

Supplementary Online Content

Kleerekooper I, Chua S, Foster PJ, et al; UK Biobank Eye and Vision Consortium. Associations of alcohol consumption and smoking with disease risk and neurodegeneration in individuals with multiple sclerosis in the United Kingdom. *JAMA Netw Open*. 2022;5(3):e220902. doi:10.1001/jamanetworkopen.2022.0902

eTable 1. Univariable and Multivariable Logistic Regression—Odds of Multiple Sclerosis Case Status

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

eTable 1. Univariable and Multivariable Logistic Regression—Odds of Multiple Sclerosis Case Status													
		Univariable logistic regression						Multivariable logistic regression					
		Healthy control group compared with multiple sclerosis			Comorbid control group compared with multiple sclerosis			Healthy control group compared with multiple sclerosis			Comorbid control group compared with multiple sclerosis		
		OR	95% CI	p-value	OR	95% CI	p-value	aOR	95% CI	p-value	aOR	95% CI	p-value
Smoking status	Never	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Previous	1.51	1.08 – 2.10	0.01	1.16	0.83 – 1.61	0.37	1.59	1.12 – 2.25	0.009	1.25	0.88 – 1.77	0.20
	Current	2.89	1.90 – 4.30	<0.001	2.34	1.54 – 3.48	<0.001	3.05	1.95 – 4.64	<0.001	2.30	1.48 – 3.51	<0.001
Alcohol consumption	Low	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Moderate	0.51	0.36 – 0.73	<0.001	0.68	0.48 – 0.97	0.03	0.62	0.43 – 0.91	0.01	0.81	0.56 – 1.18	0.26
	High	0.63	0.41 – 0.96	0.03	0.90	0.59 – 1.37	0.63	0.76	0.48 – 1.20	0.24	1.11	0.70 – 1.75	0.65
Sex	Male	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Female	2.64	1.92 – 3.70	<0.001	2.16	1.60 – 3.03	<0.001	2.97	2.10 – 4.27	<0.001	2.28	1.62 – 3.28	<0.001
Age group	40-49 years	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
	50-59 years	1.18	0.82 – 1.74	0.38	1.12	0.77 – 1.64	0.56	1.08	0.74 – 1.61	0.69	1.17	0.79 – 1.73	0.44
	60-70 years	1.08	0.74 – 1.61	0.68	0.62	0.42 – 0.92	0.02	0.98	0.65 – 1.49	0.94	0.67	0.44 – 1.01	0.05
Townsend deprivation index	Lowest quartile	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Low-middle quartile	1.47	0.94 – 2.31	0.10	1.37	0.88 – 2.16	0.17	1.40	0.88 – 2.25	0.16	1.32	0.83 – 2.11	0.24
	High-middle quartile	1.35	0.86 – 2.14	0.20	1.29	0.82 – 2.04	0.27	1.21	0.75 – 1.96	0.43	1.17	0.73 – 1.89	0.51
	Highest quartile	1.90	1.24 – 2.94	0.004	1.67	1.10 – 2.60	0.02	1.57	1.00 – 2.51	0.05	1.41	0.90 – 2.25	0.14
BMI	Low/healthy	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Overweight	1.02	0.72 – 1.46	0.89	0.86	0.61 – 1.22	0.39	1.19	0.83 – 1.71	0.34	0.99	0.69 – 1.41	0.94
	Obese	1.56	1.05 – 2.31	0.03	0.92	0.62 – 1.36	0.68	1.72	1.15 – 2.56	0.008	1.02	0.68 – 1.51	0.93

Household passive smoking	No	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Yes	1.46	0.90 – 2.27	0.11	1.37	0.84 – 2.13	0.18	NA	NA	NA	NA	NA	NA

OR = odds ratio. BMI = body mass index. aOR = adjusted odds ratio. BMI = body mass index. NA = not applicable. Alcohol intake frequency: never or special occasions only (low), drinking once per month up to 4 times per week (moderate) or daily or almost daily (high).

