier vs non-carrier	
		Lowest vs highest ω-3 index quartiles		3 highest ω-3 index quartiles	Lowest ω-3 index quartile	Lowest vs highest ω-3 index quartiles		3 highest ω-3 index quartiles	Lowest ω-3 index quartile
		unadjusted	unadjusted	adjusted <sup>1</sup>	unadjusted	unadjusted	adjusted <sup>1</sup>	unadjusted	adjusted <sup>1</sup>
		β [95% CI]	β [95% CI]	p-value	β [95% CI]	β [95% CI]	p-value	β [95% CI]	p-value
Whatever time				p=0.0696				p=0.8830	
Cortical SUVR	M0 - M-24	0.01 [0.00, 0.01]	0.01 [0.01, 0.02]	0.01 [0.00, 0.01] p=0.0394	0.02 [0.01, 0.02]	0.02 [0.02, 0.03]	0.01 [0.00, 0.02]	0.00 [-0.01, 0.01]	
	M0 - M-36	0.01 [0.00, 0.01]	0.02 [0.01, 0.02]	0.01 [0.00, 0.02] p=0.0394	0.02 [0.02, 0.03]	0.03 [0.02, 0.05]	0.01 [0.00, 0.03]	0.01 [-0.01, 0.02]	
	M0 - M-60	0.01 [0.01, 0.02]	0.03 [0.02, 0.04]	0.01 [0.00, 0.03] p=0.0394	0.04 [0.03, 0.05]	0.06 [0.04, 0.08]	0.02 [0.00, 0.04]	0.01 [-0.02, 0.03]	
	Whatever time			p=0.0394				p=0.0239	

<sup>1</sup>Adjustments: age (years), Education participant (years), History of cardiovascular disease (yes vs no), BMI (Kg/m<sup>2</sup>) + Intra-Cranial Volume (ICV only for WMH) and their interaction with time; ADAS, Alzheimer's disease assessment scale; CDR, Clinical Dementia Rating; MMSE, Mini Mental State Examination; MoCA, Montreal Cognitive Assessment; TMT, Trail Making Test; SUVR, standard uptake value ratio. Results from mixed linear regression models. <sup>2</sup>variable with log transformation;

**Supplementary Table 4.** Differences in retrospective change of cognitive, brain imaging and biomarkers variables between the lowest and the 3 highest ω-3 index quartiles according to cognitive status (longitudinal analysis)

Outcome	Time	Cognitively normal			Mild cognitive impairment (MCI)			Alzheimer's disease (AD)			MCI vs cognitively normal	AD vs cognitively normal	
		3 highest ω-3 index quartiles	Lowest ω-3 index quartile	Lowest vs highest ω-3 index quartiles	3 highest ω-3 index quartiles	Lowest ω-3 index quartile	Lowest vs highest ω-3 index quartiles	3 highest ω-3 index quartiles	Lowest ω-3 index quartile	Lowest vs highest ω-3 index quartiles	Lowest vs highest ω-3 index quartiles	Lowest vs highest ω-3 index quartiles	
