

Review of: "Low incidence of daily active tobacco smoking in patients with symptomatic COVID-19"

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I have given a low rating to this paper because, in all studies of this type, there is a significant risk that the many assumptions (explicit and implicit) are leading to an apparent correlation between non-smoking and symptomatic Covid-19 when, in reality, no such correlation exists. This requires the authors to enumerate in considerable detail the assumptions they have made, the reasons they might be incorrect and the evidence that persuades them that those assumptions are valid. However, the attempt to do this is superficial and the paper includes unsubstantiated denials of potential selection bias such as "It is, however, very unlikely that the very low SIRs that were estimated both for the out- and inpatient groups are the result of the study setting."

The key assumptions may be divided into those that relate to: -

- 1) The accuracy of the data on smoking habits of patients
- 2) The appropriateness of the reference population

In addition, even though the authors accept that correlation does not mean causation, they then proceed to speculate on the mechanism for precisely such a causative relationship. They can only reasonably do this if they have rigorously eliminated the possibility that there are no other factors which might depress smoking rates in those most likely to become symptomatic Covid-19 patients. By way of example, it is known that those dying of Covid-19 are more likely to be old, male and have comorbidities. This makes it plausible that those with comorbidities are more prone to become symptomatic Covid-19 patients. Some of those with comorbidities who have seen a doctor will have been counselled to stop smoking. The above is conjectural but, as the authors say, "Because this is a cross-sectional study, we cannot confirm the causality of this association." Accordingly, they need to do significantly more work to eliminate the possibility that smoking is reduced and risk of symptomatic Covid-19 is increased by some other parameter (e.g. comorbidities) that results in a non-causative correlation between those two factors before they can say things like "We cannot also identify which

of the many compounds of tobacco exerts the protective effect of smoking on COVID-19.”

1) Accuracy of the data on smoking habits of patients

Other reviewers have commented on the accuracy of identification of ex-smokers and one reviewer has reasonably criticised the failure to confirm smoking status biochemically. The importance of this may be judged from the Schofield and Hill paper (1) which found that “Only 63% of the patients classified as smokers on the basis of urinary cotinine levels were recorded as smokers on the computerised record created by hospital admissions staff.” One of the reasons for this is that most smokers are aware that medical staff will disapprove of smoking and there is a well-known phenomenon in market research known as the “socially desirable response” where people give answers to questions which reflect their assessment of the response the questioner would like to hear rather than the factually correct answer.

2) Appropriateness of reference population

The key assumptions here are: -

- 1) The France-wide survey of smoking from 2018 is a reasonable representation of smoking prevalence within the hospital's catchment area population.
 - a. The authors note that smoking prevalence differs across socio-professional categories but make no attempt to estimate by how much this may invalidate this assumption. Given that, on the latest available UK figures, smoking prevalence among managerial and professional occupations is less than 40% of that in routine and manual occupations, this seems surprising.
 - b. They take no account of other dimensions along which the prevalence of smoking varies by factors of over 2 in the UK (2) and which may be relevant to differences between the catchment area population and the national population in France including
 - i. Economic activity
 - ii. Relationship status
 - iii. Education
 - iv. Ethnicity
 - v. Country of birth
 - vi. Religion
 - vii. Housing tenure

1. Schofield PE and Hill DJ How accurate is in-patient smoking status data collected by hospital admissions staff? <https://doi.org/10.1111/j.1467-842X.1999.tb01555.x>
2. ONS Adult smoking habits in the UK: 2018
<https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/healthandlifeexpectancies/bulletins/adultsmokinghabitsingreatbritain/2018>