

eTable 1 Basic characteristics of 6,651 participants at study entry.

Variables	N/P ₅₀	%IQR	aMCI (5325)		naMCI (1326)	
			N/P ₅₀	%IQR	N/P ₅₀	%IQR
MCI types						
aMCI	5325	80.06				
naMCI	1326	19.94				
Sex						
Male	3354	50.43	2733	51.32	621	46.83
Female	3297	49.57	2592	48.68	705	53.17
Age (years)	73.83	12	74.33	11.83	71.83	11.66
Educational attainment (years)	16	5	16	5	16	6
Marital status						
Married	4523	68.00	3654	68.62	869	65.54
Single	2128	32.00	1671	31.38	457	34.46
Living situation						
Living alone	1619	24.34	1275	23.94	344	25.94
Living with others	5032	75.66	4050	76.06	982	74.06
Independence level						
Able to live independently	5119	76.97	4071	76.45	1047	78.96
Requiring some assistance with complex activities	1379	20.73	1140	21.41	239	18.02
Requiring some assistance with basic activities	147	2.21	112	2.10	35	2.64
Completely dependent	7	0.11	2	0.04	5	0.38
Handedness						
Left-handed	551	8.28	439	8.24	112	8.45
Right-handed	5955	89.54	4771	89.60	1184	89.29
Ambidextrous	145	2.18	115	2.16	30	2.26
APOE ε4 status						
Presence	2909	43.74	2422	45.48	487	36.73
Absence	3742	56.26	2903	54.52	839	63.27
BMI	27.11	5.02	26.29	5.93	27.06	6.37
Corrected vision						
Normal	6292	94.60	5038	94.61	1254	94.57
Abnormal	359	5.40	287	5.39	72	5.43
Corrected hearing						
Normal	5861	88.12	4692	88.11	1169	88.16
Abnormal	790	11.88	633	11.89	157	11.84
MMSE	27	4	27	4	28	4
CDR	0.5	0	0.5	0	0.5	0.5
FAQ	2	6	2	6	2	6
GDS	2	2	2	2	2	3
NPI-Q	1	4	1	4	2	4

Abbreviation: P₅₀ = median; IQR = interquartile range; MCI = mild cognitive impairment; aMCI = amnesic mild cognitive impairment; naMCI = non-amnesic mild cognitive impairment; BMI = body mass index; MMSE = Mini-Mental State Examination; CDR = Clinical Dementia Rating; FAQ = Functional Activities Questionnaire; GDS = Geriatric Depression Scale; NPI-Q = Neuropsychiatric Inventory Questionnaire.

eTable 2 Number and percentage of observed state transitions after the stratification based on MCI subtype at baseline in the merging scenario. [n(%)]

Baseline diagnosis	From To		<MCI	MCI	Dementia
			aMCI	<MCI	1783 (77.86)
	MCI	1265 (10.99)	7910 (68.74)	2332 (20.27)	
naMCI	<MCI	814 (80.59)	177 (17.52)	19 (1.88)	
	MCI	520 (18.83)	1845 (67.80)	397 (14.37)	

Abbreviation: MCI = mild cognitive impairment; <MCI = no impairment or any impairment falling below the MCI criteria threshold; aMCI = amnesic MCI; naMCI = non-amnesic MCI.

eTable 3 Estimated total length of stay over 15 years in the multivariate Markov model after the stratification based on MCI subtype at baseline in the merging scenario.

