

Smoking and obesity identified to have causal link with susceptibility to severe COVID-19 and sepsis

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An international collaboration of scientists from the UK, Norway and the U.S. have identified genetic evidence supporting a causal effect of smoking and obesity on increasing susceptibility to severe COVID-19

and sepsis.

Published online in *Circulation* today, the results show that both [smoking](#) and higher body mass index (BMI, a measure of obesity) increase risk of severe COVID-19. The same was also true for the risk of developing sepsis, which is a dangerous inflammatory response to infection, experienced by many patients with severe COVID-19.

Confirming the causal connection also highlights that stopping smoking and losing weight can be effective interventions for reducing the risk of developing severe COVID-19 and sepsis.

Led by Dr. Dipender Gill, from St George's, University of London and Imperial College London, the "Mendelian randomisation" study considered separate datasets of 3,199 patients with severe COVID-19 and 10,154 patients with sepsis. Using genetic proxies for BMI and smoking, the researchers were able to assess whether the presence of these genetic signposts in patients were related to an increased likelihood of severe COVID-19 or sepsis.

A typical observational study would examine the association of a risk factor, such as smoking or obesity, on various outcomes, such as mortality or disease risk. In contrast, this research looked at differences in DNA that are associated with smoking and obesity—known as genetic variants.

By analyzing the association of these genetic variants with severe COVID-19, other confounding factors that could also play a role in affecting disease risk, for example relating to lifestyle or environment, could be better ruled out. With such interference reduced, the results of this study represent evidence for causal effects of smoking and obesity on susceptibility to severe COVID-19.

The study also describes that there are various mechanisms by which smoking and obesity may elevate the risk of suffering from severe COVID-19 and sepsis, including inflammation and immune dysregulation.

Dr. Dipender Gill, a clinician scientist and senior author on the paper from St George's, University of London and Imperial College London, said:

"While it's already known that smoking and obesity increase the risk of many serious health conditions, including heart disease, stroke and certain types of cancer, our findings highlight that the implications of smoking and obesity are exacerbated in the current COVID-19 pandemic. Our work supports that something can be done to reduce risk of severe COVID-19, and in particular that losing excess weight and stopping smoking can make a difference. Now, more than ever, it's essential that campaigns highlighting the benefits of losing excess weight and stopping smoking remain central to public health strategies."

Dr. Mark Ponsford, Welsh clinical academic trainee at Cardiff University, and first author, said:

"Observational studies can be vulnerable to bias—for instance because of how patients are recruited or data are collected. We used an approach known as 'Mendelian Randomisation,' a technique that uses genetics to reduce the risk of bias. Studying large publicly-available genetic datasets from well-characterized UK and Norwegian populations, we calculated genetically-predicted exposure to modifiable cardiovascular risk factors. We found that smoking and obesity increased the risk of developing sepsis. Applying this approach to genetic association studies of severe COVID-19, we found the same outcome. This adds to the growing body of evidence that reducing smoking and obesity are important for public health."

Dr. Stephen Burgess, author on the paper and group leader at the Medical Research Council Biostatistics Unit, University of Cambridge, said:

"Previous research has demonstrated that those who are overweight and smoke are at higher risk of severe COVID-19. Our findings strengthen the evidence that [obesity](#) and smoking are causal risk factors, meaning that losing weight and stopping smoking will both reduce the risk of severe COVID-19."

Dr. Tormod Rogne, author on the paper from the Norwegian University of Science and Technology, said:

"A potential issue when you evaluate whether measured BMI and self-reported smoking are associated with COVID-19 is that external factors not accounted for, such as chronic diseases, may confound the associations. The genetic predisposition to BMI and smoking, on the other hand, is generally not affected by such external factors. This fact allowed us to use the study participants' genes to estimate the unconfounded association between BMI, smoking and risk of COVID-19."

More information: Mark J. Ponsford et al. Cardiometabolic Traits, Sepsis and Severe COVID-19: A Mendelian Randomization Investigation, *Circulation* (2020). [DOI: 10.1161/CIRCULATIONAHA.120.050753](https://doi.org/10.1161/CIRCULATIONAHA.120.050753)

Provided by St. George's University of London

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