

Figure S1. Residual plots for linear mixed models examining the associations between time, demographic and vascular risk factors with NART IQ and ACE-R scores by time-point

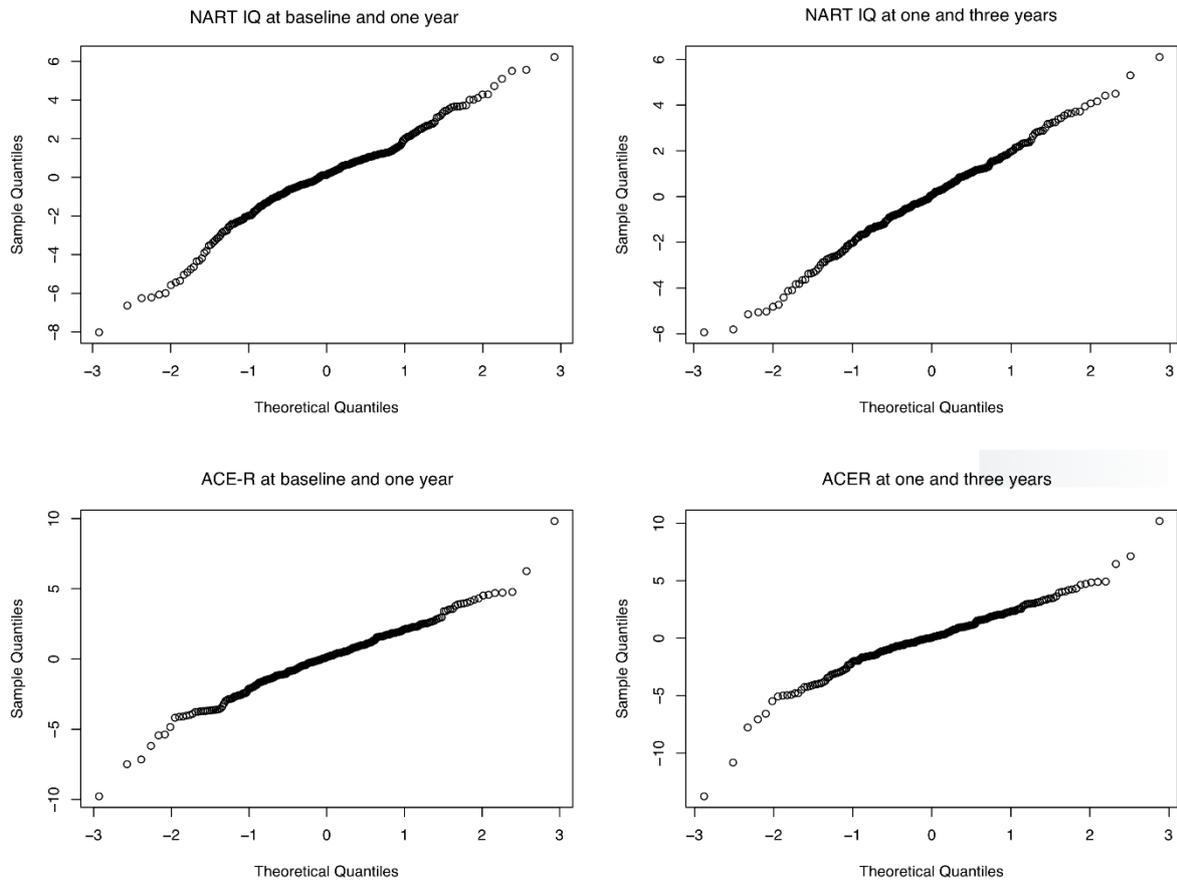


Table S1. NART IQ and ACE-R scores at and between each time-point for all patients with data available at all time-points.

