

A respiratory pandemic should focus the mind on tobacco control

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The idea that tobacco smoking may protect against COVID-19 was always an improbable one. Both wreak terrible tolls on human lives; as of 13th July 2021, COVID-19 has killed an estimated 4 million people while tobacco smoking kills 8 million people every year.^{1 2} Yet some early evidence appeared to indicate that smoking tobacco was linked to a reduced risk of COVID-19 infection and death. This finding unsurprisingly generated substantial interest among researchers, the medical profession and the public.³

The paper by Clift *et al*⁴ in this issue advances our understanding of the links between tobacco smoking and COVID-19 by combining a range of relevant data to employ two separate analytic approaches. Together, these analyses suggest a causal role for tobacco smoking in COVID-19 severity. The authors linked data from UK Biobank with primary care records, COVID-19 testing data, hospital admissions and death certificates to perform both observational and Mendelian randomisation analyses. COVID-19 testing data were available only up until August 2020, meaning that data on confirmed infections were concentrated in hospital settings. The observational analyses did not find that current smokers were more likely to have confirmed COVID-19 infection, but they were more likely to be admitted to hospital and to die from the disease. For example, in models adjusting for age and sex, current smokers were more likely than never smokers to be admitted to hospital (OR 2.19, 95% CI 1.63 to 2.92) and to die from COVID-19 (OR 5.93 (95% CI 4.22 to 8.33)). Mendelian randomisation analyses were possible only among white British participants, but these found that increased genetic propensity to start smoking was associated with being more likely to be infected with, and admitted to hospital for COVID-19. Increased risks of infection, hospitalisation and death were all found with increased genetically predicted heaviness of smoking.

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The Clift study confirms previous UK population-based studies including the UCL COVID-19 Social Study, the ZOE COVID-19 Symptom Study and the openSAFELY data.⁵⁻⁷ Analyses of data from the ZOE app up until April 2020 assessed relationships of tobacco smoking with COVID-19, using self-reported symptoms to categorise people as suspected cases.⁶ In models adjusted for age and sex, current smokers were more likely to have the then-classic COVID-19 symptoms of fever, new persistent cough and breathlessness. Associations for reporting a greater number of symptoms—a marker of disease severity—were even greater. Analyses of the *openSAFELY* data, which covers the primary care records of 40% of the UK population linked to more than 10 000 COVID-19 deaths, similarly found that both former and current smokers were more likely to die of COVID-19.⁷ What both of these studies have in common is that results and interpretations differ between statistical models adjusted only for age and sex and those that are adjusted for a wider range of factors such as pre-existing conditions. Analyses adjusted for factors including diagnosed disease found that smokers were at lower risk of COVID-19 than never smokers, stoking more interest in the notion that smoking tobacco could be protective. However, the *openSAFELY* team conducted post hoc analyses of their finding that smokers appeared less likely to die of COVID-19, which gave confidence that this apparent decrease in risk is incorrect. This apparent association was driven by collider bias, where overadjustment in fully adjusted models produces spurious results. Specifically, post hoc analyses found that the protective effect of smoking was driven primarily by adjustment for chronic respiratory disease, meaning that these analyses were adjusting out one of the primary pathways through which tobacco smoking increases risks. The Clift study adds to our confidence that tobacco smoking does not protect against COVID-19 as their Mendelian randomisation analyses are less susceptible to confounding than previous observational studies. Additionally, a *Living Review* of the existing evidence favours an association between current smoking and COVID-19 severity, while recent

data from the Real Time Assessment of Community Transmission (REACT) study finds that smoking is associated with a higher probability of persistent symptoms 12 weeks after COVID-19 infection (so-called *long COVID-19*)^{8 9} Together this evidence all reinforces the existence of the negative impacts of smoking on COVID-19 outcomes.

A respiratory pandemic should be the ideal moment to focus collective minds on tobacco control. A new Tobacco Control Plan for England is due to be published later this year, which presents an opportunity to redouble our efforts. In April, the Royal College of Physicians (RCP) marked almost 60 years since the influential Smoking and Health report with a new suite of recommendations to tackle the blight of smoking.¹⁰ While the decline in smoking in the last 60 years is a testament to previous efforts, the 1962 report noted that ‘both social custom and commercial pressure outbid the voice of caution’, and this remains true today.¹¹ The latest RCP report notes that the UK is not on track to meet goals of smoking prevalence being under 5% by 2030 and that smoking remains a major cause of health inequality. It offers 10 recommendations to correct this. These include new measures such as raising the legal age of sale to 21 years and annual increases in taxation as well as action to reduce the price gap between cigarettes and hand rolling tobacco. Further efforts to support smoking cessation are needed, combining opt-out tobacco dependency treatment in the National Health Service with tailored support for some groups. Groups highlighted for specific attention include those in the most socioeconomically deprived conditions, LGBT people and those with serious mental illnesses. Finally, the RCP recommends restricting the opportunities for the tobacco industry to exploit loopholes in regulation. The tobacco industry has a long history of such efforts that continue to this day, including recently using product innovation to circumvent the 2020 ban on menthol cigarettes. These efforts must be curtailed and the tobacco industry excluded from all policymaking if the UK is to be smokefree by 2030.

Together, the measures recommended in the RCP report offer an opportunity to make smoking history, and a respiratory pandemic is the perfect time to do so.

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