Years	aMCI						naMCI					
	Total time (years)			Percentage (%)			Total time (years)			Percentage (%)		
	<MCI	MCI	Dementia	<MCI	MCI	Dementia	<MCI	MCI	Dementia	<MCI	MCI	Dementia
Year 1	0.850	0.143	0.007	84.98	14.33	0.69	0.886	0.110	0.004	88.62	11.03	0.35
Year 2	1.473	0.479	0.048	73.66	23.93	2.42	1.604	0.372	0.024	80.18	18.61	1.22
Year 3	1.949	0.908	0.143	64.97	30.26	4.77	2.213	0.715	0.073	73.75	23.82	2.43
Year 4	2.326	1.374	0.301	58.15	34.34	7.51	2.750	1.096	0.154	68.74	27.41	3.86
Year 5	2.635	1.843	0.523	52.69	36.86	10.45	3.236	1.493	0.271	64.72	29.87	5.41
Year 6	2.894	2.297	0.808	48.24	38.29	13.47	3.685	1.892	0.423	61.42	31.53	7.05
Year 7	3.118	2.727	1.155	44.54	38.96	16.50	4.105	2.284	0.611	58.65	32.62	8.73
Year 8	3.313	3.128	1.560	41.41	39.09	19.50	4.501	2.665	0.834	56.27	33.31	10.43
Year 9	3.485	3.498	2.017	38.73	38.86	22.41	4.877	3.033	1.091	54.18	33.70	12.12
Year 10	3.639	3.837	2.523	36.39	38.37	25.23	5.233	3.387	1.380	52.33	33.87	13.80
Year 11	3.777	4.148	3.075	34.34	37.71	27.95	5.573	3.727	1.700	50.66	33.88	15.46
Year 12	3.901	4.432	3.667	32.51	36.93	30.56	5.897	4.053	2.050	49.14	33.77	17.09
Year 13	4.013	4.690	4.297	30.87	36.08	33.05	6.206	4.364	2.429	47.74	33.57	18.69
Year 14	4.115	4.925	4.960	29.39	35.18	35.43	6.502	4.662	2.836	46.44	33.30	20.26
Year 15	4.206	5.139	5.655	28.04	34.26	37.70	6.784	4.947	3.269	45.23	32.98	21.79

Abbreviation: MCI = mild cognitive impairment; <MCI = no impairment or any impairment falling below the MCI criteria threshold; aMCI = amnesic MCI; naMCI = non-amnesic MCI.

eTable 4 Estimated transition probabilities and their 95% CIs in the multivariate Markov model after the stratification based on MCI subtype at baseline in the merging scenario. The incorporated covariates for aMCI participants are sex, age, marital status, living situation, independence level, BMI, APOE ε4 status, MMSE, CDR, FAQ, GDS, and NPI-Q. The incorporated covariates for naMCI participants are sex, age, educational attainment, marital status, living situation, independence level, BMI, MMSE, CDR, FAQ, GDS, and NPI-Q.