	Scores			Difference scores		
	1-3 months	1 year	3 years	1-3 months to 1 year	1 to 3 years	1-3 months to 3 years
NART IQ (n=90)						
Mean±SD (range)	116.35±8.32 (94.66-127.70)	117.34±9.25 (9.30-127.70)	113.26±8.78 (92.18-127.70)	Mean change (95% CI) 0.991 (0.07 to 1.91)*	-4.075 (-4.98 to -3.17)**	-3.084 (-3.92 to -2.25)**
				Decreased n(%) 27 (30.34%)	72 (79.12%)	72 (77.42%)
				Increased n(%) 51 (57.30%)	12 (13.19%)	14 (15.05%)
				No change n(%) 11 (12.36%)	7 (7.69%)	7 (7.53%)
ACE-R (n=96)						
Mean±SD (range)	89.14±7.70 (69.00-100.00)	90.00±7.37 (71.00-100.00)	88.86±9.07 (54.00-100.00)	Mean change (95% CI) 0.865 (0.07 to 1.80)	-1.135 (-2.27 to -0.00)*	0.271 (-1.48 to 0.94)
No impairment n(%)^a	59 (61.46%)	64 (66.67%)	59 (61.46%)	Decreased n(%) 36 (37.50%)	40 (41.67%)	53 (55.21%)
Mild impairment n(%)^b	15 (15.63%)	16 (16.67%)	18 (18.75%)	Increased n(%) 47 (48.96%)	45 (46.88%)	38 (39.58%)
Severe impairment n(%)^c	22 (22.92%)	16 (16.67%)	19 (19.79%)	No change n(%) 13 (13.54%)	11 (11.46%)	5 (5.21%)

* $p < 0.05$

** $p < 0.001$

^a ACE-R scores ≥ 89

^b ACE-R scores 83-88

^c ACE-R scores ≤ 82

Table S2. Linear mixed effects model showing the associations between time and NART IQ and ACE-R adjusted for baseline characteristics for patients with data available at all time-points.

	Changes in scores between 1 month and 3 years			Changes in scores between 1 and 3 years		
	B	95% CI	p	B	95% CI	p
NART IQ						
<i>Time (years)</i>	0.975	(0.051, 1.898)	0.038	-4.111	(-5.019, -3.204)	<0.001
Age	0.109	(-0.083, 0.301)	0.287	0.118	(-0.078, 0.315)	0.258
Sex (male)	1.699	(-1.525, 4.923)	0.322	1.650	(-1.643, 4.943)	0.345
Baseline Fazekas	0.242	(-1.016, 1.500)	0.717	0.071	(-1.214, 1.356)	0.917
Stroke subtype (lacunar)	1.656	(-1.656, 4.968)	0.348	1.586	(-1.797, 4.969)	0.379
NIHSS	-0.537	(-1.861, 0.786)	0.446	-0.414	(-1.767, 0.938)	0.565
Hypertension (yes)	2.608	(-1.121, 6.336)	0.189	2.696	(-1.112, 6.504)	0.184
Smoker (yes)	0.169	(-3.724, 4.062)	0.935	-0.328	(-4.304, 3.648)	0.877
Years of education	1.192	(0.639, 1.745)	<0.001	1.265	(0.700, 1.830)	<0.001
ACE-R						
<i>Time (years)</i>	0.872	(-0.050, 1.795)	0.063	-1.160	(-2.296, -0.023)	0.045
Age	-0.057	(-0.213, 0.099)	0.492	-0.145	(-0.310, 0.020)	0.097
Sex (male)	-0.017	(-2.602, 2.568)	0.990	-0.585	(-3.320, 2.149)	0.687
Baseline Fazekas	-0.277	(-1.301, 0.748)	0.611	-0.293	(-1.377, 0.790)	0.610
Stroke subtype (lacunar)	0.510	(-2.179, 3.199)	0.721	1.010	(-1.834, 3.854)	0.504
NIHSS	-0.686	(-1.770, 0.398)	0.233	-0.553	(-1.700, 0.594)	0.364
Hypertension (yes)	3.213	(0.245, 6.181)	0.042	4.055	(0.916, 7.195)	0.015
Smoker (yes)	1.447	(-1.695, 4.590)	0.386	1.029	(-2.295, 4.353)	0.560
Years of education	0.993	(0.546, 1.439)	<0.001	1.061	(0.589, 1.533)	<0.001

Table S3. Full linear mixed effects models showing factors associated with changes in NART IQ at each time-point

