Supplementary Table 17. Mendelian randomization results

			P(GWAS) < $5x10^{-8}$							P(GWAS) < $5x10^{-5}$							
Outcome	Trait	Method	#SNVs	beta	beta (s.e.)	pval	het.pval	intercept	intercept (s.e)	intercept.pval	#SNVs	beta	beta (s.e.)	pval	het.pval	intercept	intercept (s.e)	intercept.pval
MS severity	25-hydroxyvitamin D level	Inverse variance weighted	81	0.010	0.059	0.871	0.133	-	-	-	322	-0.027	0.047	0.563	0.224	-	-	-
		Robust adjusted profile score	81	0.008	0.062	0.899	0.703	-	-	-	322	-0.032	0.049	0.516	0.321	-	-	-
		Weighted median	81	-0.019	0.091	0.835	-	-	-	-	322	-0.019	0.091	0.834	-	-	-	-
		Pleiotropy residual sum and outlier[a]	81	-	-	-	0.127	-	-	-	322	-	-	-	0.211	-	-	-
		MR Egger	81	-0.032	0.087	0.716	0.124	0.002	0.002	0.520	322	0.015	0.073	0.841	0.219	-0.001	0.001	0.452
	body mass index	Inverse variance weighted	446	0.039	0.038	0.307	0.676	-	-	-	732	0.018	0.035	0.611	0.157	-	-	-
		Robust adjusted profile score	446	0.048	0.039	0.226	0.975	-	-	-	732	0.019	0.037	0.607	0.990	-	-	-
		Weighted median	446	0.056	0.063	0.374	-	-	-	-	732	0.048	0.059	0.415	-	-	-	-
		Pleiotropy residual sum and outlier[a]	446	-	-	-	0.683	-	-	-	732	-	-	-	0.156	-	-	-
		MR Egger	446	0.013	0.098	0.897	0.665	4.6E-04	0.002	0.772	732	0.003	0.086	0.975	0.151	2.4E-04	0.001	0.845
	years of schooling	Inverse variance weighted[b]	263	-0.155	0.063	0.014	0.139	-	-	-	610	-0.161	0.049	9.7E-04	0.235	-	-	-
		Robust adjusted profile score	263	-0.158	0.065	0.015	0.677	-	-	-	610	-0.168	0.052	1.2E-03	0.994	-	-	-
		Weighted median	263	-0.158	0.090	0.080	-	-	-	-	610	-0.193	0.073	8.3E-03	-	-	-	-
		Pleiotropy residual sum and outlier[a]	263	-	-	-	0.136	-	-	-	610	-	-	-	0.240	-	-	-
		MR Egger	263	-0.145	0.252	0.566	0.129	-1.4E-04	0.003	0.968	610	-0.078	0.164	0.636	0.229	-0.001	0.002	0.594
Reverse direction																		
25-hydroxyvitamin D level	MS severity	Wald ratio/Inverse variance weighted	1	0.011	0.029	0.701	-	-	-	-	68	0.004	0.006	0.461	0.002	-	-	-
body mass index	MS severity	Wald ratio/Inverse variance weighted	-	missing, no proxy			-	-	-	-	15	-0.001	0.015	0.924	2.5E-04	-	-	-
years of schooling	MS severity	Wald ratio/Inverse variance weighted	1	-0.015	0.025	0.539	-	-	-	-	75	0.008	0.004	0.094	0.020	-	-	-

Results are divided by instrument selection p-value threshold (see Methods and Supplementary Table 16)

[a] A missing beta, beta (s.e.) and pval signifies that no outliers were identified, and thus the values are the same as the Inverse variance weighted method

[b] To better assess the magnitude of this association, we repeated the inverse-variance weighted MR using genetic associations with ARMSS scores on the absolute scale (results in this table are based on rank-based inverse normal transformation; see Methods). The resulting MR estimate was -0.505 (95% CI -0.845 to -0.164, P = 0.004)

pval, p-value; intercept.pval, p-value for intercept; het.pval, p-value for heterogeneity statistic; s.e., standard error