

**Supplementary Table 2. Demographic characteristics by population**

Variable	n	Discovery <sup>b</sup>	n	Replication <sup>b</sup>	p-value <sup>c</sup>	SMD
Female	12584	9023 (71.7%)	9805	7045 (71.9%)	0.81	0.003
Disease course	11626		9064		<0.0001	0.081
relapsing onset		10630 (91.4%)		8481 (93.6%)		
primary progressive		996 (8.6%)		583 (6.4%)		
Age at EDSS <sup>a</sup>	12584	51.7 (11.8)	9805	47.2 (12.4)	<0.0001	0.377
Age at onset	12453	33.6 (10.2)	8252	32.5 (10.3)	0.005	0.109
Disease duration	12453	18.2 (10.6)	8252	15.8 (10.8)	<0.0001	0.229
EDSS <sup>a</sup>	12584	3.54 (2.43)	9805	3.36 (2.37)	<0.0001	0.076
ARMSS <sup>a</sup>	12584	4.23 (2.77)	9805	4.57 (2.82)	<0.0001	0.122
Disease modifying therapy	7857		3602		<0.0001	0.911
never treated		766 (9.7%)		-		
no current treatment		983 (12.5%)		-		
glatiramer acetate		772 (9.8%)		217 (6.0%)		
interferon beta		1587 (20.2%)		594 (16.5%)		
teriflunomide		340 (4.3%)		195 (5.4%)		
dimethyl fumarate		1078 (13.7%)		534 (14.8%)		
fingolimod		870 (11.1%)		790 (21.9%)		
natalizumab		1041 (13.2%)		1107 (30.7%)		
B cell depleting therapy		128 (1.6%)		48 (1.3%)		
cladribine		3 (0.0%)		-		
alemtuzumab		73 (0.9%)		36 (1.0%)		
other		216 (2.7%)		81 (2.2%)		

The discovery population was enriched for older individuals with longer disease duration, while the replication population was composed of already collected data from unselected samples. This is reflected in the meaningful differences in age at last EDSS and disease duration. Differences in disease course, age at onset and disability scores were smaller, as indicated by the SMD, though significant given the sample sizes.

<sup>a</sup> When repeated EDSS were available, the reported age and scores correspond to the last recoded value.

<sup>b</sup> Mean (standard deviation); count (%)

<sup>c</sup> chi-square test; Fisher's exact test

ARMSS; age-related multiple sclerosis severity score; B cell depleting therapy, ocrelizumab and rituximab; EDSS, expanded disability status scale; n, non-missing observations; SMD, standardized mean difference.