	1-3 months and 1 year																								
	B	95% CI	p	B	95% CI	p	B	95% CI	p	B	95% CI	p	B	95% CI	p	B	95% CI	p	B	95% CI	p	B	95% CI	p	
	NART IQ																								
Time	1.339	(-3.545, 6.223)	0.588	1.878	(0.582, 3.173)	0.005	2.954	(1.306, 4.602)	0.001	1.122	(0.035, 2.210)	0.043	1.163	(0.066, 2.260)	0.038	1.695	(0.121, 3.269)	0.035	1.672	(0.692, 2.651)	0.001	4.277	(1.060, 7.494)	0.010	
Age	0.095	(-0.038, 0.229)	0.160	0.096	(-0.034, 0.225)	0.146	0.095	(-0.035, 0.224)	0.150	0.097	(-0.033, 0.226)	0.142	0.096	(-0.033, 0.226)	0.144	0.096	(-0.033, 0.226)	0.144	0.096	(-0.034, 0.225)	0.146	0.099	(-0.031, 0.228)	0.134	
Sex (male)	1.237	(-1.198, 3.673)	0.316	1.546	(-0.998, 4.090)	0.231	1.220	(-1.214, 3.654)	0.323	1.248	(-1.186, 3.682)	0.312	1.248	(-1.186, 3.682)	0.312	1.248	(-1.187, 3.684)	0.312	1.249	(-1.185, 3.684)	0.312	1.235	(-1.195, 3.664)	0.316	
Baseline Fazekas	0.178	(-0.656, 1.011)	0.674	0.176	(-0.657, 1.010)	0.676	0.402	(-0.458, 1.262)	0.357	0.169	(-0.664, 1.002)	0.688	0.175	(-0.657, 1.008)	0.677	0.176	(-0.657, 1.009)	0.676	0.185	(-0.648, 1.018)	0.661	0.176	(-0.655, 1.008)	0.675	
Stroke subtype (lacunar)	1.033	(-1.499, 3.564)	0.421	1.024	(-1.508, 3.555)	0.425	1.082	(-1.448, 3.612)	0.399	0.704	(-1.926, 3.334)	0.597	1.027	(-1.502, 3.557)	0.423	1.033	(-1.497, 3.564)	0.420	1.021	(-1.509, 3.552)	0.426	1.018	(-1.507, 3.544)	0.426	
NIHSS	-0.213	(-1.342, 0.916)	0.709	-0.219	(-1.348, 0.910)	0.702	-0.211	(-1.340, 0.917)	0.712	-0.218	(-1.347, 0.910)	0.702	-0.340	(-1.513, 0.833)	0.567	-0.214	(-1.342, 0.915)	0.709	-0.212	(-1.341, 0.917)	0.711	-0.220	(-1.347, 0.906)	0.699	
Hypertension (yes)	2.821	(0.139, 5.504)	0.039	2.855	(0.172, 5.538)	0.037	2.811	(0.131, 5.492)	0.040	2.828	(0.146, 5.509)	0.039	2.824	(0.143, 5.504)	0.039	2.970	(0.162, 5.778)	0.038	2.834	(0.152, 5.515)	0.039	2.815	(0.139, 5.491)	0.039	
Smoker (yes)	-0.566	(-3.275, 2.143)	0.680	-0.552	(-3.261, 2.157)	0.687	-0.512	(-3.220, 2.196)	0.709	-0.554	(-3.261, 2.154)	0.686	-0.566	(-3.273, 2.141)	0.679	-0.560	(-3.268, 2.148)	0.683	-0.256	(-3.073, 2.562)	0.858	-0.573	(-3.276, 2.129)	0.675	
Years of education	1.284	(0.860, 1.708)	<0.001	1.285	(0.861, 1.709)	<0.001	1.289	(0.865, 1.713)	<0.001	1.287	(0.863, 1.711)	<0.001	1.286	(0.862, 1.710)	0.000	1.284	(0.860, 1.708)	<0.001	1.281	(0.857, 1.706)	<0.001	1.400	(0.958, 1.842)	<0.001	
Variable + Interactions																									
Age:Time	0.097	(-0.039, 0.233)	0.160																						
Sex:Time				0.847	(-1.760, 3.453)	0.521																			
Baseline Fazekas:Time							-0.123	(-1.004, 0.758)	0.782																
Stroke subtype:Time										1.454	(-1.238, 4.145)	0.287													
NIHSS:Time													-0.062	(-1.253, 1.130)	0.918										
Hypertension:Time																2.642	(-0.222, 5.506)	0.070							
Smoker:Time																					-0.957	(-3.836, 1.923)	0.512		
