

Smoking and obesity found to increase risk of severe COVID-19 by 65% to 81%

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Researchers from the School of Public Health, LKS Faculty of Medicine of The University of Hong Kong (HKUMed), in collaboration with The Chinese University of Hong Kong (CUHK)'s Faculty of Medicine (CU



Medicine), confirmed smoking, obesity and lower socioeconomic position (SEP) likely increase the risk of contracting mild to severe COVID-19, using data from large scale genome-wide association studies.

Other exposures thought to be related to COVID-19 risk, such as glycemic traits, type 2 diabetes, and vitamin D, are likely unrelated. The researchers also found angiotensin-converting enzyme 2 (ACE2), the key receptor of SARS-CoV-2, mediates part of the detrimental effect of obesity and SEP. The findings have been published in the *Journal of Medical Virology*.

Epidemiologic studies show a variety of factors related to increased risk of COVID-19, such as type 2 diabetes, although <u>paradoxical findings</u> have also been reported, such as an inverse association of smoking with COVID-19 severity.

However, these associations may not be causal due to limitations in <u>observational studies</u>. Using better designs to understand the determinants of COVID-19 risk would be particularly important to devise effective mitigation measures to reduce the risk of COVID-19 in the population.

In this regard, the research team conducted a comprehensive assessment of the role of multiple risk factors (vitamin D, glycemic traits, <u>blood</u> <u>pressure</u>, smoking, obesity and SEP) in various severities of COVID-19 risk using a method called Mendelian randomization. As genetic variants are used, this approach might circumvent some of the limitations of conventional observational epidemiologic studies. The research team also explored whether ACE2 mediates any of these detrimental effects.

Using Mendelian randomization, researchers extracted genetic variants related to the various risk factors described above (N



The research team found that smoking, obesity and lower SEP likely increase the risk of COVID-19.

For example, one standard deviation (SD) increase of body mass index (BMI) likely:

- increases risk of severe COVID-19 by 81%
- Increases risk of COVID-19 hospitalization by 55%
- increases risk of contracting COVID-19 by 18%

Strong social gradations were also found in COVID-19 risks, with people of lower SEP tending to have a higher risk of all forms of COVID-19. Previous findings on the harm associated with smoking were also confirmed.

"Using a less biased design, our study confirms the importance of smoking and obesity in increasing the risk of contracting all forms of COVID-19. Our study also shows that targeting ACE2 may be a way to mitigate the risk of COVID-19 among those who are obese or overweight, or of low SEP, and may help inform corresponding drug development," said Dr. Ryan Au Yeung Shiu-lun, Assistant Professor, Division of Epidemiology and Biostatistics of the School of Public Health, HKUMed.

"SARS-CoV-2 enters the host cells via ACE2. Recently, various therapeutic approaches have been developed for COVID-19 patients with the utilization of ACE2-modulating medications to effectively control viral entry. Our findings will enhance research into several therapeutic targets for COVID-19 treatment," said Professor Kwok Kinon, Assistant Professor, the Jockey Club School of Public Health and Primary Care, CU Medicine.

This is one of the largest studies to explore the role of various risk



factors in different severities of COVID-19 using Mendelian randomization. It reiterates the relevance of obesity and smoking, which are key factors contributing to disease burden, according to the World Health Organization.

"The strong social gradient associated with COVID-19 risk highlights clearly the inequalities embedded in societies that need to be urgently addressed, and it is likely relevant to other diseases too," added Dr. Au Yeung.

"It is understandable that smokers and people who have high BMI may have difficulty in quitting smoking or losing weight immediately to reduce their COVID-19 risk. Therefore, these high-risk groups are strongly encouraged to receive the booster dose of the COVID-19 vaccine as soon as possible to mitigate any severe COVID-19 outcomes.

"This study highlights the importance of genomics and big data analytics in understanding the causes of diseases. In particular, it is an exemplar of enhancing the understanding of the interaction between infectious diseases and non-communicable diseases," said Professor Kwok.

More information: Shiu Lun Au Yeung et al, Does ACE2 mediate the detrimental effect of exposures related to COVID-19 risk: A Mendelian randomization investigation, *Journal of Medical Virology* (2022). DOI: 10.1002/jmv.28205

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