Review of "Smoking, vaping and hospitalization for COVID-19"

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The authors searched PubMed on 1 April 2020 for studies reporting the prevalence of smoking in patients hospitalised with COVID-19 in China. From 432 studies, they identified 13, that reported smoking status of 5960 patients. The pooled prevalence of current smoking was 6.5%, substantially lower than Chinese population smoking prevalence of 26.6%, 50.5% in males and 2.1% in females. This (alongside similar recent data from the US Centres for Disease Control) has raised a question as to whether current smoking is protective against COVID-19 hospitalisation

The reviewed studies are cross-sectional in design, i.e., offer a snapshot of data at a condensed point in time. Cross-sectional designs are the weakest form of observational study in epidemiology. Taken on their own, such data cannot prove that smoking protects against COVID-19 hospitalisation.

A significant weakness of the reports is that they are not accompanied by statements of reliability of the data on current smoking. The reliability of hospital inpatient smoking surveys is poorly reported in the literature as a whole. Twenty one years ago a study from Australia found that about two-thirds of smokers could be correctly identified at admission (https://www.ncbi.nlm.nih.gov/pubmed/10641361). One can't assume that such a figure holds true for China or the USA in the context of a pandemic crisis. In the absence of reliability data, "current smoking status", a primary endpoint for these analyses, has to be viewed as unvalidated.

For example in the case of the Chinese data, male gender in that country is strongly associated with smoking. Chinese COVID-19 hospitalisations by gender reveal a 23% excess for male (3286) versus female (2673).   Gender is a robust classifier. It is much more likely to be accurately and thoroughly recorded, than is self-reported smoking status at admission. If smoking were truly protective against hospitalisation, one would expect to see more Chinese women than men admitted with COVID-19. The reverse is true.

Another thing to undermine inference from smoking status to COVID-19 hospitalisation would be any difference in structure of the reported populations from the national average. For example it is possible the studied populations might have lower smoking

prevalence in relation to factors such as age, ethnicity, or economic status. Such information is not available in the reports.

In general it is understood that smoking increases the risk of hospitalisation with respiratory disease. For example, in 2019 Han and colleagues found that current smoking increased the odds of influenza hospitalisation by 50% (odds ratio of 1.5, 95% confidence interval 1.3–1.9, https://www.ncbi.nlm.nih.gov/pubmed/30789425). This work was based on a pooled analysis from 12 studies, some using the more reliable case-control designs.

The authors hypothesise that nicotine might be protective against SARS-CoV-2. There is a prior literature about nicotine's effects on expression of angiotensin converting enzyme 2 (ACE2) receptors, that the virus uses for cell entry. This is an hypothesis worthy of study. But obviously smoking involves many exposures, of which nicotine is only a part. There could be any number of mechanisms at work.

In conclusion, the report is worthy of publication in light of its startling finding of lower than expected prevalence of current smoking in these patients. The apparent link is weakened by an unvalidated endpoint (current smoking status), and absence of supporting evidence by gender. Further investigation is warranted.

PS as a reviewer I'm not a fan of the star system. Some further comments are on our website https://www.endsmoking.nz/?p=436.