Years of education:Time																							1.165	(0.721, 1.608)	<0.001
1-3 years																									
Time	-2.107	(-4.706, 0.492)	0.111	-2.327	(-2.997, -1.657)	<0.001	-2.633	(-3.551, -1.716)	<0.001	-1.723	(-2.283, -1.164)	<0.001	-2.129	(-2.727, -1.531)	<0.001	-2.36	(-3.215, -1.505)	<0.001	-2.152	(-2.658, -1.646)	<0.001	-4.332	(-6.003, -2.661)	<0.001	
Age	0.098	(-0.061, 0.257)	0.223	0.095	(-0.048, 0.238)	0.191	0.094	(-0.049, 0.237)	0.193	0.095	(-0.048, 0.239)	0.191	0.095	(-0.048, 0.238)	0.188	0.095	(-0.048, 0.238)	0.191	0.094	(-0.049, 0.237)	0.193	0.101	(-0.042, 0.243)	0.165	
Sex (male)	1.504	(-1.098, 4.107)	0.254	1.214	(-1.866, 4.293)	0.436	1.502	(-1.100, 4.104)	0.255	1.531	(-1.081, 4.142)	0.248	1.509	(-1.093, 4.110)	0.252	1.501	(-1.101, 4.103)	0.255	1.496	(-1.106, 4.098)	0.257	1.502	(-1.096, 4.099)	0.254	
Baseline Fazekas	0.010	(-0.892, 0.913)	0.982	0.010	(-0.892, 0.912)	0.983	-0.242	(-1.281, 0.797)	0.644	-0.030	(-0.936, 0.876)	0.947	0.006	(-0.896, 0.909)	0.989	0.009	(-0.893, 0.912)	0.984	0.001	(-0.907, 0.904)	0.998	-0.023	(-0.924, 0.878)	0.961	
Stroke subtype (lacunar)	0.875	(-1.846, 3.596)	0.525	0.877	(-1.842, 3.596)	0.524	0.931	(-1.791, 3.653)	0.499	2.980	(-0.160, 6.119)	0.063	0.880	(-1.839, 3.599)	0.522	0.886	(-1.834, 3.607)	0.519	0.882	(-1.838, 3.601)	0.521	0.846	(-1.869, 3.561)	0.538	
NIHSS	0.034	(-1.163, 1.232)	0.955	0.032	(-1.165, 1.229)	0.958	0.028	(-1.169, 1.226)	0.963	0.035	(-1.167, 1.237)	0.954	0.213	(-1.166, 1.592)	0.760	0.031	(-1.166, 1.229)	0.959	0.037	(-1.161, 1.234)	0.952	0.041	(-1.155, 1.236)	0.946	
Hypertension (yes)	2.311	(-0.571, 5.192)	0.115	2.311	(-0.569, 5.191)	0.115	2.309	(-0.573, 5.190)	0.115	2.283	(-0.609, 5.174)	0.120	2.315	(-0.565, 5.195)	0.114	2.012	(-1.383, 5.406)	0.242	2.302	(-0.579, 5.183)	0.116	2.343	(-0.533, 5.218)	0.109	
Smoker (yes)	-1.610	(-4.546, 1.326)	0.279	-1.599	(-4.533, 1.335)	0.282	-1.559	(-4.495, 1.378)	0.295	-1.596	(-4.540, 1.349)	0.285	-1.598	(-4.532, 1.336)	0.282	-1.598	(-4.534, 1.337)	0.282	-1.051	(-4.446, 2.344)	0.540	-1.584	(-4.513, 1.345)	0.286	
Years of education	1.190	(0.754, 1.625)	<0.001	1.191	(0.756, 1.626)	<0.001	1.189	(0.754, 1.624)	<0.001	1.197	(0.760, 1.634)	<0.001	1.191	(0.756, 1.626)	<0.001	1.191	(0.756, 1.627)	<0.001	1.190	(0.755, 1.625)	<0.001	0.873	(0.375, 1.372)	0.001	
Variable + Interactions																									
Age:Time	0.0963	(-0.050, 0.243)	0.194																						
Sex:Time				1.3677	(-1.345, 4.081)	0.319																			
Baseline Fazekas:Time							-0.103	(-1.035, 0.828)	0.826																
Stroke subtype:Time										1.842	(-0.979, 4.663)	0.198													
NIHSS:Time													0.116	(-1.122, 1.354)	0.852										
Hypertension:Time																2.176	(-0.815, 5.168)	0.152							
Smoker:Time																					-1.369	(-4.393, 1.656)	0.371		
Years of education:Time																							1.046	(0.598, 1.495)	<0.001

