27-Feb-2021
BMJ-2021-064273.R2
Post-COVID syndrome in individuals hospitalised with COVID-19: a retrospective cohort study

Dear Mr. Ayoubkhani

Thank you for sending us your revised paper, which is considerably stronger and clearer. We appreciate the changes you have made and your responsiveness to the comments made by our editors and the reviewers. We sent it back to our statistical editor and the following issues were raised that require clarification before we can finalize our decision:

- Missing values are handled by the missing indicator approach (i.e., using an 'unknown' category) – this is widely considered as being potentially problematic, as it can lead to unpredictable bias outside a randomized controlled setting (Knol et al J Clin Epidemiol 2010; Henry et al J Vasc Surg 2013; Groenwold et al CMAJ 2012); Pedersen et al Clin Epidemiol 2017 and many more). There is a non-ignorable amount of missing data for some covariates. Please provide additional justification for using the missing indicator approach and address the limitations of this approach in your Discussion.
- Continuous predictors (age, BMI) handled by arbitrary (coarse) categorisation (losing information) for the main analysis, unclear why this was done, keeping them on their continuous scale would've been more appropriate, and not assuming a functional form and examined using splines. A sensitivity analysis was done using polynomials (for age) though not BMI (why not) – these results are not presented, if they are making claims that the results remain unchanged, then these should be presented in the supplementary material (unless I missed them). At the very least, please further justify these decisions.
- Some justification is needed for examining by <70 versus >70 years of age in the Methods. One would normally keep this on the continuous scale and handle with an interaction and possibly a spline. However, I appreciate interest in this cut-off might have been driven by other considerations.
- The analyses examining white versus non-white, how were the 'unknowns' handled?

While we are not expecting you to redo your analyses to address these comments - unless your research team expects that making these changes would alter the conclusions drawn from your analysis, we hope very much that you will be willing and able to revise your paper in response, so that we will be in a better position to understand your study and decide whether the BMJ is the right journal for it. We are looking forward to reading the revised version and, we hope, reaching a decision.

In addition to the statistical editor comments, please address these minor comments:
- Rather than using the phrase "compared with background levels", please instead say "when compared with expected general population risk".
- Please write out post-COVID syndrome rather than use the acronym PCS.
- Please clarify how readmission risk was assessed when compared to the general population. Since these patients were not hospitalized, we presume that they were simply "admitted" (as opposed to being readmitted).
- Rather than using the phrases "adverse events", we would prefer you consistently use the phrase or "post-discharge multi-organ dysfunction".

When you return your revised manuscript, please note that The BMJ requires an ORCID ID for corresponding authors of all research articles. If you do not have an ORCID ID, registration is free and takes a matter of seconds.

Yours sincerely,

Joseph S Ross MD MHS
Associate Editor BMJ