

Supplementary material

Table S1. Variables included in the propensity score models for each analysis in association with outcome for age groups for multiple sclerosis patients

Patient group	Sex	Age at MS clinical onset	Age at treatment start	Number of relapses	EDSS	Year of MS onset	MS Center
Propensity score model adjusting for age at MS clinical onset							
<i>All</i>	x	x		0.698	x	x	x
<i>≤40 years old group</i>	x	x		0.533	x	x	x
<i>>40 years old group</i>	x	x		0.259	x	x	x
Propensity score model adjusting for age at treatment start							
<i>All</i>	x		x	0.234	x	x	x
<i>≤40 years old group</i>	x		x	0.978	x	x	x
<i>>40 years old group</i>	0.983		x	0.141	x	x	x

MS; multiple sclerosis, PS; propensity score

Legend: Bold dark cross in the table means the variable in column met the criterion of $p \leq 20\%$, else the exact p value is indicated. Grey areas mean that the variable was not considered in the analyses (i.e. not applicable)

Table S2: Multiple sclerosis (MS) patient characteristics at first treatment start by earliness status before and after stabilized inverse probability of treatment weighting for

	<i>Before PS</i>			<i>After PS model adjusting for age at MS clinical onset</i>			<i>After PS model adjusting for age at treatment start</i>		
	Early N= 1,882	Late N= 3,397	Difference*	Early	Late	Difference*	Early	Late	Difference*
Sex (Female)	1,445 (76.8%)	2,565 (75.5%)	3.0	76.3%	76%	0.8	76.8%	76%	1.9
Age at MS clinical onset	32.1±9.1	32.3±8.7	1.4	32.2±9	32.2±8.8	0.3			
Age at treatment start	32.7±9.1	36.1±9.0	38.4				34.6±9.4	34.9±8.9	2.6
Number of relapses within 12 months before treatment start**	1.7±0.8	1.1±0.8	80.4	1.8±0.8	1.0±0.8	93.8	1.8±0.81	1.0±0.80	90.2
EDSS within 12 months before treatment start									
[0; 1.5]	642 (34.1%)	1,098 (32.3%)	7.6	31.6%	32.8%	2.8	32.1%	32.9%	2.8
[2; 3.5]	377 (20.0%)	784 (23.1%)		22.4%	22.1%		21.7%	22.0%	
≥4	38 (2.0%)	73 (2.1%)		1.9%	2.0%		1.9%	2.0%	
Missing	825 (43.8%)	1,442 (42.4%)		44.1%	43.1%		44.3%	43.0%	
Year of MS onset									
1996	31 (1.6%)	248 (7.3%)	74.9	5.4%	5.3%	1.2	5.0%	5.3%	4.2
1997	35 (1.9%)	279 (8.2%)		5.8%	5.9%		5.4%	5.9%	
1998	51 (2.7%)	289 (8.5%)		6.3%	6.4%		5.7%	6.4%	
1999	62 (3.3%)	264 (7.8%)		6.3%	6.2%		6.4%	6.2%	
2000	94 (5.0%)	267 (7.9%)		6.8%	6.8%		6.9%	6.8%	
2001	106 (5.6%)	237 (7.0%)		6.5%	6.5%		6.5%	6.4%	
2002	121 (6.4%)	259 (7.6%)		7.1%	7.2%		6.9%	7.1%	
2003	106 (5.6%)	222 (6.5%)		6.2%	6.2%		6.4%	6.2%	
2004	152 (8.1%)	232 (6.8%)		7.3%	7.3%		7.5%	7.3%	
2005	132 (7.0%)	213 (6.3%)		6.6%	6.5%		6.6%	6.5%	
2006	164 (8.7%)	196 (5.8%)		6.9%	6.8%		7.0%	6.9%	
2007	137 (7.3%)	172 (5.1%)		5.8%	5.9%		6.1%	5.9%	
2008	171 (9.1%)	158 (4.7%)		6.3%	6.3%		6.4%	6.2%	
2009	160 (8.5%)	127 (3.7%)		5.4%	5.4%		5.6%	5.5%	
2010	121 (6.4%)	123 (3.6%)		4.7%	4.6%		4.9%	4.7%	
2011	119 (6.3%)	85 (2.5%)		3.9%	3.9%		4.0%	4.0%	
2012	120 (6.4%)	26 (0.8%)		2.8%	2.7%		2.8%	2.8%	
MS Center									
Center 1	93 (4.9%)	152 (4.5%)	10.5	4.6%	4.6%	2.6	4.7%	4.6%	2.6
Center 2	187 (9.9%)	360 (10.6%)		10.1%	10.2%		10.0%	10.2%	
Center 3	149 (7.9%)	252 (7.4%)		7.7%	7.6%		7.8%	7.6%	
Center 4	72 (3.8%)	116 (3.4%)		3.8%	3.5%		3.7%	3.5%	
Center 5	555 (29.5%)	976 (28.7%)		28.9%	29.1%		29.4%	29.3%	
Center 6	137 (7.3%)	196 (5.8%)		6.9%	6.4%		7.1%	6.6%	
Center 7	186 (9.9%)	328 (9.7%)		9.4%	9.7%		9.3%	9.6%	
Center 8	182 (9.7%)	350 (10.3%)		9.7%	9.9%		9.7%	9.9%	
Center 9	110 (5.8%)	199 (5.9%)		5.9%	5.9%		5.7%	5.9%	
Center 10	211 (11.2%)	468 (13.8%)		13.1%	12.9%		12.7%	12.8%	