Table S4. Full linear mixed effects models showing factors associated with changes in current ACE-R scores at each time-point.

	1-3 months and 1 year																										
	B	95% CI	p	B	95% CI	p	B	95% CI	p	B	95% CI	p	B	95% CI	p	B	95% CI	p	B	95% CI	p	B	95% CI	p			
Time	-2.191	(-7.337, 2.954)	0.401	-0.001	(-1.389, 1.387)	0.999	0.207	(1.597, 2.011)	0.820	-0.020	(-1.177, 1.137)	0.973	-0.536	(-1.683, 0.612)	0.357	0.073	(-1.601, 1.746)	0.932	0.595	(-0.452, 1.642)	0.263	-6.217	(-18.303, 5.869)	0.310	-2.157	(-5.616, 1.302)	0.219
Age	-0.239	(-0.345, -0.133)	<0.001	-0.223	(-0.323, -0.122)	<0.001	-0.223	(-0.323, -0.122)	<0.001	-0.222	(-0.323, -0.122)	0.000	-0.222	(-0.323, -0.122)	<0.011	-0.223	(-0.323, -0.122)	<0.001	-0.223	(-0.324, -0.122)	0.000	-0.224	(-0.324, -0.123)	0.000	-0.225	(-0.326, -0.125)	<0.001
Sex (male)	-0.202	(-2.085, 1.681)	0.832	-0.370	(-2.417, 1.677)	0.721	-0.216	(-2.104, 1.671)	0.821	-0.207	(-2.097, 1.683)	0.829	-0.176	(-2.068, 1.715)	0.854	-0.222	(-2.111, 1.666)	0.816	-0.187	(-2.078, 1.703)	0.845	-0.218	(-2.105, 1.669)	0.819	-0.222	(-2.107, 1.663)	0.816
Baseline Fazekas	-0.214	(-0.862, 0.435)	0.515	-0.221	(-0.870, 0.428)	0.502	-0.221	(-0.915, 0.473)	0.529	-0.225	(-0.876, 0.425)	0.494	-0.224	(-0.875, 0.427)	0.498	-0.221	(-0.871, 0.429)	0.502	-0.208	(-0.859, 0.443)	0.528	-0.202	(-0.853, 0.448)	0.539	-0.222	(-0.871, 0.427)	0.500
Stroke subtype (lacunar)	-0.107	(-2.061, 1.847)	0.914	-0.097	(-2.053, 1.860)	0.922	-0.099	(-2.058, 1.861)	0.921	-0.327	(-2.433, 1.778)	0.759	-0.105	(-2.068, 1.858)	0.916	-0.099	(-2.058, 1.860)	0.921	-0.112	(-2.074, 1.850)	0.910	-0.113	(-2.072, 1.845)	0.909	-0.094	(-2.050, 1.862)	0.925
NIHSS	-0.277	(-1.141, 0.587)	0.527	-0.272	(-1.138, 0.593)	0.534	-0.275	(-1.142, 0.591)	0.530	-0.279	(-1.146, 0.588)	0.525	-0.609	(-1.541, 0.323)	0.198	-0.275	(-1.141, 0.591)	0.530	-0.275	(-1.142, 0.593)	0.532	-0.280	(-1.146, 0.586)	0.523	-0.268	(-1.133, 0.597)	0.541
Hypertension (yes)	2.845	(0.762, 4.928)	0.008	2.826	(0.738, 4.915)	0.008	2.844	(0.755, 4.933)	0.008	2.856	(0.765, 4.947)	0.008	2.875	(0.783, 4.968)	0.007	2.761	(0.499, 5.033)	0.018	2.879	(0.787, 4.972)	0.007	2.878	(0.789, 4.967)	0.007	2.833	(0.747, 4.919)	0.008
Smoker (yes)	-0.159	(-2.243, 1.924)	0.880	-0.156	(-2.243, 1.930)	0.882	-0.151	(-2.240, 1.938)	0.887	-0.147	(-2.238, 1.944)	0.890	-0.164	(-2.257, 1.929)	0.877	-0.154	(-2.242, 1.935)	0.885	0.388	(-1.859, 2.635)	0.733	-0.141	(-2.229, 1.948)	0.894	-0.143	(-2.229, 1.943)	0.892