Baseline diagnosis	Years	<MCI→<MCI	<MCI→MCI	<MCI→Dementia	MCI→<MCI	MCI→MCI	MCI→Dementia
aMCI	Year 1	0.720 (0.694, 0.747)	0.260 (0.236, 0.284)	0.020 (0.018, 0.022)	0.080 (0.075, 0.085)	0.797 (0.789, 0.804)	0.123 (0.118, 0.129)
	Year 2	0.540 (0.499, 0.575)	0.395 (0.365, 0.428)	0.066 (0.060, 0.073)	0.121 (0.113, 0.130)	0.656 (0.644, 0.667)	0.223 (0.214, 0.233)
	Year 3	0.420 (0.377, 0.459)	0.455 (0.426, 0.488)	0.125 (0.114, 0.138)	0.140 (0.130, 0.150)	0.554 (0.541, 0.566)	0.306 (0.294, 0.318)
	Year 4	0.339 (0.302, 0.377)	0.472 (0.447, 0.496)	0.190 (0.173, 0.207)	0.145 (0.134, 0.156)	0.478 (0.464, 0.492)	0.377 (0.362, 0.392)
	Year 5	0.282 (0.247, 0.316)	0.464 (0.444, 0.484)	0.254 (0.236, 0.273)	0.143 (0.132, 0.154)	0.419 (0.402, 0.435)	0.439 (0.424, 0.455)
	Year 6	0.240 (0.211, 0.271)	0.443 (0.427, 0.458)	0.317 (0.296, 0.339)	0.136 (0.125, 0.148)	0.371 (0.356, 0.385)	0.493 (0.476, 0.511)
	Year 7	0.208 (0.185, 0.238)	0.416 (0.402, 0.429)	0.376 (0.352, 0.398)	0.128 (0.116, 0.140)	0.331 (0.316, 0.345)	0.541 (0.524, 0.559)
	Year 8	0.183 (0.159, 0.209)	0.385 (0.372, 0.398)	0.432 (0.407, 0.455)	0.118 (0.106, 0.130)	0.297 (0.282, 0.312)	0.585 (0.567, 0.603)
	Year 9	0.163 (0.141, 0.188)	0.355 (0.342, 0.367)	0.483 (0.455, 0.507)	0.109 (0.098, 0.122)	0.268 (0.254, 0.281)	0.624 (0.605, 0.642)
	Year 10	0.145 (0.125, 0.168)	0.325 (0.312, 0.339)	0.530 (0.503, 0.556)	0.100 (0.089, 0.112)	0.242 (0.228, 0.257)	0.659 (0.639, 0.678)
	Year 11	0.131 (0.114, 0.152)	0.297 (0.284, 0.310)	0.572 (0.545, 0.597)	0.091 (0.081, 0.104)	0.219 (0.205, 0.232)	0.690 (0.672, 0.708)
	Year 12	0.118 (0.101, 0.137)	0.271 (0.257, 0.283)	0.612 (0.585, 0.637)	0.083 (0.073, 0.094)	0.198 (0.185, 0.211)	0.719 (0.702, 0.737)
	Year 13	0.107 (0.092, 0.124)	0.246 (0.233, 0.258)	0.647 (0.623, 0.671)	0.076 (0.067, 0.085)	0.179 (0.167, 0.191)	0.745 (0.728, 0.763)
	Year 14	0.096 (0.082, 0.114)	0.224 (0.210, 0.237)	0.680 (0.654, 0.703)	0.069 (0.060, 0.079)	0.163 (0.150, 0.175)	0.769 (0.752, 0.787)
	Year 15	0.087 (0.075, 0.103)	0.204 (0.190, 0.218)	0.709 (0.683, 0.733)	0.063 (0.054, 0.072)	0.148 (0.136, 0.160)	0.790 (0.773, 0.807)
naMCI	Year 1	0.789 (0.758, 0.817)	0.201 (0.175, 0.230)	0.010 (0.008, 0.012)	0.165 (0.151, 0.180)	0.757 (0.741, 0.773)	0.078 (0.069, 0.089)
	Year 2	0.656 (0.610, 0.697)	0.311 (0.275, 0.352)	0.034 (0.028, 0.040)	0.255 (0.236, 0.275)	0.606 (0.583, 0.629)	0.139 (0.123, 0.156)
	Year 3	0.568 (0.523, 0.609)	0.367 (0.334, 0.405)	0.064 (0.054, 0.076)	0.301 (0.279, 0.323)	0.510 (0.486, 0.534)	0.189 (0.169, 0.213)
	Year 4	0.509 (0.463, 0.554)	0.392 (0.357, 0.429)	0.099 (0.084, 0.115)	0.322 (0.296, 0.346)	0.447 (0.420, 0.474)	0.232 (0.205, 0.260)
	Year 5	0.466 (0.418, 0.515)	0.399 (0.363, 0.435)	0.134 (0.116, 0.160)	0.327 (0.297, 0.356)	0.403 (0.373, 0.433)	0.270 (0.243, 0.304)
	Year 6	0.434 (0.391, 0.478)	0.396 (0.366, 0.427)	0.170 (0.148, 0.197)	0.325 (0.295, 0.353)	0.371 (0.341, 0.399)	0.305 (0.274, 0.340)

