Rapid Reviews COVID-19

Review 2: "SSRIs and SNRIs and Risk of Death or Intubation in COVID-19: Results from an Observational Study"

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RR:C19 Evidence Scale rating by reviewer:

- **Potentially informative.** The main claims made are not strongly justified by the methods and data, but may yield some insight. The results and conclusions of the study may resemble those from the hypothetical ideal study, but there is substantial room for doubt. Decision-makers should consider this evidence only with a thorough understanding of its weaknesses, alongside other evidence and theory. Decision-makers should not consider this actionable, unless the weaknesses are clearly understood and there is other theory and evidence to further support it.

Review:

This observational study has tried to assess the use of SSRIs and SNRIs and risk of death or intubation in COVID-19 patients.

In the abstract section, some background information would be helpful in addition to the importance provided. The other part of the abstract seems fine.

The introduction provided is fine. It provides the background information on COVID-19. It focuses on the absence of a vaccine or curative treatment and the need of effective treatment for COVID-19. Evidences on the use of antidepressants to lower the plasma levels of cytokines involved in pathogenesis of COVID-19 has been explained. Based on the evidences, the study has hypothesized that use of antidepressants would be associated with reduced risk of intubation or death.

In the methods part, the settings of the study is well described. The data sources is fine and the variables assessed is sufficiently presented. In the section 2.4 exposure to antidepressants, it would be better to describe the number of persons exposed to antidepressants and the rationale for it. The schedule of provision of antidepressants or its different types are not clear. The section of statistical analysis is fine.

The results have been presented in different subheadings. The characteristics of the cohort and the study endpoints have been well described. Necessary tables and figures have been presented. However, I am not quite sure about the e-tables and e-figures as there was no access to them.

The discussion seems fine.

In the present context of COVID-19, the findings can be considered novel. The use of antidepressant may be associated with lower risk of intubation and death. However, this association has not been established. This provides the insights that further studies and clinical trials are required. Also, the findings can be considered interesting as the preliminary findings from this study indicated that use of antidepressants can lower the risk of intubation and deaths from COVID-19. So more evidences are required to prove this. This call for more research and clinical trials to see the association between use of antidepressants and low risk of intubation and death. The societal impact is that the use of antidepressants could save lives of people from COVID-19.

The study design and analysis requires more descriptions in terms of provision of antidepressants. The schedule/interval, doses, follow up etc needs to be explained.

The conclusions drawn are supported by the results.

The article cites the current literature. The article has discussed about its limitations as well.

The structure of the paper can be improved. The article seems a little long, hence it should focus on only the major parts to be covered in the article. Other parts of the paper is fine.

The tables and figures mentioned in the article are not accessible. The data and code used are also not accessible.

Regarding ethical concerns, the authors mentions about getting approval from IRB and that the study has adhered to all ethical standards but not adequately described.

Based on the review, the article can be considered for publications with minor revisions as mentioned above.