Reviewer’s report

Title: The age distribution of mortality due to influenza: pandemic and peri-pandemic

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Reviewer: Alessandro Vespignani

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The paper provides the analysis of influenza mortality in the pandemic, pre-pandemic and post-pandemic periods considering the H2N2 pandemic of 1957 and the H3N2 pandemic of 1968 in six different countries. The analysis aims at the assessment of variations in the age-specific mortality rate determined by the new virus emergence.

Authors compare the exponential fit of the age-specific excess mortality rates for the pandemics with the ones for the preceding and the following seasons. By analyzing variations in the exponential growth they address the phenomenon of shifting mortality toward younger age groups in order to assess underlying mechanisms and implications.

The analysis presented in the manuscript is accurate and the comparison presented among the H2 and H3 pandemics in different countries allows a comprehensive discussion of the mechanisms involved in the mortality shift such as previous exposure of elderly people to the emerging virus and following immune escape.

In summary the paper is sound and interesting and shall be published after the authors have considered the following comments.

Minor essential revisions

1. The organization of the manuscript can be improved in order to make the contents more accessible to the reader. The presentation of the results is often fragmented and repetitive, and contents are not properly distributed in the sections Methods, Results, Discussion and Conclusion. I will give some example:

   a. The Methods section should contain more details including part of the information given in the Supplementary Material (SM), like e.g. the time period spanned by each country dataset.

   b. I would include the contents of the Addendum in the SM, since the current subdivision makes the presentation of work fragmented and thus not easily readable.

   c. Description of Figure 5 should be included in the section Results.

   d. The comparison between the two H2 and H3 pandemics in Canada should be addressed in the section Discussion.

2. The analysis of the pandemics’ attack rates should be discussed more
extensively. Details on the datasets used for the plot of Figure 6 (like e.g. the extent of the datasets) should be given in the SM. Despite the different curves collapse pretty well, I think that a more extensive data collection and analysis should be needed in order to support a pan-pandemic model for the attack rate distribution. Data are rather scant, and in addition to that it is not clear why the data from Davis et al are discrepant. Moreover the sentence “If such viruses are so highly transmissible that only gross features of social contact among individuals determine the case age distribution, there could be significant similarities in attack rates across pandemics” seems to me quite strong and vague at the same time. What do authors mean by “gross features”? Variation in the demographic composition of the population among different years and different countries may potentially have a strong impact on the pandemic outcome. Authors should comment on that.

3. I do not understand the advice in the paragraph “Immunoprotection may be a key to pandemic survival… for organizations, too”. Authors suggest to “consider prospectively recruiting AARPs for positions critical to the missions of their enterprises”. It is not clear to me the motivation behind the advise, considered that, as shown in the analysis, these age groups are still characterized by the highest mortality ratio compared to the whole population.

4. For each country and each pandemic, authors should provide tables summarizing the results of the exponential fitting, including fitting parameters with relative uncertainty, R2 and p-value. This could help the comparison among different seasons and different countries.

5. Figures 1, 2 and 3 are not easily readable. Datasets plotted are too many and it is difficult to discern a particular season. I suggest to restrict the number of seasons included in the plots to 3 or 4 at most, and to report in the tables the results of the fit (as suggested in point 4) for all the seasons.

6. The list of Reference in the SM is missing.

7. The two representations for C&S mortality rate are both presented in the main paper (Figure 5) while one should be presented in the SM. I do not think it is necessary to show all the six countries in the main paper, authors can present the case of US as paradigmatic example and move the others to the SM.

8. Figures do not appear in the same order as they are mentioned in the text.

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

no competing interests