Year 7	0.407 (0.365, 0.450)	0.387 (0.358, 0.415)	0.206 (0.179, 0.235)	0.317 (0.287, 0.347)	0.346 (0.316, 0.375)	0.337 (0.302, 0.373)
Year 8	0.385 (0.344, 0.431)	0.375 (0.347, 0.401)	0.240 (0.210, 0.273)	0.307 (0.276, 0.341)	0.326 (0.296, 0.352)	0.367 (0.332, 0.409)
Year 9	0.366 (0.324, 0.409)	0.361 (0.335, 0.388)	0.273 (0.239, 0.309)	0.296 (0.264, 0.328)	0.308 (0.279, 0.338)	0.396 (0.356, 0.435)
Year 10	0.348 (0.308, 0.389)	0.347 (0.322, 0.373)	0.305 (0.269, 0.344)	0.284 (0.252, 0.316)	0.293 (0.266, 0.321)	0.423 (0.382, 0.463)
Year 11	0.332 (0.293, 0.375)	0.333 (0.308, 0.357)	0.336 (0.296, 0.378)	0.273 (0.241, 0.308)	0.279 (0.253, 0.306)	0.449 (0.405, 0.490)
Year 12	0.317 (0.278, 0.358)	0.319 (0.294, 0.342)	0.365 (0.322, 0.408)	0.261 (0.229, 0.294)	0.266 (0.240, 0.293)	0.473 (0.429, 0.517)
Year 13	0.302 (0.261, 0.344)	0.305 (0.281, 0.331)	0.393 (0.350, 0.441)	0.250 (0.217, 0.284)	0.254 (0.227, 0.282)	0.496 (0.449, 0.540)
Year 14	0.289 (0.246, 0.331)	0.292 (0.264, 0.318)	0.420 (0.373, 0.467)	0.239 (0.205, 0.272)	0.242 (0.214, 0.272)	0.519 (0.472, 0.566)
Year 15	0.276 (0.236, 0.317)	0.279 (0.252, 0.302)	0.445 (0.396, 0.499)	0.228 (0.195, 0.262)	0.232 (0.205, 0.258)	0.540 (0.491, 0.593)

eTable 5 Estimated HRs and their 95% CIs in the multivariate Markov model after the stratification based on MCI subtype at baseline in the merging scenario.

Baseline diagnosis	Covariates	HR		
		<MCI→MCI	MCI→<MCI	MCI→Dementia
aMCI	Sex (male)	0.853 (0.695, 1.047)	1.059 (0.930, 1.207)	1.063 (0.973, 1.161)
	Age	1.026 (1.015, 1.038) ^a	0.979 (0.972, 0.986) ^a	1.012 (1.007, 1.017) ^a
	Marital status (single)	1.210 (0.890, 1.646)	1.039 (0.849, 1.272)	0.743 (0.645, 0.857) ^a
	Living situation (living with others)	0.901 (0.658, 1.234)	0.975 (0.787, 1.207)	0.864 (0.742, 1.005)
	Independence level	1.275 (1.012, 1.607) ^a	0.629 (0.514, 0.769) ^a	1.256 (1.164, 1.356) ^a
	<i>APOE</i> ε4 (absence)	0.862 (0.710, 1.047)	1.460 (1.279, 1.668) ^a	0.734 (0.676, 0.798) ^a
	BMI	0.981 (0.962, 1.001)	1.001 (0.989, 1.013)	0.974 (0.965, 0.983) ^a
	MMSE	0.972 (0.938, 1.007)	1.129 (1.098, 1.160) ^a	0.940 (0.928, 0.951) ^a
	CDR	2.378 (1.611, 3.510) ^a	0.250 (0.181, 0.347) ^a	1.390 (1.093, 1.767) ^a
	FAQ	1.005 (0.976, 1.035)	0.894 (0.872, 0.917) ^a	1.067 (1.058, 1.076) ^a
	GDS	1.035 (0.999, 1.072)	1.033 (1.007, 1.060) ^a	1.020 (1.004, 1.036) ^a
	NPI-Q	0.995 (0.958, 1.033)	0.987 (0.962, 1.012)	1.018 (1.006, 1.031) ^a
	Sex (male)	0.832 (0.584, 1.186)	0.871 (0.698, 1.087)	1.037 (0.833, 1.289)
	Age	1.011 (0.992, 1.030)	0.990 (0.979, 1.001)	1.003 (0.993, 1.012)
naMCI	Educational attainment (years)	0.973 (0.931, 1.016)	0.974 (0.945, 1.004)	1.046 (1.017, 1.076) ^a
	Marital status (single)	1.810 (1.077, 3.042) ^a	1.170 (0.836, 1.639)	0.822 (0.585, 1.153)
	Living situation (living with others)	1.404 (0.857, 2.299)	1.021 (0.724, 1.440)	1.096 (0.720, 1.599)
	Independence level	1.283 (0.883, 1.866)	1.035 (0.786, 1.362)	1.279 (1.069, 1.531) ^a
	BMI	1.002 (0.973, 1.032)	1.007 (0.990, 1.024)	0.967 (0.948, 0.987) ^a
	MMSE	0.997 (0.948, 1.049)	1.089 (1.048, 1.132) ^a	0.928 (0.904, 0.952) ^a
	CDR	2.067 (1.156, 3.695) ^a	0.346 (0.230, 0.520) ^a	2.972 (1.827, 4.834) ^a
	FAQ	1.016 (0.968, 1.065)	0.938 (0.906, 0.970) ^a	1.051 (1.029, 1.073) ^a
	GDS	1.045 (0.976, 1.120)	0.969 (0.926, 1.014)	1.018 (0.983, 1.054)
	NPI-Q	0.981 (0.916, 1.051)	0.996 (0.959, 1.034)	1.016 (0.989, 1.044)

