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Associations of alcohol consumption and smoking with disease risk and neurodegeneration in multiple sclerosis; a UK cohort of 72,101 subjects

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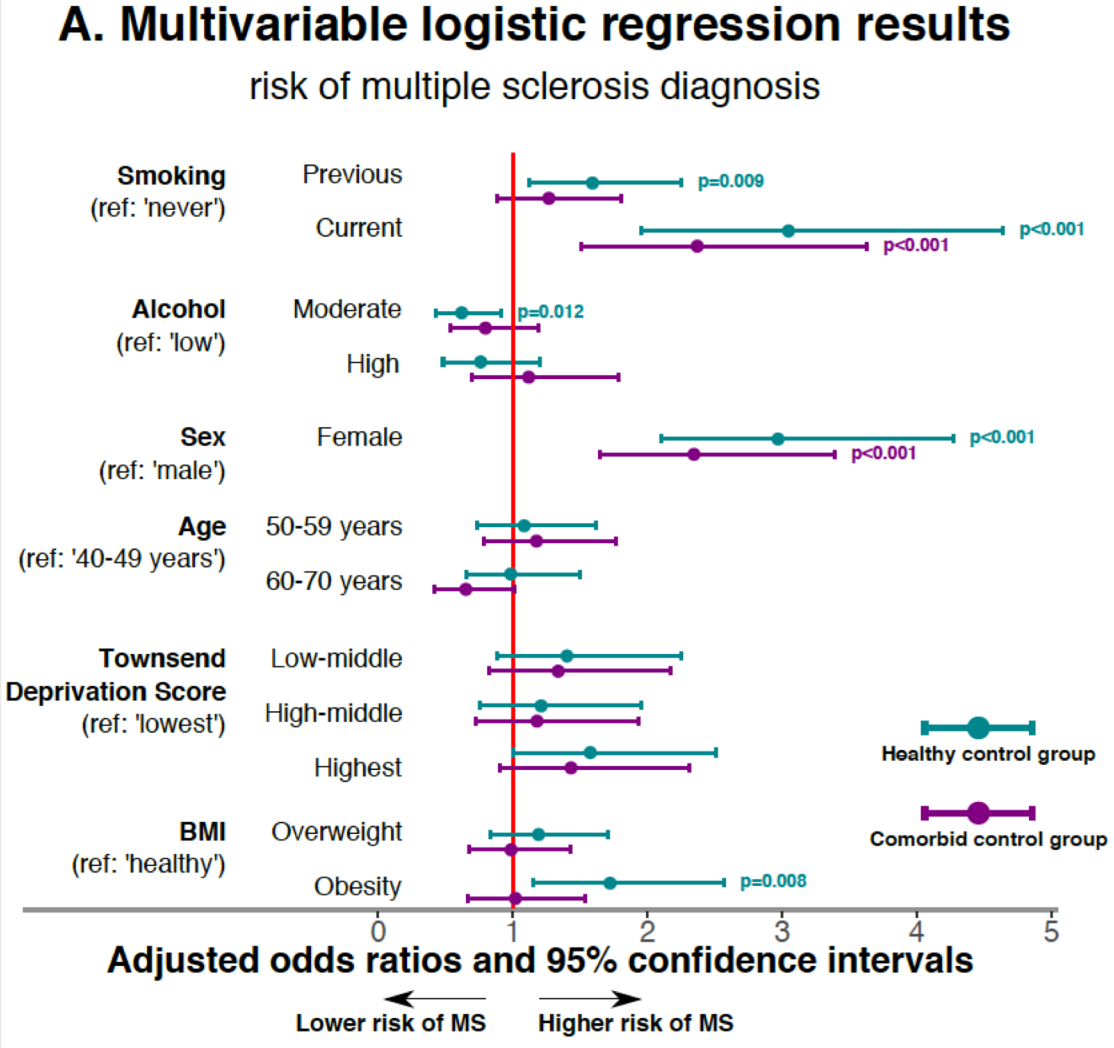
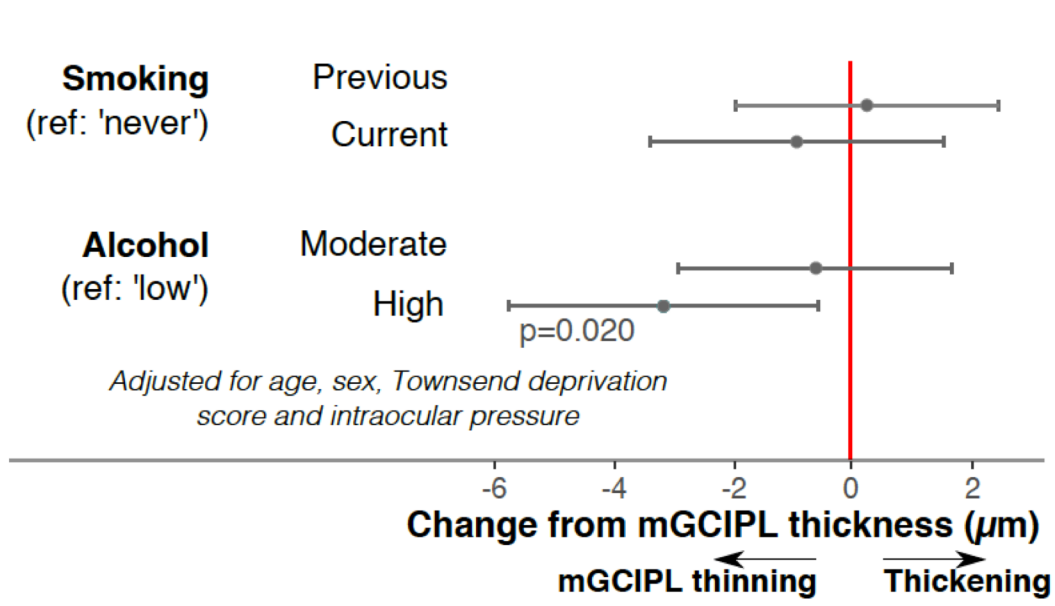
Introduction Understanding the effects of modifiable risk factors on multiple sclerosis (MS) risk and associated neurodegeneration is important to guide clinical counselling. Here, the associations of alcohol use and smoking with odds of being diagnosed with MS and with macular ganglion cell layer and inner plexiform layer (mGCIPL) thickness, are investigated.