NART	0.320	(0.215, 0.425)	<0.001	0.321	(0.215, 0.426)	<0.001	0.319	(0.214, 0.426)	<0.001	0.317	(0.212, 0.423)	0.000	0.311	(0.206, 0.416)	<0.011	0.320	(0.214, 0.425)	<0.001	0.315	(0.209, 0.420)	0.000	0.290	(0.171, 0.408)	0.000	0.326	(0.220, 0.431)	<0.001
Years of education	0.506	(0.155, 0.856)	0.005	0.509	(0.158, 0.860)	0.005	0.511	(0.159, 0.863)	0.005	0.516	(0.164, 0.868)	0.004	0.526	(0.174, 0.878)	0.004	0.511	(-0.159, 0.862)	0.005	0.512	(0.160, 0.864)	0.005	0.519	(0.168, 0.871)	0.004	0.407	(0.026, 0.788)	0.037
Variable + Interactions																											
Age:Time	-0.202	(-0.311, -0.093)	<0.001																								
Sex:Time				-0.030	(-2.150, 2.090)	0.977																					
Baseline Fazekas:Time							-0.222	(-0.937, 0.494)	0.541																		
Stroke subtype:Time										0.191	(-1.995, 2.377)	0.863															
NIHSS:Time												0.115	(-0.840, 1.070)	0.812													
Hypertension:Time															2.943	(0.605, 5.280)	0.014										
Smoker:Time																		-0.835	(-3.165, 1.494)	0.479							
NART:Time																					0.345	(0.229, 0.461)	<0.001				
Years of education:Time																									0.603	(0.229, 0.977)	0.002
1-3 years																											
Time	5.771	(2.560, 8.981)	0.001	0.803	(-0.114, 1.720)	0.085	1.250	(0.018, 2.482)	0.047	<0.001	(-0.783, 0.783)	1.000	0.683	(-0.138, 1.504)	0.102	0.444	(-0.709, 1.598)	0.446	0.089	(-0.619, 0.796)	0.804	-3.704	(-11.427, 4.020)	0.343	1.019	(-1.312, 3.350)	0.387
Age	-0.054	(-0.196, 0.087)	0.447	-0.204	(-0.315, -0.093)	0.000	-0.203	(-0.314, -0.092)	0.000	-0.205	(-0.315, -0.094)	0.000	-0.202	(-0.313, -0.091)	0.000	-0.203	(-0.314, -0.093)	<0.001	-0.201	(-0.312, -0.091)	<0.001	-0.203	(-0.313, -0.093)	<0.001	-0.205	(-0.316, -0.095)	<0.001
Sex (male)	-0.136	(-2.160, 1.888)	0.894	1.016	(-1.928, 3.960)	0.495	-0.202	(-2.209, 1.805)	0.842	-0.230	(-2.237, 1.776)	0.820	-0.192	(-2.199, 1.815)	0.850	-0.205	(-2.212, 1.802)	0.839	-0.167	(-2.175, 1.841)	0.869	-0.232	(-2.230, 1.765)	0.818	-0.210	(-2.215, 1.795)	0.836
Baseline Fazekas	-0.609	(-1.312, 0.094)	0.089	-0.639	(-1.340, 0.061)	0.073	-0.123	(-1.088, 0.842)	0.801	-0.610	(-1.308, 0.088)	0.086	-0.647	(-1.345, 0.051)	0.069	-0.641	(-1.338, 0.057)	0.071	-0.615	(-1.313, 0.083)	0.084	-0.653	(-1.348, 0.041)	0.065	-0.633	(-1.330, 0.065)	0.075