		unadjusted	unadjusted	adjusted <sup>1</sup>	unadjusted	unadjusted	adjusted <sup>1</sup>	unadjusted	unadjusted	adjusted <sup>1</sup>	adjusted <sup>1</sup>	adjusted <sup>1</sup>	
		β [95% CI]	β [95% CI]	β [95% CI] p-value	β [95% CI]	β [95% CI]	β [95% CI] p-value	β [95% CI]	β [95% CI]	β [95% CI] p-value	β [95% CI] p-value	β [95% CI] p-value	
Composite cognitive score	M0 - M-24	-0.13 [-0.38, 0.12]	0.00 [-0.47, 0.48]	0.12 [-0.41, 0.66] p=0.6517	-0.58 [-0.89, -0.26]	-0.96 [-1.50, -0.41]	-0.45 [-1.10, 0.19] p=0.1655	-4.39 [-5.03, -3.76]	-3.00 [-3.79, -2.20]	1.25 [0.24, 2.27] p=0.0155	-0.58 [-1.40, 0.25] p=0.1706	1.13 [-0.01, 2.27] p=0.0513	
		-0.17 [-0.52, 0.18]	-0.00 [-0.65, 0.65]	0.17 [-0.57, 0.91] p=0.6543	-0.83 [-1.26, -0.39]	-1.35 [-2.11, -0.60]	-0.61 [-1.50, 0.27] p=0.1736	-6.23 [-7.10, -5.36]	-4.31 [-5.41, -3.22]	1.72 [0.33, 3.11] p=0.0156	-0.78 [-1.92, 0.36] p=0.1777	1.55 [-0.01, 3.11] p=0.0512	
	M0 - M-36	-0.19 [-0.67, 0.29]	-0.02 [-0.92, 0.89]	0.22 [-0.80, 1.24] p=0.6686	-1.24 [-1.85, -0.64]	-1.98 [-3.04, -0.93]	-0.79 [-2.02, 0.43] p=0.2040	-9.20 [-10.41, -7.98]	-6.57 [-8.08, -5.06]	2.33 [0.41, 4.25] p=0.0173	-1.02 [-2.59, 0.56] p=0.2060	2.11 [-0.04, 4.26] p=0.0547	
		Whatever time		p=0.9023			p=0.3527			p=0.0542	p=0.3712	p=0.1504	
		-0.09 [-0.24, 0.06]	0.04 [-0.24, 0.32]	0.16 [-0.17, 0.49] p=0.3395	-0.23 [-0.41, -0.04]	-0.44 [-0.75, -0.12]	-0.18 [-0.56, 0.21] p=0.3740	-3.23 [-3.57, -2.89]	-2.05 [-2.49, -1.60]	1.19 [0.62, 1.75] <b>p=&lt;0.001</b>	-0.34 [-0.84, 0.17] p=0.1893	1.03 [0.38, 1.68] <b>p=0.0019</b>	
Total MMSE	M0 - M-24	-0.12 [-0.33, 0.08]	0.06 [-0.32, 0.44]	0.22 [-0.23, 0.67] p=0.3403	-0.33 [-0.59, -0.08]	-0.63 [-1.07, -0.19]	-0.26 [-0.79, 0.27] p=0.3424	-4.54 [-5.01, -4.06]	-2.91 [-3.52, -2.30]	1.62 [0.84, 2.40] <b>p=&lt;0.001</b>	-0.47 [-1.16, 0.21] p=0.1751	1.40 [0.51, 2.29] <b>p=0.0020</b>	
		-0.17 [-0.46, 0.11]	0.09 [-0.45, 0.62]	0.29 [-0.33, 0.91] p=0.3638	-0.54 [-0.89, -0.18]	-0.99 [-1.61, -0.37]	-0.41 [-1.15, 0.34] p=0.2818	-6.52 [-7.19, -5.85]	-4.32 [-5.17, -3.47]	2.17 [1.08, 3.26] <b>p=0.0001</b>	-0.70 [-1.66, 0.26] p=0.1551	1.88 [0.63, 3.13] <b>p=0.0032</b>	
