

Supplemental Online Content

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This supplemental material has been provided by the authors to give readers additional information about their work.

Supplementary material 1: Full model estimates, main model

eTable 1. Effect of 1-Year Premorbid Socioeconomic Status on EDSS and MSIS

Relapsing onset	EDSS				MSIS physical				MSIS psychological			
	Est	LL	UL	p	Est [‡]	LL	UL	p	Est [‡]	LL	UL	p
(Intercept)	2.21	2.07	2.36	<0.001	25.13	21.53	29.34	<0.001	44.92	39.54	51.04	<0.001
Male sex	0.15	0.05	0.24	0.002	0.83	0.75	0.92	0.001	0.83	0.76	0.90	<0.001
Age at onset (years)	0.04	0.03	0.04	<0.001	1.02	1.02	1.03	<0.001	1.00	1.00	1.01	0.39
Disease duration (years)	0.06	0.05	0.06	<0.001	1.01	1.00	1.02	<0.001	0.98	0.98	0.99	<0.001
Number of early relapses	0.11	0.07	0.15	<0.001	1.05	1.01	1.09	0.02	1.03	1.00	1.07	0.05
Proportion of disease time on high-efficacy therapy [§]	-0.04	-0.05	-0.04	<0.001	0.94	0.94	0.95	<0.001	0.95	0.94	0.96	<0.001
Proportion of disease time on lower-efficacy therapy [§]	-0.03	-0.03	-0.03	<0.001	0.96	0.95	0.96	<0.001	0.96	0.95	0.96	<0.001
Income quartile	-0.16	-0.20	-0.12	<0.001	0.86	0.82	0.89	<0.001	0.88	0.84	0.91	<0.001
Secondary education*	-0.30	-0.40	-0.19	<0.001	0.82	0.73	0.92	0.001	0.92	0.84	1.01	0.09
Tertiary education*	-0.47	-0.59	-0.35	<0.001	0.57	0.50	0.65	<0.001	0.75	0.67	0.83	<0.001
Partnered [#]	-0.04	-0.14	0.05	0.38	1.00	0.90	1.11	0.99	1.00	0.91	1.09	0.94
Separated [#]	0.34	0.18	0.51	<0.001	1.35	1.12	1.62	0.002	1.25	1.08	1.46	0.004
Progressive onset	EDSS				MSIS physical				MSIS psychological			
	Est	LL	UL	P	Est	LL	UL	P	Est	LL	UL	P
(Intercept)	3.63	3.01	4.26	<0.001	36.89	22.67	60.05	<0.001	42.26	25.87	69.02	<0.001
Male sex	0.14	-0.27	0.54	0.51	0.93	0.70	1.25	0.64	0.81	0.61	1.09	0.16
Age at onset	0.03	0.00	0.05	0.04	1.00	0.98	1.02	0.93	0.99	0.98	1.01	0.54
Disease duration	0.22	0.21	0.24	<0.001	1.04	1.02	1.06	<0.001	1.01	0.99	1.03	0.41
Income quartile	-0.30	-0.48	-0.11	0.002	0.98	0.85	1.12	0.72	0.96	0.84	1.10	0.58
Secondary education*	-0.26	-0.72	0.20	0.26	0.66	0.47	0.93	0.02	0.71	0.51	1.00	0.05
Tertiary education*	-0.25	-0.80	0.30	0.37	0.69	0.47	1.03	0.07	0.67	0.46	0.99	0.05
Partnered [#]	-0.21	-0.66	0.23	0.35	1.01	0.74	1.39	0.93	1.07	0.79	1.46	0.65
Separated [#]	-0.05	-0.68	0.58	0.88	1.14	0.71	1.85	0.59	1.28	0.80	2.05	0.31

§ Estimates are for every additional 10% of disease time spent treated.

* reference group: did not complete secondary education

reference group: Unmarried

‡ Estimates are multiplicative of reference value; estimates <1 indicate lower symptom burden, >1 indicate higher symptom burden