Abbreviation: MCI = mild cognitive impairment; <MCI = no impairment or any impairment falling below the MCI criteria threshold; aMCI = amnesic MCI; naMCI = non-amnesic MCI; BMI = body mass index; MMSE = Mini-Mental State Examination; CDR = Clinical Dementia Rating; FAQ = Functional Activities Questionnaire; GDS = Geriatric Depression Scale; NPI-Q = Neuropsychiatric Inventory Questionnaire; HR = hazard ratio; CI = confidence intervals.

^a Statistically significant results.

eTable 6 Number and percentage of observed state transitions for the post-reversion in the merging scenario. [n(%)]

From To	<MCI	MCI	Dementia
<MCI	2595 (78.71)	629 (19.08)	73 (2.21)
MCI	207 (24.41)	562 (66.27)	79 (9.32)

Abbreviation: MCI = mild cognitive impairment; <MCI = no impairment or any impairment falling below the MCI criteria threshold.

eTable 7 Estimated total length of stay for post-reversion over 15 years in the merging scenario.

Years	Total time (years)			Percentage (%)		
	<MCI	MCI	Dementia	<MCI	MCI	Dementia
Year 1	0.88	0.117	0.003	88.00	11.70	0.30
Year 2	1.612	0.368	0.02	80.60	18.40	1.00
Year 3	2.271	0.671	0.058	75.70	22.37	1.93
Year 4	2.889	0.992	0.118	72.23	24.80	2.95
Year 5	3.482	1.315	0.202	69.64	26.30	4.04
Year 6	4.056	1.634	0.31	67.60	27.23	5.17
Year 7	4.612	1.947	0.44	65.89	27.81	6.29
Year 8	5.154	2.253	0.593	64.43	28.16	7.41
Year 9	5.681	2.551	0.768	63.12	28.34	8.53
Year 10	6.194	2.841	0.965	61.94	28.41	9.65
Year 11	6.694	3.124	1.182	60.85	28.40	10.75
Year 12	7.181	3.399	1.42	59.84	28.33	11.83
Year 13	7.655	3.668	1.677	58.88	28.22	12.90
Year 14	8.117	3.929	1.954	57.98	28.06	13.96
Year 15	8.566	4.184	2.25	57.11	27.89	15.00

Abbreviation: MCI = mild cognitive impairment; <MCI = no impairment or any impairment falling below the MCI criteria threshold.