	M0 - M-36	Whatever time		p=0.6336			p=0.4985			p=0.0002	p=0.3604	p=0.0085	
		M0 - M-24	0.48 [0.42, 0.53]	0.37 [0.27, 0.48]	-0.10 [-0.22, 0.02] p=0.1169	0.32 [0.26, 0.39]	0.25 [0.13, 0.36]	-0.08 [-0.22, 0.06] p=0.2676	0.32 [0.18, 0.45]	0.23 [0.07, 0.40]	-0.05 [-0.26, 0.16] p=0.6442	0.02 [-0.17, 0.20] p=0.8574	0.05 [-0.19, 0.29] p=0.7013
			0.59	0.43	-0.14	0.40	0.33	-0.07	0.46	0.36	-0.06	0.06	0.08

		[0.52, 0.65]	[0.32, 0.55]	[-0.27, -0.00] p=0.0468	[0.32, 0.48]	[0.19, 0.47]	[-0.23, 0.09] p=0.3752	[0.30, 0.61]	[0.17, 0.55]	[-0.30, 0.18] p=0.6223	[-0.14, 0.27] p=0.5530	[-0.20, 0.35] p=0.5862
	M0 - M-60	0.62	0.42	-0.18 p=0.0106	0.45	0.43	-0.01 p=0.8607	0.69	0.59	-0.06 p=0.6074	0.16 p=0.1333	0.11 p=0.4266
	Whatever time	[0.55, 0.68]	[0.30, 0.54]	[-0.31, -0.04] p=0.0026	[0.37, 0.53]	[0.29, 0.58]	[-0.18, 0.15] p=0.3121	[0.53, 0.85]	[0.40, 0.79]	[-0.31, 0.18] p=0.9655	[-0.05, 0.37] p=0.0094	[-0.16, 0.39] p=0.3257
<b>ADAS-Cog delayed recall</b>		0.16	-0.17	-0.26 p=0.1298	0.33	0.32	0.04 p=0.8468	0.95	0.58	-0.30 p=0.3051	0.30 p=0.2550	-0.04 p=0.8958
	M0 - M-24	[0.01, 0.32]	[-0.45, 0.12]	[-0.59, 0.08] p=0.1355	[0.13, 0.52]	[-0.01, 0.65]	[-0.36, 0.43] p=0.8773	[0.59, 1.30]	[0.13, 1.03]	[-0.88, 0.27] p=0.2992	[-0.21, 0.80] p=0.2760	[-0.70, 0.61] p=0.8737
	M0 - M-36	0.22	-0.21	-0.34 p=0.1355	0.46	0.46	0.04 p=0.8773	1.38	0.86	-0.41 p=0.2978	0.38 p=0.3585	-0.07 p=0.8184
	M0 - M-60	[0.01, 0.42]	[-0.60, 0.18]	[-0.79, 0.11] p=0.1721	[0.21, 0.72]	[0.01, 0.90]	[-0.49, 0.58] p=0.9648	[0.90, 1.86]	[0.25, 1.48]	[-1.19, 0.37] p=0.5790	[-0.31, 1.07] p=0.4523	[-0.97, 0.82] p=0.9311
	Whatever time			p=0.3132			p=0.8739					
<b>Wechsler Memory Scale-Delayed recall</b>		0.15	-0.06	-0.29 p=0.4311	-0.19	-0.99	-1.02 p=0.0182	-2.01	-1.85	0.01 p=0.9936	-0.73 p=0.1864	0.29 p=0.6909
	M0 - M-24	[-0.19, 0.49]	[-0.71, 0.58]	[-1.00, 0.43] p=0.3915	[-0.62, 0.23]	[-1.73, -0.25]	[-1.86, -0.17] p=0.0198	[-2.83, -1.20]	[-2.87, -0.83]	[-1.25, 1.26] p=0.9931	[-1.82, 0.36] p=0.2094	[-1.14, 1.72] p=0.6669
	M0 - M-36	0.29	-0.06	-0.42 p=0.3915	-0.22	-1.31	-1.37 p=0.0198	-2.93	-2.70	0.01 p=0.9919	-0.95 p=0.3005	0.43 p=0.6129
