

Review of: "The association of smoking status with SARS-CoV-2 infection, hospitalisation and mortality from COVID-19: A living rapid evidence review with Bayesian meta-analyses (version 11)"

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Potential competing interests: The author(s) declared that no potential competing interests exist.

Overall, I find this review of high quality, with major strengths due to the progressive inclusion of studies with Bayesian analytical approach.

However, I think that the contribution would benefit of addressing some unclear points and of improving the presentation of the results in the tables.

Eligibility criteria and search strategy

If the primary question of this review concerned the association between smoking and Covid-19 outcomes why to include among the exposures vaping, medicinal nicotine, etc? A rationale should be given and eventually separate PICO questions should be formulated and reflected in the title.

On the same note, why to include RCTs? (smoking as an exposure is hardly randomized)

[From the flow-chart on study selection and from quality appraisal it seems again that only smoking exposure was considered].

Presentation of the results

While the figures are quite informative and easy to grasp, the tables (2-4) are not.

1. I do not understand the purpose of presenting the data in the way the authors do, i.e. giving % of current/former/never smokers among positive or negative respectively to the outcome of choice. It would be logical to present the % with the outcome in categories of the exposure, i.e. % of Covid 19 positive (or negative) among current, former and never smokers. In this way the reader would link the associations presented in the figures with the table data in a much more intuitive fashion. In addition, one may be able to save some columns.

As an example: in the first study in table 2 (Rentsch) one would be able to read

% of tested positive among CS = 9.9; among FS=20.3; among NS=20.7, therefore immediately linked to the RR of 0.49 given in the forest plot

1. I do not understand the purpose of the column labelled "current/former smokers (%)", which is by the way mostly left empty even if the information is extracted
2. I suggest also to report the study design in all tables, (now given only in supplementary table 2). It would help the

readers to judge on the potential limitations of the presented associations (e.g. the word "risk" should be restricted to longitudinal studies with prospective assessment of the exposure)

3. On the same note, the authors state that the majority of the included studies were observational (paragraph results, lines 8-9). From table S2 (not S1, as stated in the paragraph) I counted 6 RCT in the list, the majority pharmaceutical. How were these studies used in the review?
4. A typo in table 3 title should be corrected
5. The expression "risk of" (e.g. hospitalization) should be confined to longitudinal studies that follow up cases to the event. I guess that this is not the case in all studies included in the metaanalysis. To my knowledge, many studies just compared the prevalence of exposure among cases hospitalized and non hospitalized, respectively
6. Severity/progression of the disease and deaths are only related to hospitalized patients – this should be clarified in all tables and text (including abstract).

Discussion

Overall, I find the discussion well structured and balanced.

A few notes:

1. Occupation should be cited as a likely confounder (strong determinant of infection probability (see point 2 I) and correlate (negative or positive) of exposure (e.g. hospital workers); as well as a selection factor (e.g. opportunity to get tested) that would differ among smokers and non smokers
2. I do not understand the relevance of point 2II in the context of explanation of the negative association current smoking-Covid 19 infection. Are smokers exposed to a different micro-climate than non-smokers? If air humidity is a moderator of the risk then one would expect a different association in humid climate compared to dry climate. Does the geography of the studies support this hypothesis?
3. One of the most important reasons for the adverse disease course among former smokers may be pre-Covid 19 smoking-related morbidity, a cause of disease severity and a determinant of quitting smoking. In other words: the adverse outcomes among former smokers may be mediated by smoking-related diseases while current smokers may represent a selected subgroup of relatively "healthy" smokers.