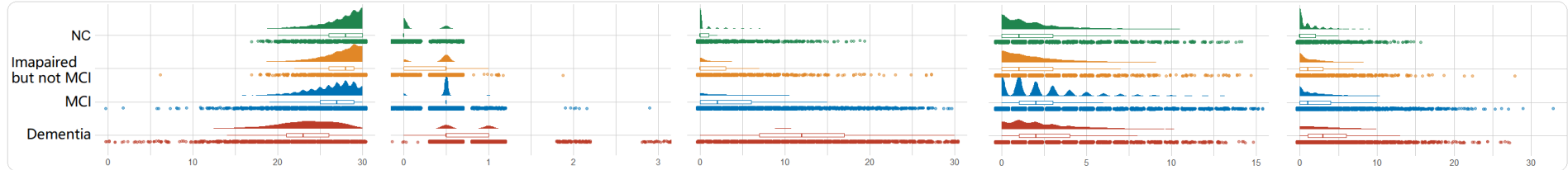
eTable 8 Estimated transition probabilities and their 95% CIs over 15 years for the post-reversion in the merging scenario.

Years	<MCI→<MCI	<MCI→MCI	<MCI→Dementia	MCI→<MCI	MCI→MCI	MCI→Dementia
Year 1	0.788 (0.772, 0.803)	0.204 (0.189, 0.219)	0.009 (0.007, 0.011)	0.329 (0.287, 0.372)	0.614 (0.572, 0.655)	0.057 (0.044, 0.073)
Year 2	0.687 (0.668, 0.706)	0.286 (0.267, 0.305)	0.027 (0.021, 0.034)	0.461 (0.418, 0.507)	0.444 (0.402, 0.482)	0.095 (0.073, 0.121)
Year 3	0.636 (0.612, 0.657)	0.316 (0.294, 0.337)	0.049 (0.037, 0.063)	0.510 (0.465, 0.550)	0.367 (0.332, 0.404)	0.124 (0.096, 0.161)
Year 4	0.604 (0.576, 0.629)	0.323 (0.298, 0.348)	0.072 (0.057, 0.095)	0.522 (0.480, 0.559)	0.329 (0.296, 0.361)	0.149 (0.116, 0.193)
Year 5	0.582 (0.556, 0.612)	0.322 (0.295, 0.345)	0.096 (0.076, 0.120)	0.519 (0.482, 0.558)	0.308 (0.278, 0.336)	0.172 (0.136, 0.215)
Year 6	0.565 (0.534, 0.596)	0.316 (0.291, 0.341)	0.119 (0.094, 0.152)	0.511 (0.468, 0.550)	0.295 (0.267, 0.322)	0.194 (0.152, 0.246)
Year 7	0.549 (0.514, 0.579)	0.309 (0.284, 0.335)	0.142 (0.112, 0.180)	0.499 (0.456, 0.537)	0.285 (0.256, 0.314)	0.215 (0.169, 0.274)
Year 8	0.534 (0.498, 0.566)	0.302 (0.275, 0.327)	0.164 (0.131, 0.206)	0.487 (0.442, 0.525)	0.277 (0.248, 0.304)	0.236 (0.188, 0.296)
Year 9	0.520 (0.482, 0.555)	0.294 (0.265, 0.321)	0.186 (0.147, 0.231)	0.475 (0.429, 0.517)	0.269 (0.238, 0.298)	0.256 (0.205, 0.318)
Year 10	0.506 (0.466, 0.545)	0.287 (0.258, 0.313)	0.207 (0.162, 0.259)	0.463 (0.415, 0.508)	0.262 (0.233, 0.291)	0.275 (0.216, 0.342)
Year 11	0.493 (0.452, 0.536)	0.279 (0.253, 0.305)	0.228 (0.178, 0.283)	0.451 (0.401, 0.500)	0.255 (0.227, 0.284)	0.294 (0.229, 0.364)
Year 12	0.480 (0.437, 0.522)	0.272 (0.242, 0.299)	0.248 (0.197, 0.314)	0.439 (0.387, 0.488)	0.249 (0.215, 0.277)	0.312 (0.251, 0.392)
Year 13	0.468 (0.421, 0.511)	0.265 (0.239, 0.293)	0.267 (0.213, 0.330)	0.428 (0.373, 0.477)	0.242 (0.213, 0.272)	0.330 (0.265, 0.406)
Year 14	0.456 (0.406, 0.498)	0.258 (0.229, 0.288)	0.287 (0.228, 0.355)	0.417 (0.359, 0.465)	0.236 (0.204, 0.267)	0.348 (0.279, 0.430)
Year 15	0.444 (0.392, 0.488)	0.251 (0.219, 0.281)	0.305 (0.245, 0.380)	0.406 (0.350, 0.454)	0.230 (0.194, 0.261)	0.365 (0.296, 0.452)