	M0 - M-60	[-0.17, 0.76]	[-0.93, 0.81]	[-1.38, 0.54] p=0.3117	[-0.80, 0.36]	[-2.31, -0.31]	[-2.51, -0.22] p=0.0297	[-4.04, -1.82]	[-4.08, -1.31]	[-1.71, 1.72] p=0.9999	[-2.43, 0.53] p=0.3128	[-1.52, 2.38] p=0.8378
	Whatever time			p=0.5264			p=0.0597					
<b>Wechsler Memory Scale-Immediate recall</b>		0.17	-0.16	-0.32 p=0.3409	-0.02	-0.77	-0.88 p=0.0270	-2.03	-1.14	0.84 p=0.1563	-0.56 p=0.2742	1.16 p=0.0862
	M0 - M-24	[-0.14, 0.48]	[-0.75, 0.42]	[-0.98, 0.34] p=0.2888	[-0.41, 0.36]	[-1.44, -0.10]	[-1.66, -0.10] p=0.0301	[-2.75, -1.30]	[-2.08, -0.21]	[-0.32, 2.00] p=0.1778	[-1.57, 0.45] p=0.3202	[-0.17, 2.48] p=0.0879
	M0 - M-36	0.29	-0.22	-0.48 p=0.2888	-0.01	-1.04	-1.18 p=0.0301	-2.90	-1.74	1.09 p=0.1778	-0.70 p=0.3202	1.58 p=0.0879
	M0 - M-60	[-0.13, 0.72]	[-1.02, 0.57]	[-1.38, 0.41] p=0.2888	[-0.54, 0.52]	[-1.95, -0.12]	[-2.25, -0.11] p=0.0301	[-3.90, -1.91]	[-3.02, -0.46]	[-0.50, 2.69] p=0.2742	[-2.08, 0.68] p=0.3202	[-0.24, 3.39] p=0.0879
	Whatever time	0.65	-0.31	-0.83 p=0.2888	0.07	-1.33	-1.52 p=0.0301	-4.37	-2.99	1.27 p=0.1778	-0.69 p=0.3202	2.10 p=0.0879

	[0.06, 1.23]	[-1.41, 0.79]	[-2.06, 0.41] p=0.1873	[-0.66, 0.81]	[-2.60, -0.06]	[-3.00, -0.04] p=0.0442	[-5.75, -2.99]	[-4.75, -1.22]	[-0.93, 3.47] p=0.2559	[-2.60, 1.22] p=0.4783	[-0.40, 4.60] p=0.0995	
Whatever time			p=0.2212			p=0.0744			p=0.2052	p=0.2010	p=0.2297	
<b>Category</b>	-0.09	-0.31	-0.22	-0.63	-0.50	0.09	-1.66	-1.23	0.37	0.31	0.59	
<b>Fluency test (words)</b>	M0 - M-24	[-0.29, 0.10]	[-0.68, 0.07]	[-0.64, 0.21] p=0.3180	[-0.86, -0.40]	[-0.89, -0.11]	[-0.37, 0.56] p=0.6923	[-2.09, -1.24]	[-1.75, -0.70]	[-0.30, 1.05] p=0.2720	[-0.31, 0.93] p=0.3273	[-0.20, 1.38] p=0.1408
	-0.14	-0.46	-0.32	-0.95	-0.75	0.14	-2.50	-1.84	0.56	0.46	0.89	
M0 - M-36	[-0.43, 0.15]	[-1.01, 0.10]	[-0.96, 0.31] p=0.3180	[-1.30, -0.59]	[-1.33, -0.16]	[-0.56, 0.83] p=0.6923	[-3.13, -1.86]	[-2.63, -1.05]	[-0.44, 1.57] p=0.2720	[-0.47, 1.39] p=0.3273	[-0.30, 2.07] p=0.1408	
	-0.23	-0.76	-0.54	-1.58	-1.24	0.23	-4.16	-3.06	0.94	0.77	1.48	
M0 - M-60	[-0.72, 0.26]	[-1.69, 0.16]	[-1.60, 0.52] p=0.3180	[-2.16, -0.99]	[-2.22, -0.27]	[-0.93, 1.39] p=0.6923	[-5.22, -3.10]	[-4.38, -1.75]	[-0.74, 2.61] p=0.2720	[-0.78, 2.32] p=0.3273	[-0.49, 3.44] p=0.1408	