eTable 2. Effect of 5-Year Premorbid Socioeconomic Status on EDSS and MSIS

	EDSS				MSIS physical				MSIS psychological			
	Est	LL	UL	p	Est [⌘]	LL	UL	p	Est [⌘]	LL	UL	p
Relapsing onset												
(Intercept)	2.03	1.87	2.20	<0.001	22.35	18.89	26.44	<0.001	41.67	36.23	47.94	<0.001
Male sex	0.20	0.09	0.30	<0.001	0.84	0.75	0.94	0.003	0.83	0.76	0.91	<0.001
Age at onset	0.05	0.04	0.05	<0.001	1.03	1.02	1.04	<0.001	1.00	0.99	1.01	0.746
Disease duration	0.06	0.06	0.07	<0.001	1.01	1.01	1.02	<0.001	0.98	0.98	0.99	<0.001
Number of early relapses	0.10	0.06	0.14	<0.001	1.04	1.00	1.09	0.068	1.03	0.99	1.07	0.139
Proportion of disease time on high-efficacy therapy [§]	-0.03	-0.04	-0.02	<0.001	0.94	0.94	0.95	<0.001	0.95	0.94	0.96	<0.001
Proportion of disease time on lower-efficacy therapy [§]	-0.03	-0.03	-0.03	<0.001	0.96	0.95	0.97	<0.001	0.96	0.95	0.96	<0.001
Income quartile	-0.12	-0.17	-0.08	<0.001	0.87	0.83	0.91	<0.001	0.90	0.87	0.94	<0.001
Secondary education*	-0.29	-0.41	-0.18	<0.001	0.79	0.70	0.90	<0.001	0.87	0.79	0.97	0.010
Tertiary education*	-0.50	-0.63	-0.37	<0.001	0.57	0.50	0.66	<0.001	0.71	0.63	0.80	<0.001
Partnered [#]	-0.02	-0.13	0.09	0.740	1.06	0.94	1.19	0.335	1.03	0.94	1.14	0.519
Separated [#]	0.29	0.09	0.49	0.005	1.44	1.15	1.80	0.001	1.24	1.03	1.49	0.022
	EDSS				MSIS physical				MSIS psychological			
Progressive onset												
(Intercept)	3.21	2.60	3.82	<0.001	42.81	26.07	70.29	<0.001	49.48	30.07	81.40	<0.001
Male sex	0.09	-0.31	0.49	0.658	0.86	0.64	1.15	0.300	0.79	0.59	1.05	0.103
Age at onset	0.04	0.01	0.06	0.008	1.01	0.99	1.03	0.601	1.00	0.98	1.02	0.955
Disease duration	0.22	0.21	0.24	<0.001	1.04	1.01	1.06	0.001	1.00	0.98	1.03	0.691
Income quartile	-0.13	-0.31	0.06	0.175	0.93	0.81	1.06	0.279	0.91	0.80	1.04	0.150
Secondary education*	-0.33	-0.77	0.11	0.147	0.72	0.52	1.00	0.047	0.77	0.56	1.07	0.118
Tertiary education*	-0.29	-0.86	0.28	0.316	0.78	0.52	1.19	0.249	0.69	0.46	1.04	0.077
Partnered [#]	-0.30	-0.74	0.13	0.173	0.93	0.68	1.27	0.668	0.97	0.72	1.32	0.847
Separated [#]	-0.09	-0.74	0.55	0.776	1.00	0.62	1.61	1.000	1.19	0.74	1.90	0.470

§ Estimates are for every additional 10% of disease time spent treated.

* reference group: did not complete secondary education

reference group: unmarried

⌘ Estimates are multiplicative of reference value; estimates <1 indicate lower symptom burden, >1 indicate higher symptom burden

Supplementary material 2: Patient baseline characteristics five years prior to multiple sclerosis onset

	EDSS analysis		MSIS-29 analysis	
	Progressive onset	Relapse onset	Progressive onset	Relapse onset
n	362	3394	190	2899
Age at onset (mean (SD))	47.67 (8.40)	39.56 (8.22)	45.38 (7.96)	38.92 (7.90)
Male sex, n (%)	171 (47.2)	1026 (30.2)	91 (47.9)	878 (30.3)
Female sex, n (%)	191 (52.8)	2368 (69.8)	99 (52.1)	2021 (69.7)
Income Quartile, n(%)				
1 (least affluent)	71 (20.0)	706 (21.9)	37 (19.8)	595 (21.6)
2	56 (15.8)	778 (24.2)	37 (19.8)	673 (24.4)
3	103 (29.0)	840 (26.1)	52 (27.8)	716 (26.0)
4 (most affluent)	125 (35.2)	896 (27.8)	61 (32.6)	775 (28.1)
Marital status, n (%)				
Single	155 (43.7)	1877 (58.3)	88 (47.1)	1654 (59.9)
Partnered	151 (42.5)	1121 (34.8)	76 (40.6)	931 (33.7)
Separated	49 (13.8)	222 (6.9)	23 (12.3)	174 (6.3)
Highest educational attainment, n (%)				
Pre-secondary	171 (48.4)	1045 (32.6)	77 (41.4)	860 (31.3)
Secondary education	125 (35.4)	1364 (42.5)	77 (41.4)	1179 (42.9)
Tertiary	57 (16.1)	799 (24.9)	32 (17.2)	712 (25.9)
Charlson comorbidity index (%)				
0	261 (91.6)	2559 (94.0)	149 (95.5)	2205 (93.9)
>1	24 (8.4)	162 (5.9)	7 (4.5)	144 (6.1)
Number of EDSS scores recorded during follow-up (median [IQR])	4 [2-7]	6 [4-9]		
Number of MSIS-29 scores recorded during follow-up (median [IQR])			2 [1-4]	5 [3-7]
Follow-up time (mean (SD))	8.29 (3.35)	8.17 (3.42)	7.30 (3.18)	8.03 (3.37)

EDSS: Expanded disability status scale score.

