

Appendix e-1. Potential confounding variables

All analyses were adjusted for age, sex, residential area, ancestry, and when appropriate, smoking habits. Other potential confounding factors taken into account had minor influence on the results and were not retained in the final analyses. These were heredity of MS, educational level, socioeconomic status, snuff use, alcohol consumption, body mass index at age 20, UVR exposure habits, supplemental vitamin D intake during the last five years, vitamin D status at inclusion, and a history of infectious mononucleosis. Self reported heredity was dichotomized into having or not having a first or second degree relative with MS. Educational level was categorized into no post-secondary education, post-secondary education without university degree, or university degree. The last occupation during the year before the index year was used as a marker for socioeconomic class which was categorized into the following strata: 1, workers in goods production; 2, workers in service production; 3, employees at lower and intermediate levels; 4, employees at higher levels, executives, university graduates, and 5; others such as pensioners, students, and unemployed. Snuff use was dichotomized into ever- or never snuff users. Alcohol consumption was categorized into low, moderate or high consumption based on the number of drinks per week at inclusion in the study. BMI at age 20 was calculated by dividing self-reported weight in kilograms by self-reported height in meters squared¹⁶. Based on three questions regarding exposure to UVR where each answer alternative was given a number ranging from 1 (the lowest exposure) to 4 (the highest exposure), we constructed an index by adding the numbers together and thus acquired a value between 3 and 12. UVR exposure was then dichotomized into high or low exposure (index value more or less than 6). Vitamin D status was categorised into sufficient levels (50 nmol/L or higher), vitamin D deficiency (less than 50 nmol/L), or unknown. A history of infectious mononucleosis was dichotomized into yes or no.

Appendix e-2

OR with 95% CI of developing MS **among never smokers** categorized by exposure to organic solvents, HLA-DRB1*15 and HLA-A*02, compared with non-exposed participants without the MS risk HLA genes. Attributable proportion due to overall interaction (TotAP) between HLA-DRB1*15, absence of HLA-A*02 and organic solvents.

HLA-DRB1*15	HLA-A02-	Organic solvents	ca/co*	OR (95% CI)#	p value	TotAP (95% CI)
-	+	-	139/525	1.0 (reference)	1.0 (reference)	
-	-	-	238/550	1.6 (1.3-2.1)	<0.0001	
+	+	-	200/231	3.3 (2.5-4.3)	<0.0001	
+	-	-	279/196	5.3 (4.1-6.9)	<0.0001	
-	+	+	12/42	1.1 (0.6-2.2)	0.7	
-	-	+	26/56	1.8 (1.1-3.0)	0.02	
+	+	+	22/20	4.4 (2.3-8.3)	<0.0001	
+	-	+	34/19	6.9 (3.8-12.6)	<0.0001	0.4 (0.07-0.7)

* number of cases and controls

adjusted for age, gender, residential area, and ancestry.

Appendix e-3

OR with 95% CI of developing MS **among smokers** categorized by exposure to organic solvents, HLA-DRB1*15 and HLA-A*02, compared with non-exposed participants without the MS risk HLA genes. Attributable proportion due to overall interaction (TotAP) between HLA-DRB1*15, absence of HLA-A*02 and organic solvents.

HLA-DRB1*15	HLA-A02-	Organic solvents	ca/co*	OR (95% CI)#	p value	TotAP (95% CI)
-	+	-	165/423	1.0 (reference)		
-	-	-	278/443	1.6 (1.3-2.0)	<0.0001	
+	+	-	229/208	2.9 (2.2-3.7)	<0.0001	
+	-	-	281/139	5.2 (4.0-6.9)	<0.0001	
-	+	+	22/39	1.4 (0.8-2.5)	0.2	
-	-	+	40/30	3.1 (1.8-5.1)	<0.0001	
+	+	+	37/21	4.0 (2.2-7.1)	<0.0001	
+	-	+	40/5	19.0 (7.3-49.1)	<0.0001	0.7 (0.4-1.0)

* number of cases and controls

adjusted for age, gender, residential area, and ancestry.