Whatever time			p=0.3180			p=0.6923			p=0.2720	p=0.3273	p=0.1408	
<b>TMT-A (seconds)<sup>2</sup></b>	0.01	0.03	0.02	0.02	0.05	0.04	0.26	0.12	-0.12	0.02	-0.14	
M0 - M-24	[-0.02, 0.03]	[-0.02, 0.07]	[-0.03, 0.07] p=0.4774	[-0.01, 0.05]	[-0.00, 0.10]	[-0.02, 0.10] p=0.2156	[0.20, 0.31]	[0.05, 0.20]	[-0.21, -0.03] <b>p=0.0095</b>	[-0.06, 0.10] p=0.6227	[-0.24, -0.03] <b>p=0.0087</b>	
	0.01	0.04	0.02	0.03	0.07	0.05	0.36	0.18	-0.17	0.03	-0.19	
M0 - M-36	[-0.03, 0.04]	[-0.03, 0.10]	[-0.05, 0.09] p=0.5067	[-0.01, 0.07]	[-0.01, 0.14]	[-0.03, 0.13] p=0.2410	[0.28, 0.44]	[0.08, 0.27]	[-0.29, -0.05] <b>p=0.0075</b>	[-0.08, 0.13] p=0.6352	[-0.33, -0.05] <b>p=0.0075</b>	
	0.01	0.04	0.03	0.05	0.09	0.06	0.53	0.26	-0.24	0.03	-0.27	
M0 - M-60	[-0.04, 0.05]	[-0.05, 0.12]	[-0.07, 0.12] p=0.6031	[-0.01, 0.10]	[-0.01, 0.19]	[-0.06, 0.17] p=0.3299	[0.42, 0.63]	[0.12, 0.39]	[-0.41, -0.08] <b>p=0.0045</b>	[-0.12, 0.18] p=0.6769	[-0.46, -0.08] <b>p=0.0060</b>	
Whatever time			p=0.6589			p=0.2913			<b>p=0.0139</b>	p=0.8606	<b>p=0.0234</b>	
<b>TMT-B (seconds)<sup>2</sup></b>	0.03	0.06	0.02	0.05	0.11	0.07	0.34	0.16	-0.18	0.04	-0.20	
M0 - M-24	[-0.00, 0.06]	[-0.00, 0.11]	[-0.04, 0.09] p=0.4930	[0.02, 0.09]	[0.04, 0.17]	[-0.01, 0.14] p=0.0841	[0.26, 0.41]	[0.07, 0.25]	[-0.30, -0.06] <b>p=0.0028</b>	[-0.05, 0.14] p=0.3765	[-0.33, -0.07] <b>p=0.0028</b>	
	0.04	0.08	0.03	0.08	0.15	0.09	0.48	0.23	-0.25	0.06	-0.28	
M0 - M-36	[-0.00, 0.08]	[-0.00, 0.15]	[-0.06, 0.11] p=0.5184	[0.03, 0.13]	[0.06, 0.24]	[-0.02, 0.19] p=0.0958	[0.38, 0.58]	[0.10, 0.36]	[-0.41, -0.09] <b>p=0.0020</b>	[-0.07, 0.19] p=0.3869	[-0.46, -0.10] <b>p=0.0023</b>	
	0.06	0.11	0.03	0.12	0.22	0.10	0.71	0.35	-0.37	0.07	-0.40	
M0 - M-60	[0.01, 0.12]	[0.00, 0.21]	[-0.09, 0.15] p=0.6001	[0.05, 0.19]	[0.10, 0.34]	[-0.03, 0.24] p=0.1408	[0.57, 0.85]	[0.18, 0.53]	[-0.58, -0.15] <b>p=0.0010</b>	[-0.11, 0.25] p=0.4247	[-0.64, -0.15] <b>p=0.0015</b>	
Whatever time			p=0.6710			p=0.1365			<b>p=0.0023</b>	p=0.6482	<b>p=0.0057</b>	

		0.00	-0.17	-0.39	-0.42	-0.83	-0.50	-3.99	-2.09	1.63	-0.11	2.02