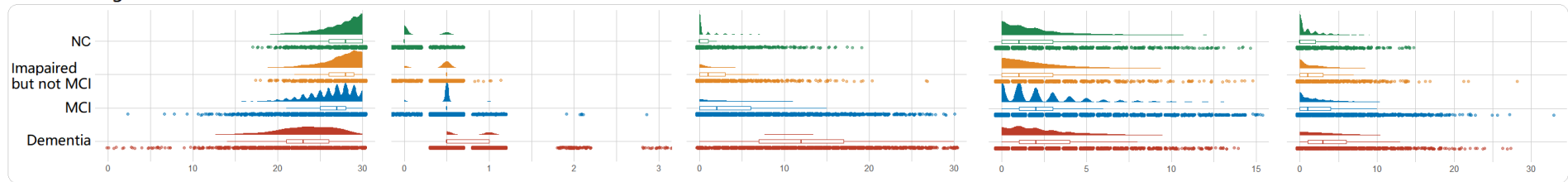
Abbreviation: MCI = mild cognitive impairment; <MCI = no impairment or any impairment falling below the MCI criteria threshold; CI = confidence intervals.

eFigure 1 The raincloud plot of the clinical assessments of four cognitive states, including NC; “impaired but not MCI”; MCI; dementia. The different rows referred to the clinical assessment of participants with baseline diagnosis of MCI, aMCI, and naMCI, respectively. The different columns referred to the clinical assessment scores of participants, including MMSE, CDR, FAQ, GDS and NPI-Q.

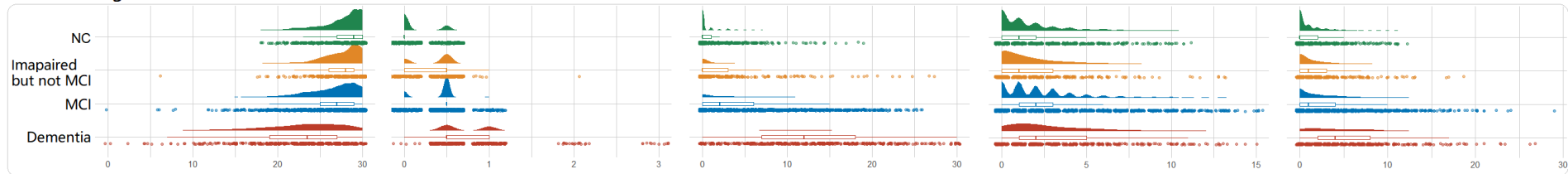
A Baseline diagnosis: MCI



B Baseline diagnosis: aMCI



C Baseline diagnosis: naMCI



MMSE

CDR

FAQ

GDS

NPI-Q

Abbreviation: NC = normal cognition; MCI = mild cognitive impairment; aMCI = amnesic MCI; naMCI = non-amnesic MCI; MMSE = Mini-Mental State Examination; CDR = Clinical Dementia Rating; FAQ = Functional Activities Questionnaire; GDS = the 15-item Geriatric Depression Scale; NPI-Q = Neuropsychiatric Inventory Questionnaire.

