

## Sex difference and smoking predisposition in patients with COVID-19

The outbreak of novel coronavirus disease 2019 (COVID-19) is quickly turning into a pandemic. Although the disease is now better contained in China, 32 702 cases remain as of March 2, 2020. 10 566 cases and 166 deaths outside of China had been reported as of March 3 (WHO situation report 43), which is a large increase from the 2918 cases and 44 deaths reported on Feb 26 (WHO situation report 37). Rapid progress has been made with diagnostic reagents (eg, nucleic acid detection and detection of IgM or IgG, or both), drug repurposing (eg, remdesivir and chloroquine), and vaccine production. Studies on the biology of viral infection and clinical management of the disease have also been published, some of which have demonstrated that differences in COVID-19 disease prevalence and severity are associated with sex, and smoking is related to higher expression of ACE2 (the receptor for severe acute respiratory syndrome coronavirus 2 [SARS-CoV-2]), so that might also be a factor. One study (preprint),<sup>1</sup> using single-cell sequencing, found that expression of ACE2 was more predominant in Asian men, which might be the reason for the higher prevalence of COVID-19 in this subgroup of patients than in women and patients of other ethnicities. One study of 140 patients with COVID-19 in China,<sup>2</sup> found the sex distribution equal; whereas, in a study of critically ill patients,<sup>3</sup> more men were affected (67%) than women. In a latest report<sup>4</sup>

of 1099 patients with COVID-19 from 552 hospitals in 30 provinces in China, 58% of the patients were men. Taken together, these data seem to indicate that there might be a sex predisposition to COVID-19, with men more prone to being affected.

This sex predisposition might be associated with the much higher smoking rate in men than in women in China (288 million men vs 12.6 million women were smokers in 2018). Of note, one study (preprint)<sup>5</sup> found that although ACE2 expression was not significantly different between Asian and white people, men and women, or subgroups aged older and younger than 60 years, it was significantly higher in current smokers of Asian ethnicity than Asian non-smokers; although no difference was found between smokers and non-smokers who were white. Nonetheless, the current literature does not support smoking as a predisposing factor in men or any subgroup for infection with SARS-CoV-2. In the study by Zhang and colleagues,<sup>2</sup> only 1.4% of patients were current smokers, although this number was much higher at 12.6% in the study by Guan and colleagues.<sup>4</sup> The relatively small proportion of current smokers in each of these two studies compared with the proportion of male smokers in China (50.5%) are unlikely to be associated with incidence or severity of COVID-19. A trend towards an association was seen between smoking and severity of COVID-19 in the study by Guan and colleagues<sup>4</sup> (11.8% of patients with non-severe disease were smokers vs 16.9% who had severe disease), but it was not significant. Without strong evidence of an association between smoking and prevalence or severity of COVID-19 in Asian men compared with other

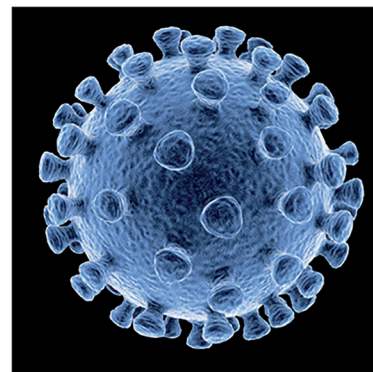
subgroups, no firm conclusions can be drawn. With more cases being examined from different ethnic and genetic backgrounds worldwide, ACE2 expression variation can be better analysed and compared to establish whether it contributes to susceptibility to COVID-19 across the different subgroups.

I declare no competing interests.

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For the WHO COVID-19 report 43 see [https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200303-sitrep-43-covid-19.pdf?sfvrsn=2c21c09c\\_2](https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200303-sitrep-43-covid-19.pdf?sfvrsn=2c21c09c_2)

For the WHO COVID-19 report 37 see <https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200226-sitrep-37-covid-19.pdf>