Methods This cross-sectional study analysed data from the community-based United Kingdom Biobank (UKBB) study on health behaviours (obtained through questionnaires) and retinal thickness (measured by optical coherence tomography (OCT)) in individuals aged 40-69 years. Exposures are smoking status and alcohol intake frequency, while outcomes are MS diagnosis status and mGCIPL thickness. Multivariable logistic regression analyses were used to identify risk factors for MS diagnosis by calculating odds ratios (ORs) and 95% confidence intervals (CI). Multivariable generalised estimating equations (GEEs) were used to explore the associations of alcohol use and smoking with mGCIPL thickness in individuals with MS, following adjustment for confounding factors. Finally, interaction models explored if the correlations of alcohol and smoking with mGCIPL thickness were modified by MS diagnosis.

A. Multivariable logistic regression results
risk of multiple sclerosis diagnosis



B. GEE results: change in mGCIPL thickness
in individuals with multiple sclerosis



Results 72,101 individuals were included (20,065 healthy, 51,737 with comorbidities and 179 with MS). Modifiable risk factors significantly associated with MS diagnosis were smoking (OR 3.05; 95% CI 1.95 – 4.64), moderate alcohol intake (OR 0.62; 95% CI 0.43 – 0.91) and obesity (OR 1.72; 95% CI 1.15 – 2.56) compared to healthy controls (Figure A). Using the comorbid control group, the only modifiable risk factor showing a significant association with MS diagnosis was smoking (OR 2.10; 95% CI 1.35 – 3.20). High alcohol intake was associated with decreased mGCIPL thickness in individuals with MS (beta=-3.09µm; p=0.020), with a significant trend effect across the alcohol intake levels (p=0.021) (Figure B). The effects of high alcohol intake on mGCIPL thickness trended to being more severe in MS compared with controls (beta=-2.27µm, p=0.074 vs. beta=-0.91µm, p<0.001, resp.). Smoking was not associated with mGCIPL thickness in MS. However, there was suggestion of effect modification in the interaction model, with smoking being associated with an increase in mGCIPL thickness in controls (beta=0.87µm, p<0.001), but a negative trend in MS (beta=-2.14µm, p=0.077).

Conclusion In this large community-based cohort investigating modifiable risk factors in MS, high alcohol intake was associated with retinal features indicative of more severe neurodegeneration while smoking was associated with higher odds of being diagnosed with MS.

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