Rapid Reviews COVID-19

Review 2: "Factors Driving Extensive Spatial and Temporal Fluctuations in COVID-19 Fatality Rates in Brazilian Hospitals"

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RR:C19 Evidence Scale rating by reviewer:

- **Reliable.** The main study claims are generally justified by its methods and data. The results and conclusions are likely to be similar to the hypothetical ideal study. There are some minor caveats or limitations, but they would/do not change the major claims of the study. The study provides sufficient strength of evidence on its own that its main claims should be considered actionable, with some room for future revision.

Review:

Summary of the paper

This manuscript studies the fluctuations in COVID-19 Gamma variant fatality rate, and correlates such fluctuations with spatial characteristics including inequity, and healthcare capacity. The authors first show the increased frequency of the gamma variant within each of the studied cities. They limited the study on unvaccinated admitted COVID patients that are resident in their respective city and found that the fatality rate among these patients was 24.87% (before adding additional estimated fatalities to take underreporting into consideration). Using such data, the authors visualise the weekly fatality rate in each city, for each age group, and found a transient increase in COVID fatality rate following the Gamma variant, however, fluctuation also existed prior to the Gamma spread. These findings were consistent among age groups and cities. Next, the authors estimated age-standardised fatality rate for each city, by giving a weight for each age-specific trend that depicts the proportion of the population within the corresponding age group. The goal of estimating age-standardised fatality rate is to study the spatio-temporal variation of fatality rates, after removing the age effects on such fluctuation. The authors introduced indices that depict pandemic healthcare pressure at the city level, in order to study the correlation between fatality rate, and healthcare capacity. Each pressure index represents hospital demand (ICU admission) per a specific available resource. Resources include physicians, intensive care specialists, ICU beds, critical care beds, ventilators, nurses, nurse assistants, and physiotherapists. The authors show the correlation (Pearson Correlation) between each pressure index and the weekly fatality rates, for each city. The authors used a regression equation to map the health care pressure effects, non-parametric location effects, and gamma variant effects to the age-specific fatality rate. The authors estimated a 28.8% reduction in the number of deaths after removing

health care pressure effects (pandemic resource limitation) from the regression equation. Overall, the authors conclude that the main drivers of fatality rate fluctuation are the increased health care pressure brought by the pandemic, and the pre-pandemic inequities.

Commentary

Correlation Between Pressure Indices and Fatality Rate

The first finding of the authors is the correlation between the pressure indices and the weekly fatality rates. The authors stated: “We find that all healthcare pressure indices are strongly correlated with the age- standardised, weekly COVID- 19 in- hospital fatality rates in most cities” (page 9). However, looking at Figure 3B and Figure S6 A-J in the supplementary materials, the strong correlation is only apparent in the city of Manaus. Also, when observing the average correlation of each pressure index over all cities, one finds that the correlation ranges from 0.49 to 0.54 only. There are 8 cities where the correlation reached a maximum of about 0.6.

Drivers of Fluctuation and Avoidable Deaths

The authors argue that healthcare pressure and inequity are the main drivers of the fluctuation in the weekly COVID fatality rate, and that a quarter of the reported fatalities could have been avoided if there were no healthcare limitations. The authors’ argument is inferred from a fitted model that estimate COVID fatalities based on healthcare pressure and location-specific pre-pandemic inequities. Although the model was able to adequately replicate the observations (Figure 4), the argument concerning avoidable fatalities needs more analysis and support as such conclusion constitute a major leap, especially with the absence of a strong correlation between pressure indices and fatality in every city. For example, consider ICU admission per ventilators (Figure S6 D). Although the demand on ventilators is fluctuating, we see that the ratio is less than 1 (and less than 0.6 for most cities during the studied period). This indicates that there might not be a shortage of ventilators and adding more ventilators (removing the limitation) will not necessarily lead to a reduction in fatalities. For this to be the case, an additional analysis should take place, one that takes into consideration whether the deceased patient needed a ventilator and was not able to get one. Because if that was not the case, adding more ventilators might be ineffective. This applies for each healthcare resource studied by the authors (physicians, ICU beds,, nurses, etc.). It is possible that the lack of ventilators represented poor management with dire implications that don’t have much to do with ventilators.

In summary, it is expected that the normalised number of deaths increased with the level of resources (one would be surprised if it does not). However, the study, although extensive (as one notes from the supplementary material), did not provide major new insights into the underlying factors for the heterogeneous distribution of COVID19.