

Supplementary table 1. Prediction of clinically relevant reduction in SDMT during 5 years from baseline (31 cases, 35 non-cases)

Baseline predictor	Univariable				Multivariable					
	OR (95% CI)	p	C	R ² (%)	OR (95% CI)	p	C	R ² (%)	ΔC	ΔR ²
					<i>Best model clin/dem</i>					
Age	1.45 (0.85, 2.45)	0.17	0.60	3.9						
Sex (female)	0.63 (0.23, 1.77)	0.39	0.55	1.5						
Center (SUS)	6.07 (2.08, 17.66)	0.001	0.71	22.3	8.71 (2.55, 29.78)	0.001	0.81	36.9		
Education (high)	0.78 (0.28, 2.23)	0.65	0.53	0.4						
Log disease duration	1.62 (0.82, 3.19)	0.16	0.60	4.0	2.03 (0.91, 4.53)	0.083				
MS type progressive	1.41 (0.42, 4.76)	0.58	0.53	0.6						
EDSS	1.62 (1.06, 2.47)	0.026	0.64	10.9	1.72 (1.03, 2.88)	0.037				
SDMT	1.00 (0.97, 1.04)	0.90	0.51	0.0						
					<i>When added to best model clin/dem</i>					
Whole brain	0.989 (0.981, 0.996)	0.003	0.72	21.0	0.993 (0.984, 1.002)	0.11	0.83	40.9	0.02	4.0
Grey matter	0.987 (0.977, 0.998)	0.015	0.67	13.0	0.991 (0.978, 1.004)	0.17	0.82	39.9	0.01	3.0
White matter	0.980 (0.966, 0.994)	0.006	0.70	18.5	0.989 (0.972, 1.006)	0.20	0.82	39.4	0.01	2.5
Ventricular	1.00 (0.98, 1.03)	0.80	0.51	0.1	1.01 (0.98, 1.05)	0.40	0.81	38.0	0.00	1.1
Cortical	0.980 (0.967, 0.994)	0.004	0.70	19.6	0.988 (0.973, 1.004)	0.14	0.83	40.3	0.02	3.4
T2 LV	1.05 (1.00, 1.10)	0.032	0.67	10.0	1.07 (1.00, 1.14)	0.043	0.84	43.5	0.03	6.6
T1 LV	1.10 (1.01, 1.21)	0.037	0.70	10.4	1.11 (0.98, 1.26)	0.10	0.83	41.4	0.02	4.5
Subcortical	0.94 (0.86, 1.03)	0.19	0.59	3.6	0.99 (0.88, 1.12)	0.88	0.80	37.0	-0.01	0.1
Caudate	0.89 (0.53, 1.51)	0.67	0.56	0.4	1.35 (0.69, 2.64)	0.38	0.81	38.1	0.00	1.2
Putamen	0.87 (0.59, 1.27)	0.47	0.53	1.1	0.97 (0.58, 1.62)	0.90	0.80	37.0	-0.01	0.1
Thalamus	0.76 (0.57, 1.01)	0.059	0.65	7.5	0.88 (0.62, 1.26)	0.49	0.81	37.6	0.00	0.7
Pallidus	1.10 (0.38, 3.19)	0.86	0.50	0.1	1.46 (0.38, 5.62)	0.59	0.81	37.4	0.00	0.5
Hippocampus	0.77 (0.49, 1.21)	0.26	0.57	2.7	0.93 (0.54, 1.62)	0.81	0.80	37.0	-0.01	0.1
Amygdala	0.29 (0.09, 0.95)	0.040	0.63	9.2	0.75 (0.18, 3.07)	0.69	0.81	37.2	0.00	0.3

Legend: MS = Multiple Sclerosis (progressive=primary and secondary progressive combined); EDSS = Expanded Disability Status Scale; SDMT = Symbol Digit Modalities Test; LV = Lesion Volume; OR = Odds Ratio; CI = Confidence Interval.

Effect estimates from logistic regression analysis with reduction in SDMT greater than 4 points during 5 years (yes/no) as outcome, and baseline variables as predictors. An OR>1 means that a higher value of the predictor is associated with a greater odds of having a clinically significant decline in CPS. Predictive power of each model is estimated by the concordance index (C) and by Nagelkerke R², and the contribution of each predictor by the change in these statistics (ΔC and ΔR², respectively). Bold values denotes statistical significance at the p< 0.05 level.

Supplementary table 2. Prediction of clinically relevant reduction in SDMT during 10 years from baseline (13 cases, 37 non-cases)

Predictor	Univariable			
	OR (95% CI)	p	C	R ² (%)
Age	1.24 (0.61, 2.50)	0.55	0.55	1.1
Sex (female)	0.44 (0.11, 1.73)	0.24	0.58	3.9
Center (SUS)	1.69 (0.44, 6.39)	0.44	0.56	1.7
Education (high)	1.30 (0.35, 4.84)	0.69	0.53	0.5
Log disease duration	1.11 (0.48, 2.59)	0.80	0.62	0.2
MS type progressive	1.92 (0.39, 9.49)	0.42	0.55	1.8
EDSS	1.00 (0.62, 1.61)	1.00	0.51	0.0
SDMT	1.03 (0.97, 1.08)	0.33	0.59	2.8
Whole brain	0.997 (0.989, 1.005)	0.46	0.58	1.6
Grey matter	0.992 (0.981, 1.004)	0.19	0.60	5.3
White matter	1.003 (0.988, 1.017)	0.72	0.50	0.4
Ventricular	0.999 (0.970, 1.028)	0.92	0.51	0.0
Cortical	0.992 (0.978, 1.006)	0.24	0.60	4.3
T2 LV	1.05 (1.00, 1.10)	0.044	0.68	12.0
T1 LV	1.14 (1.01, 1.29)	0.037	0.72	12.9
Subcortical	0.95 (0.84, 1.07)	0.41	0.57	2.0
Caudate	0.97 (0.48, 1.95)	0.93	0.52	0.0
Putamen	0.83 (0.50, 1.39)	0.49	0.54	1.4
Thalamus	0.85 (0.59, 1.23)	0.39	0.59	2.2
Pallidus	0.61 (0.14, 2.71)	0.51	0.55	1.3
Hippocampus	0.75 (0.42, 1.36)	0.35	0.44	2.6
Amygdala	0.63 (0.15, 2.66)	0.53	0.51	1.2

Legend: MS = Multiple Sclerosis (progressive=primary and secondary progressive combined); EDSS = Expanded Disability Status Scale; SDMT = Symbol Digit Modalities Test; LV = Lesion Volume; OR = Odds Ratio; CI = Confidence Interval.

Effect estimates from logistic regression analysis with reduction in SDMT greater than 4 points during 5 years (yes/no) as outcome, and baseline variables as predictors. An OR>1 means that a higher value of the predictor is associated with a greater odds of having a clinically significant decline in CPS. Predictive power of each model is estimated by the concordance index (C) and by Nagelkerke R². Bold values denotes statistical significance at the p< 0.05 level.