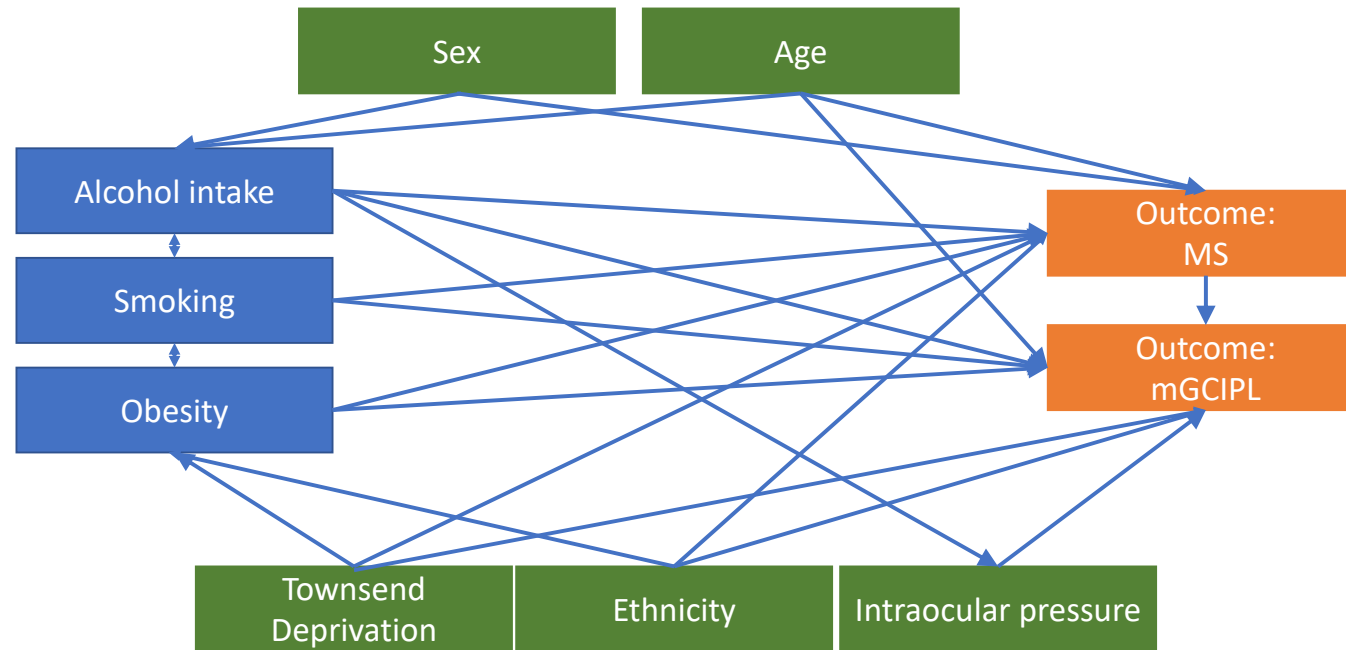
eTable 2. Testing for multiplicative effects of Alcohol and Smoking in multiple sclerosis					
		MS cohort			
		mGCIPL change	p-value	Trend p-value	Observations (n)
Smoking status	Never	NA	NA	NA	176
	Previous	-1.68	0.41		
	Current	-2.26	0.28		
Alcohol consumption	Low	NA	NA	NA	
	Moderate	-1.32	0.43		
	High	-4.21	0.02		
Interaction terms	Previous smoking + Moderate alcohol	1.91	0.45	NA	
	Previous smoking + High alcohol	2.27	0.43		
	Current smoking + Moderate alcohol	2.54	0.36		
	Current smoking + High alcohol	1.65	0.56		

Alcohol intake frequency: never or special occasions only (low), drinking once per month up to 4 times per week (moderate) or daily or almost daily (high). MS = multiple sclerosis. mGCIPL = macular ganglion cell and inner plexiform layer. NA = not applicable.

eTable 3. Effect Modification of Alcohol and Smoking Effects by Multiple Sclerosis Diagnosis					
		mGCIPL μ m change	p-value	Observations	
Model 1: interaction smoking with multiple sclerosis (adjusted for alcohol intake)					
Controls					
Smoking status	Never	NA	NA	72,101	
	Previous	-0.04	0.437		
	Current	0.89	<0.001		
Multiple sclerosis cases					
Smoking status	Never	-4.00	<0.001		
	Previous	-0.29	0.784		
	Current	-2.14	0.077		
Model 2: interaction alcohol use with multiple sclerosis (adjusted for smoking)					
Controls					
Alcohol consumption	Low	NA	NA	72,101	
	Moderate	-0.33	<0.001		
	High	-0.93	<0.001		
Multiple sclerosis cases					
Alcohol status	Low	-3.99	<0.001		
	Moderate	0.03	0.979		
	High	-2.27	0.074		

Alcohol intake frequency: never or special occasions only (low), drinking once per month up to 4 times per week (moderate) or daily or almost daily (high). mGCIPL = macular ganglion cell and inner plexiform layer. NA = not applicable.

eFigure. Directed Acyclic Graph (DAG) Visualizing the Assumed Associations Among the Exposures, Outcomes and Potential Confounders in This Study



MS = multiple sclerosis. mGCIPL = macular ganglion cell and inner plexiform layer.