MS; Multiple sclerosis, PS; propensity score, * Difference: Standardized mean differences or Mahalanobis distances for more than two categorical variables

**Variable not included in the propensity score model since only variable associated with outcome were included in the PS model

each propensity score (PS) model

Table S3. Multiple sclerosis (MS) patient characteristics at first treatment start according to availability of baseline Expanded Disability Status Scale (EDSS) score

	EDSS ^a available	EDSS ^a missing	Difference ^b
	N=3,012	N= 2,267	
Female	2310 (76.7%)	1700 (75.0%)	4%
Age at MS clinical onset	31.1 (25.3-38.6)	30.5 (25.1-38.1)	3%
Age at treatment start	34.1 (27.9-41.4)	33.6 (27.5 - 40.8)	4%
MS duration at treatment start	1.6 (0.7-3.7)	1.7 (0.7-3.7)	3%
Number of relapses within 12 months before treatment start			10%
0	392 (13%)	363 (16%)	
1	1547 (51.4%)	1169 (51.6%)	
2	829 (27.5%)	581 (25.6%)	
≥3	244 (8.1%)	154 (6.8%)	
Year of MS onset			24%
1996-2000	811 (26.9%)	809 (35.7%)	
2001-2005	996 (33.1%)	784 (34.6%)	
2006-2012	1205 (40%)	674 (29.7%)	
Treatment start			
Early (within 12 months)	1955 (64.9%)	1442 (63.6%)	3%
Later	1057 (35.1%)	825 (36.4%)	

^aEDSS: Expanded Disability Status Scale

^b Difference: Standardized mean differences or Manahalobis distances for more than two categorical variables

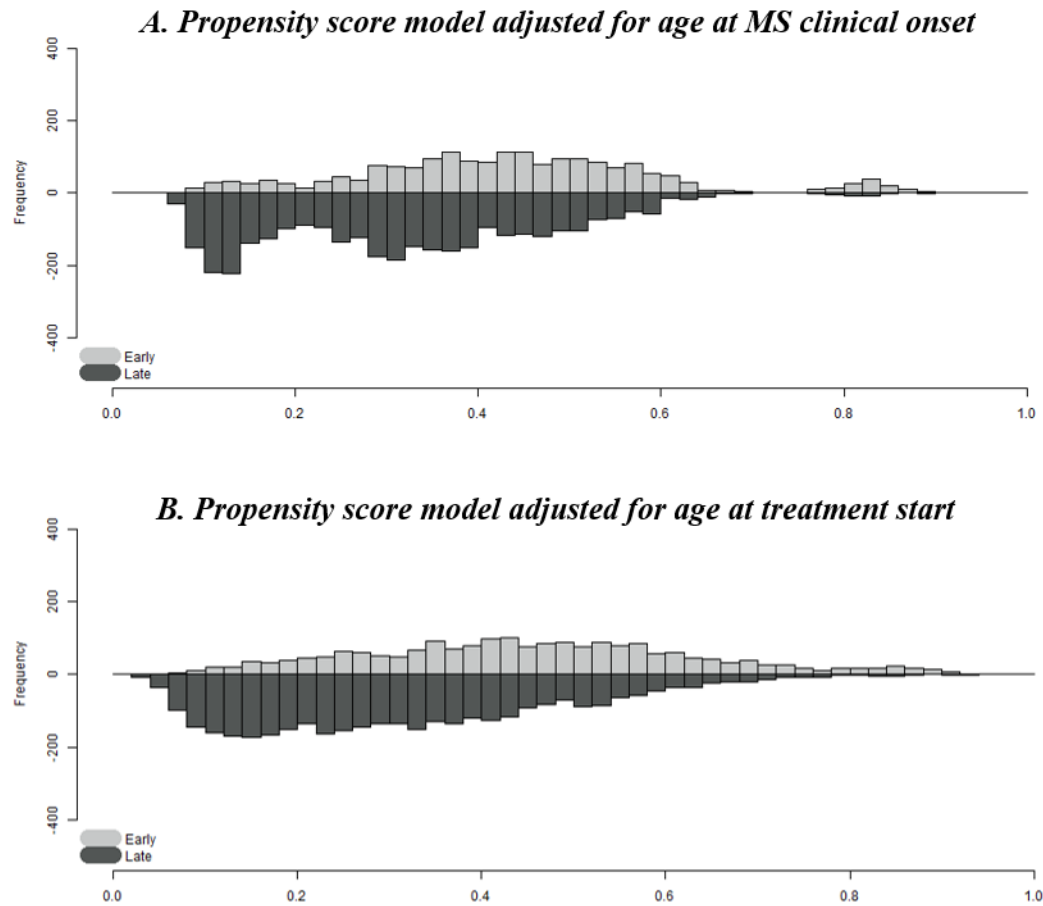


Figure S1. Propensity score distributions adjusted for age at clinical onset and treatment start for multiple sclerosis (MS) patients