MoCA total score	M0 - M-24	[−0.29, 0.30]	[−0.72, 0.39]	[−1.01, 0.23] p=0.2162	[−0.77, −0.07]	[−1.47, −0.19]	[−1.23, 0.23] p=0.1822	[−4.71, −3.27]	[−2.96, −1.22]	[0.54, 2.72] <b>p=0.0033</b>	[−1.05, 0.84] p=0.8247	[0.78, 3.26] <b>p=0.0014</b>
		0.04	-0.21	-0.49	-0.57	-1.17	-0.70	-5.41	-2.91	2.17	-0.21	2.66
	M0 - M-36	[−0.33, 0.41]	[−0.91, 0.48]	[−1.25, 0.28] p=0.2132	[−1.03, −0.12]	[−1.98, −0.36]	[−1.62, 0.23] p=0.1391	[−6.31, −4.50]	[−4.02, −1.81]	[0.80, 3.54] <b>p=0.0020</b>	[−1.40, 0.98] p=0.7270	[1.10, 4.22] <b>p=0.0009</b>
		0.17	-0.23	-0.48	-0.76	-1.69	-1.01	-7.08	-4.09	2.68	-0.52	3.17
	M0 - M-60	[−0.27, 0.60]	[−1.05, 0.59]	[−1.39, 0.42] p=0.2942	[−1.32, −0.21]	[−2.65, −0.73]	[−2.12, 0.10] p=0.0747	[−8.14, −6.02]	[−5.40, −2.77]	[1.06, 4.31] <b>p=0.0013</b>	[−1.94, 0.89] p=0.4678	[1.32, 5.02] <b>p=0.0008</b>
	Whatever time			p=0.4605			p=0.1916			<b>p=0.0050</b>	p=0.6218	<b>p=0.0027</b>
CDR sum of boxes	M0 - M-24	-0.02	-0.00	0.06	0.43	0.19	-0.11	2.48	2.44	0.03	-0.17	-0.03
		[−0.15, 0.11]	[−0.25, 0.24]	[−0.22, 0.34] p=0.6760	[0.27, 0.59]	[−0.09, 0.48]	[−0.45, 0.24] p=0.5412	[2.17, 2.79]	[2.06, 2.83]	[−0.47, 0.53] p=0.9110	[−0.61, 0.27] p=0.4566	[−0.60, 0.54] p=0.9127
		-0.04	-0.01	0.08	0.54	0.26	-0.13	3.40	3.19	-0.13	-0.21	-0.21
	M0 - M-36	[−0.21, 0.13]	[−0.32, 0.30]	[−0.28, 0.44] p=0.6698	[0.33, 0.75]	[−0.11, 0.63]	[−0.57, 0.31] p=0.5620	[3.01, 3.80]	[2.69, 3.69]	[−0.77, 0.51] p=0.6912	[−0.77, 0.36] p=0.4679	[−0.94, 0.52] p=0.5762
		-0.09	-0.02	0.09	0.63	0.37	-0.15	4.75	4.03	-0.64	-0.24	-0.73
White matter hyperintensities (cm3) <sup>2</sup>	M0 - M-60	[−0.30, 0.12]	[−0.41, 0.38]	[−0.37, 0.55] p=0.7028	[0.36, 0.91]	[−0.11, 0.84]	[−0.72, 0.42] p=0.6086	[4.23, 5.26]	[3.39, 4.67]	[−1.47, 0.19] p=0.1323	[−0.97, 0.49] p=0.5194	[−1.67, 0.22] p=0.1302
		Whatever time		p=0.8757			p=0.6823			p=<.0001	p=0.8948	p=0.0015
	M0 - M-24	-0.46	-0.48	-0.04	-0.16	-0.35	-0.10	-0.21	0.16	0.31	-0.06	0.35
		[−0.63, −0.30]	[−0.77, −0.19]	[−0.35, 0.27] p=0.8031	[−0.37, 0.05]	[−0.71, 0.02]	[−0.51, 0.30] p=0.6095	[−0.61, 0.20]	[−0.38, 0.70]	[−0.34, 0.95] p=0.3507	[−0.57, 0.44] p=0.8006	[−0.36, 1.06] p=0.3384
		-0.44	-0.40	0.02	-0.13	-0.29	-0.08	-0.14	0.29	0.41	-0.10	0.39