MSIS-29: Multiple sclerosis impact scale score.

Supplementary material 3: Secondary analysis adjusted for comorbidity

eTable 3. Effect of 1-Year Premorbid Socioeconomic Status on EDSS and MSIS, Adjusted for Comorbidity

Relapsing onset	EDSS				MSIS physical				MSIS psychological			
	Est	LL	UL	p	Est ^a	LL	UL	p	Est ^a	LL	UL	p
(Intercept)	2.26	2.10	2.41	<0.001	27.64	23.39	32.65	<0.001	47.09	41.07	53.98	<0.001
Male sex	0.16	0.05	0.27	0.004	0.86	0.76	0.96	0.009	0.89	0.81	0.98	0.017
Age at onset	0.04	0.03	0.04	<0.001	1.02	1.02	1.03	<0.001	1.00	1.00	1.01	0.17
Disease duration	0.06	0.06	0.07	<0.001	1.01	1.00	1.01	0.001	0.98	0.98	0.99	<0.001
Number of early relapses	0.11	0.07	0.15	<0.001	1.05	1.00	1.09	0.04	1.04	1.01	1.08	0.02
Proportion of disease time on high-efficacy therapy [§]	-0.04	-0.05	-0.04	<0.001	0.95	0.94	0.96	<0.001	0.95	0.94	0.96	<0.001
Proportion of disease time on lower-efficacy therapy [§]	-0.03	-0.03	-0.02	<0.001	0.96	0.95	0.96	<0.001	0.96	0.95	0.96	<0.001
Income quartile	-0.18	-0.22	-0.13	<0.001	0.83	0.79	0.87	<0.001	0.86	0.83	0.89	<0.001
Secondary education*	-0.34	-0.46	-0.22	<0.001	0.79	0.70	0.90	<0.001	0.91	0.82	1.01	0.06
Tertiary education*	-0.47	-0.60	-0.34	<0.001	0.58	0.50	0.66	<0.001	0.75	0.67	0.84	<0.001
Partnered [#]	-0.03	-0.13	0.08	0.638	1.00	0.89	1.12	0.97	1.02	0.93	1.12	0.70
Separated [#]	0.35	0.16	0.53	<0.001	1.34	1.10	1.63	0.004	1.24	1.06	1.46	0.008
Comorbidity index >1	0.38	0.17	0.58	<0.001	1.34	1.08	1.66	0.008	1.16	0.97	1.38	0.10

Progressive onset	EDSS				MSIS physical				MSIS psychological			
	Est	LL	UL	p	Est [‡]	LL	UL	p	Est [‡]	LL	UL	p
(Intercept)	2.94	2.07	3.81	<0.001	34.5	20.2	58.8	<0.001	43.0	26.6	69.5	<0.001
Male sex	0.29	-0.17	0.75	0.21	0.87	0.62	1.21	0.41	0.78	0.58	1.05	0.10
Age at onset	0.03	0.00	0.06	0.02	1.01	0.99	1.03	0.38	1.00	0.98	1.02	0.95
Disease duration	0.21	0.20	0.23	<0.001	1.04	1.02	1.06	<0.001	1.01	0.98	1.03	0.64
Income quartile	-0.28	-0.49	-0.07	0.009	0.98	0.84	1.15	0.83	0.96	0.84	1.10	0.56
Secondary education*	-0.06	-0.57	0.46	0.83	0.73	0.49	1.07	0.11	0.83	0.59	1.17	0.30
Tertiary education*	-0.26	-0.89	0.36	0.41	0.63	0.41	0.99	0.047	0.66	0.44	0.98	0.04
Partnered#	-0.25	-0.75	0.26	0.33	1.05	0.73	1.50	0.81	1.05	0.76	1.44	0.78
Separated#	-0.09	-0.79	0.61	0.80	1.11	0.64	1.91	0.71	1.27	0.78	2.05	0.34
Comorbidity index >1	0.90	0.08	1.73	0.03	0.82	0.37	1.78	0.61	1.00	0.50	2.00	1.00

§ Estimates are for every additional 10% of disease time spent treated.