Stroke subtype (lacunar)	0.776	(-1.336, 2.889)	0.467	0.916	(-1.186, 3.018)	0.389	0.818	(-1.278, 2.914)	0.440	-1.008	(-3.990, 1.974)	0.504	0.912	(-1.181, 3.005)	0.389	0.910	(-1.184, 3.004)	0.390	0.919	(-1.174, 3.013)	0.385	0.913	(-1.169, 2.996)	0.386	0.915	(-1.176, 3.006)	0.387
NIHSS	-0.177	(-1.097, 0.744)	0.704	-0.203	(-1.118, 0.712)	0.660	-0.198	(-1.109, 0.713)	0.667	-0.207	(-1.118, 0.703)	0.652	0.227	(-1.063, 1.517)	0.727	-0.209	(-1.120, 0.702)	0.650	-0.218	(-1.129, 0.694)	0.636	-0.205	(-1.111, 0.701)	0.654	-0.210	(-1.120, 0.700)	0.648
Hypertension (yes)	2.404	(0.153, 4.654)	0.037	2.356	(0.114, 1.720)	0.040	2.359	(0.127, 4.591)	0.039	2.368	(0.136, 4.599)	0.038	2.373	(0.140, 4.605)	0.037	2.378	(-0.875, 5.632)	0.150	2.398	(0.165, 4.631)	0.036	2.356	(0.135, 4.577)	0.038	2.343	(0.111, 4.574)	0.040
Smoker (yes)	0.553	(-1.745, 2.852)	0.634	0.697	(-1.593, 2.988)	0.547	0.654	(-1.628, 2.937)	0.571	0.745	(-1.534, 3.025)	0.518	0.746	(-1.535, 3.027)	0.518	0.737	(-1.545, 3.019)	0.523	-1.491	(-4.670, 1.689)	0.354	0.749	(-1.521, 3.020)	0.514	0.738	(-1.541, 3.017)	0.522
NART	0.430	(0.312, 0.548)	<0.001	0.443	(0.324, 0.562)	0.000	0.446	(0.327, 0.564)	0.000	0.451	(0.333, 0.570)	<0.001	0.442	(0.323, 0.560)	0.000	0.444	(0.326, 0.563)	<0.001	0.442	(0.324, 0.561)	<0.001	0.380	(0.211, 0.549)	<0.001	0.448	(0.329, 0.567)	<0.001
Years of education	0.455	(0.090, 0.820)	0.015	0.464	(0.100, 0.828)	0.013	0.465	(0.103, 0.828)	0.012	0.450	(0.088, 0.813)	0.015	0.469	(0.106, 0.831)	0.012	0.465	(0.102, 0.827)	0.013	0.468	(0.106, 0.831)	0.012	0.456	(0.096, 0.817)	0.014	0.548	(0.064, 1.032)	0.027
Variable + Interactions																											
Age:Time	-0.137	(-0.255, -0.019)	0.024																								
Sex:Time				0.370	(-1.882, 2.622)	0.745																					
Baseline Fazekas:Time							-0.407	(-1.167, 0.353)	0.291																		
Stroke subtype:Time										0.022	(-2.291, 2.335)	0.985															
NIHSS:Time												-0.005	(-1.011, 1.000)	0.992													
Hypertension:Time															2.367	(-0.108, 4.843)	0.061										
Smoker:Time																		-0.226	(-2.697, 2.245)	0.856							
NART:Time																					0.416	(0.286, 0.546)	<0.001				
Years of education:Time																									0.501	(0.113, 0.888)	0.012