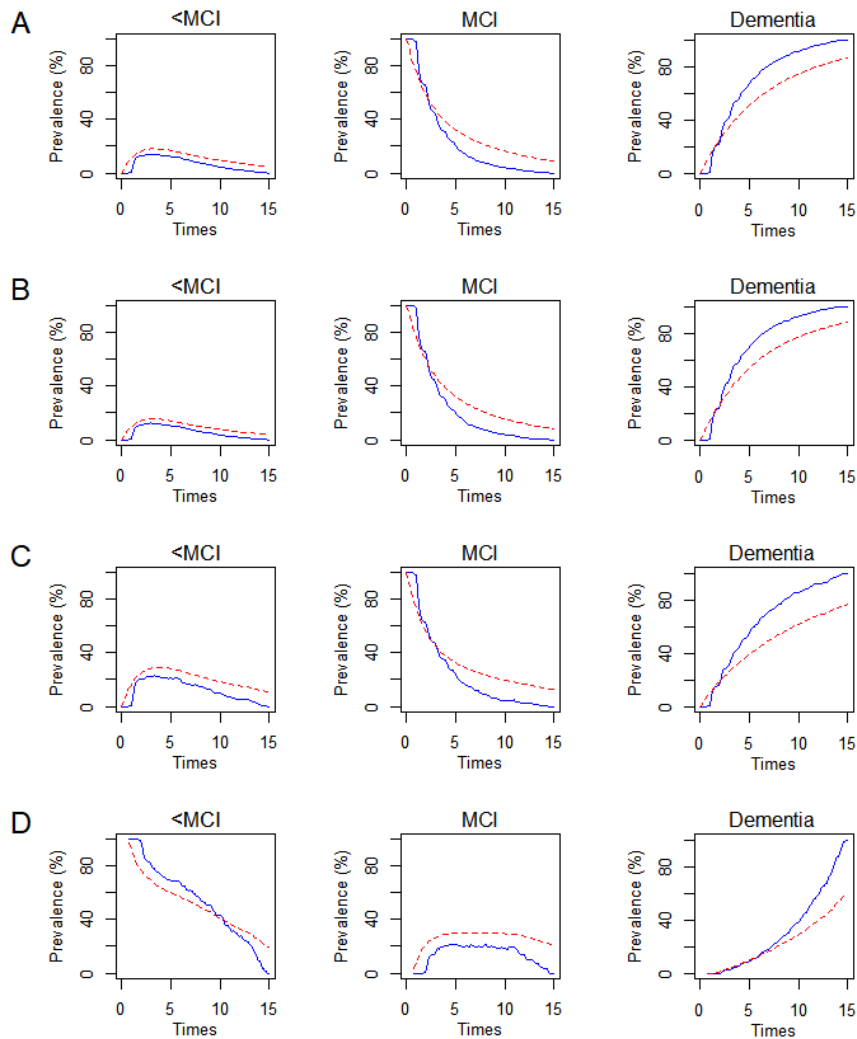
eFigure 2 Observed (solid line) and simulated (dotted line) prevalence transition of each state. The figure demonstrates the observed and simulated prevalence transition of each state from four multi-state Markov models constructed in this study:

Figure 6 (A): bidirectional transitions of subjects with an MCI diagnosis at baseline;

Figure 6 (B): bidirectional transitions of subjects with an aMCI diagnosis at baseline;

Figure 6 (C): bidirectional transitions of subjects with an naMCI diagnosis at baseline;

Figure 6 (D): transitions of the post-reversion.



Abbreviation: MCI = mild cognitive impairment; <MCI = no impairment or any impairment falling below the MCI criteria threshold.