* reference group: did not complete secondary education

reference group: Unmarried

‡ Estimates are multiplicative of reference value; estimates <1 indicate lower symptom burden, >1 indicate higher symptom burden

Supplementary material 4: Unadjusted analyses of individual sociodemographic factors

eTable 4: Estimated Effect of 1 Year Premorbid Sociodemographic Factors on Multiple Sclerosis Severity, Unadjusted Analyses

Relapse onset	EDSS			MSIS-29 Physical symptoms			MSIS-29 Psychological symptoms		
	Estimate	95% CI	p	Estimate	95% CI	p	Estimate	95% CI	p
Income quartile	-0.10	-0.14 - -0.06	<0.001	0.85	0.82 – 0.89	<0.000	0.85	0.85 – 0.85	<0.001
Educational attainment									
Secondary	-0.53	-0.64 - -0.43	<0.001	0.71	0.63 – 0.79	<0.001	0.90	0.82 – 0.99	0.03
Tertiary	-0.73	-0.85 - -0.62	<0.001	0.49	0.43 – 0.55	<0.001	0.71	0.64 – 0.78	<0.001
Marital status									
Partnered	0.16	0.07 - 0.25	<0.001	0.95	0.85 – 1.05	0.31	0.96	0.88 – 1.04	0.32
Separated	0.70	0.53 - 0.86	<0.001	1.43	1.18 – 1.73	<0.001	1.30	1.12 – 1.52	0.001

Progressive onset	EDSS			MSIS-29 Physical symptoms			MSIS-29 Psychological symptoms		
	Estimate	95% CI	p	Estimate	95% CI	p	Estimate	95% CI	P
Income quartile	-0.25	-0.43 - -0.07	0.007	1.00	0.88 – 1.14	0.99	0.95	0.84 – 1.09	0.48
Educational attainment									
Secondary	-0.40	-0.86 - 0.06	0.09	0.67	0.48 – 0.92	0.02	0.77	0.76 – 0.77	<0.001
Tertiary	-0.49	-1.04 - 0.06	0.08	0.69	0.47 – 1.01	0.06	0.69	0.69 – 0.69	<0.001
Marital status									
Partnered	-0.33	-0.77 - 0.11	0.14	0.95	0.69 – 1.31	0.75	1.02	0.75 – 1.39	0.91
Separated	0.20	-0.43 - 0.83	0.53	1.15	0.70 – 1.90	0.57	1.32	0.81 – 2.13	0.26

Linear mixed models with patient ID and calendar year of onset as random intercepts.

EDSS estimates are linear (additive). Estimates >0 indicate higher disability severity.

MSIS-29 estimates are coefficients (multiplicative). Estimates >1 indicate higher symptom severity.

eTable 5. Estimated Effect of 5 Year Premorbid Sociodemographic Factors on Multiple Sclerosis Severity, Unadjusted Analyses

Relapse onset	EDSS			MSIS-29 Physical symptoms			MSIS-29 Psychological symptoms		
	Estimate	95% CI	p	Estimate	95% CI	P	Estimate	95% CI	P
Income quartile	-0.13	-0.18 - -0.09	<0.001	0.88	0.84 – 0.92	<0.001	0.88	0.85 – 0.92	<0.001
Educational attainment									
Secondary	-0.52	-0.64 - -0.41	<0.001	0.68	0.61 – 0.77	<0.001	0.88	0.79 – 0.97	0.01
Tertiary	-0.73	-0.87 - -0.60	<0.001	0.49	0.43 – 0.56	<0.001	0.70	0.63 – 0.79	<0.001
Marital status									
Partnered	0.23	0.12 - 0.34	<0.001	1.03	0.92 – 1.16	0.62	1.01	1.00 – 1.01	<0.001
Separated	0.75	0.55 - 0.95	<0.001	1.55	1.24 – 1.94	<0.001	1.31	1.31 – 1.32	<0.001

Progressive onset	EDSS			MSIS-29 Physical symptoms			MSIS-29 Psychological symptoms		
	Estimate	95% CI	p	Estimate	95% CI	p	Estimate	95% CI	p
Income quartile	-0.22	-0.40 - -0.05	0.01	0.94	0.83 – 1.08	0.38	0.90	0.79 – 1.02	0.09
Educational attainment									
Secondary	-0.52	-0.96 - -0.09	0.02	0.72	0.53 – 0.98	0.04	0.81	0.80 – 0.81	<0.001
Tertiary	-0.53	-1.09 - 0.03	0.07	0.76	0.50 – 1.15	0.20	0.66	0.66 – 0.67	<0.001
Marital status									
Partnered	-0.19	-0.61 - 0.23	0.38	0.92	0.67 – 1.26	0.59	0.95	0.70 – 1.30	0.75
Separated	0.30	-0.32 - 0.91	0.35	1.02	0.62 – 1.68	0.94	1.25	0.77 – 2.03	0.36

Linear mixed models with patient ID and calendar year of onset as random intercepts.

EDSS estimates are linear (additive). Estimates >0 indicate higher disability severity.

MSIS-29 estimates are coefficients (multiplicative). Estimates >1 indicate higher symptom severity.