Cortical SUVR	M0 - M-36	-0.44	-0.40	0.02	-0.13	-0.29	-0.08	-0.14	0.29	0.41	-0.10	0.39
		[−0.60, −0.27]	[−0.68, −0.11]	[−0.29, 0.33] p=0.8927	[−0.34, 0.08]	[−0.65, 0.08]	[−0.48, 0.32] p=0.6899	[−0.54, 0.27]	[−0.24, 0.82]	[−0.21, 1.04] p=0.1944	[−0.60, 0.40] p=0.6876	[−0.30, 1.08] p=0.2644
		-0.25	-0.20	0.05	-0.02	-0.04	0.03	0.11	0.48	0.45	-0.03	0.40
	M0 - M-60	[−0.39, −0.11]	[−0.45, 0.06]	[−0.22, 0.32] p=0.7134	[−0.20, 0.16]	[−0.36, 0.28]	[−0.33, 0.38] p=0.8877	[−0.24, 0.46]	[0.02, 0.93]	[−0.10, 1.00] p=0.1066	[−0.47, 0.42] p=0.9109	[−0.21, 1.01] p=0.1965
		Whatever time		p=0.1210			p=0.5816			p=0.2834	p=0.1401	p=0.6411
Cortical SUVR	M0 - M-24	0.01	0.01	0.01	0.01	0.02	0.01	0.01	0.02	0.01	0.00	0.01

	[0.00, 0.01]	[0.01, 0.02]	[-0.00, 0.01] p=0.0844	[0.00, 0.01]	[0.01, 0.02]	[-0.00, 0.01] p=0.1647	[0.00, 0.02]	[0.01, 0.03]	[0.00, 0.02] p=0.0360	[-0.01, 0.01] p=0.9984	[-0.01, 0.02] p=0.3030
M0 - M-36	0.01	0.02	0.01 p=0.0844	0.01	0.02	0.01 p=0.1647	0.02	0.03	0.02 p=0.0360	0.00 p=0.9984	0.01 p=0.3030
	[0.01, 0.02]	[0.01, 0.03]	[-0.00, 0.02] p=0.0844	[0.01, 0.02]	[0.01, 0.03]	[-0.00, 0.02] p=0.1647	[0.01, 0.03]	[0.02, 0.05]	[0.00, 0.04] p=0.0360	[-0.02, 0.02] p=0.9984	[-0.01, 0.03] p=0.3030
	0.02	0.03	0.01 p=0.0844	0.02	0.04	0.01 p=0.1647	0.03	0.05	0.03 p=0.0360	0.00 p=0.9984	0.02 p=0.3030
M0 - M-60	[0.01, 0.03]	[0.02, 0.05]	[-0.00, 0.03] p=0.0844	[0.01, 0.03]	[0.02, 0.06]	[-0.01, 0.03] p=0.1647	[0.01, 0.05]	[0.03, 0.08]	[0.00, 0.06] p=0.0360	[-0.03, 0.03] p=0.9984	[-0.02, 0.05] p=0.3030
	Whatever time		p=0.0844			p=0.1647			p=0.0360	p=0.9984	p=0.3030

<sup>1</sup>Adjustments: age (years), Education participant (years), ApoE4 (yes vs no), History of cardiovascular disease (yes vs no), BMI (Kg/m2) + Intra-Cranial Volume (ICV only for WMH) and their interaction with time; ADAS, Alzheimer's disease assessment scale; CDR, Clinical Dementia Rating; MMSE, Mini Mental State Examination; MoCA, Montreal Cognitive Assessment; TMT, Trail Making Test; SUVR, standard uptake value ratio. Results from mixed linear regression models. <sup>2</sup>variable with log transformation;

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