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# Evidence for causal effects of lifetime smoking on risk for depression and schizophrenia: a Mendelian randomisation study

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## **Abstract**

**Background**

Smoking prevalence is higher amongst individuals with schizophrenia and depression compared with the general population. Mendelian randomisation (MR) can examine whether this association is causal using genetic variants identified in genome-wide association studies (GWAS).

**Methods**

We conducted two-sample MR to explore the bi-directional effects of smoking on schizophrenia and depression. For smoking behaviour, we used (1) smoking initiation GWAS from the GSCAN consortium and (2) we conducted our own GWAS of lifetime smoking behaviour (which captures smoking duration, heaviness and cessation) in a sample of 462690 individuals from the UK Biobank. We validated this instrument using positive control outcomes (e.g. lung cancer). For schizophrenia and depression we used GWAS from the PGC consortium.

**Results**

There was strong evidence to suggest smoking is a risk factor for both schizophrenia (odds ratio (OR) 2.27, 95% confidence interval (CI) 1.67–3.08, *p* < 0.001) and depression (OR 1.99, 95% CI 1.71–2.32, *p* < 0.001). Results were consistent across both lifetime smoking and smoking initiation. We found some evidence that genetic liability to depression increases smoking (*β* = 0.091, 95% CI 0.027–0.155, *p* = 0.005) but evidence was mixed for schizophrenia (*β* = 0.022, 95% CI 0.005–0.038, *p* = 0.009) with very weak evidence for an effect on smoking initiation.

**Conclusions**

These findings suggest that the association between smoking, schizophrenia and depression is due, at least in part, to a causal effect of smoking, providing further evidence for the detrimental consequences of smoking on mental health.

https://www.cambridge.org/core/journals/psychological-medicine/article/evidence-for-causal-effects-of-lifetime-smoking-on-risk-for-depression-and-schizophrenia-a-mendelian-randomisation-study/AA82945360EC59FEC4331A7A567309C9