Author's response to reviews

Title: Population Mortality during the Outbreak of Severe Acute Respiratory Syndrome in Toronto

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Author's response to reviews: see over
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Editorial Board
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Re: Population Mortality during the Outbreak of Severe Acute Respiratory Syndrome in Toronto

Thank you for the opportunity to revise and resubmit the above manuscript. We have provided detailed responses to the reviewers’ comments.

Reviewer 1: Christopher Booth

Discretionary Revisions:

1. Page 2 Para 1. Add word: "the period of THESE infection control measures..."

We have made this change.

2. Page 6. Do the authors have data to support their assertion that clinical services were not restricted outside Toronto?

The public health order suspending elective surgery and other non-urgent hospital-based services was specifically directed only at the Greater Toronto area. We do not have empiric data on the volume of clinical services delivered outside Toronto during the SARS outbreak.

3. Page 10 Para 3. Agree with the statement that this study does not account for longer term mortality. One major concern during the SARS outbreak was whether the delay of cancer surgery, and adjuvant chemotherapy/radiation would lead to increased relapses in patients who were treated during the SARS outbreak. Although this data may be hard to obtain and sample size may small it would be of interest to know if longer-term cancer-related outcomes were worse for patients diagnosed/treated in the spring of 2003.

We agree that this is a very interesting and plausible hypothesis, and we are in the process of conducting the study suggested by the reviewer.

4. Page 11 Para 1. Line 14. Once again – do the authors have data/information related to curtailing of clinical services in jurisdictions outside Toronto?

See response to #2 above.

5. Page 12. Para 1. If (as the authors suggest) future research is needed in this area it might be worthwhile to propose that data capture systems are established in advance of future pandemics/disasters so that rising mortality/morbidity associated with restricted access to routine health care is monitored during such an event. In a
prolonged outbreak this would be very useful information to the disaster response team and aid in planning which services should be prioritized during a period of severely restricted health services. We were fortunate in 2003 that the SARS outbreak was relatively short-lived. In the event of an influenza (or other infectious disease) outbreak the duration of infection control measures could be considerably longer.

We have added a statement to this effect in the discussion section of our paper.

**Reviewer 2: Gerardo Chowell**

**Major Compulsory Revisions:**

1. The interrupted time-series analyses undertaken by the authors need some more work. The authors need to show the mortality time-series predicted by their analyses and compare with the observed mortality. From Figure 1, one can see a significant increase in mortality in 2003 around weeks 24-25 relative to mortality in 2001 and 2002. However, the authors claim no significant increase in mortality during the SARS outbreak in Ontario, Canada. This might be the result of the four-week lag chosen by the authors to the pulse-function effect used in their interrupted time-series analyses. The authors should conduct a sensitivity analysis on this lag because changes on this could lead to different conclusions. Also, how the adjustments on seasonality were performed were not clearly explained in the text. Claiming that the time-series analyses did not reveal significant change in mortality is not sufficient. This statement should be supported quantitatively.

The apparent increase in mortality in weeks 24-25 (based on the reviewer's visual inspection of the graph) was not supported by the time-series analysis (see Figure 2 in the revised manuscript).

We have conducted a sensitivity analysis looking at the effects of using a 2-week and 6-week lag.

In the methods section, we have clarified how adjustments for seasonality were performed.

2. Data of the population of Ontario outside the Greater Toronto Area are not shown.

Data on mortality rates outside the Greater Toronto Area are given in Table 1, which shows the results of our Poisson regression analysis. We do not think it is necessary to show these data in a figure.

3. More informative figures: The authors are encouraged to plot the mortality curve in 2003 and the mortality curves in 2001 and 2002 with the corresponding 95% confidence intervals. This plot will help reveal any significant increases in mortality during the SARS outbreak.
In our revised Figure 2, we have plotted the mortality rates for 2001-2003 and the 95% confidence intervals for mortality rates after the onset of the SARS period. This figure shows that there was no significant increase in mortality during the SARS outbreak.

4. The following studies are relevant to this study:
   - Lee et al. BMC Public Health (2005). The immediate effects of the severe acute respiratory syndrome (SARS) epidemic on childbirth in Taiwan

We now reference these papers in the discussion section and present our findings in the context of these studies.

5. The end date of the SARS epidemic defined by the authors to be July 2, 2003, the date that WHO removed Toronto from the list of SARS-affected areas does not match the date indicated in the figures.

   July 2 is the midpoint of the 52-week calendar year and thus marks the beginning of the 27\textsuperscript{th} week of the year. In the figures, the broken line indicating the end date of the SARS outbreak is placed at week 27.

6. Figures 1 and 2 appear to be exactly the same. Figure 2 is supposed to show weekly mortality rate per 100,000 population in the Greater Toronto area.

   There was an error in the preparation of the figures. Figure 1 (showing the number of deaths) was used twice. We are submitting a revised Figure 2 that shows mortality rates for 2001-2003 (see response to #3 above).

Reviewer 3: Sik To Lai

General:

The lack of increase in general mortality may not be accounted for by the maintenance of access for life-threatening conditions during the SARS outbreak alone. In a study published by Lo JYC, et al. (Respiratory Infections during SARS Outbreak, Hong Kong, 2003\textsuperscript{a}; Emerg Infect Dis 2005; 11:1738-1741) showed a possible association between population-based hygienic measures and the reduced incidence of influenza and other acute viral respiratory infections. Complications in patients suffering from chronic medical problems precipitated by acute viral respiratory infection are thus decreased in incidence. This possibility can affect the overall mortality rate and warrants some discussion.

We have referenced this paper in our discussion, and we mention this possible beneficial side effect of the SARS outbreak.

Minor Essential Revisions:
The legends on the left side of the graphs in Figures 1 and 2 appear the same though one is on the actual number of deaths and one is on the number who died per 100,000 of the population. Amendment is required.

Please see our response to Reviewer 3, Comment #6.

**Reviewer 4: Shan-Chwen Chang**

Major Compulsory Revisions:

1. *Figure 1 and Figure 2 are totally the same. There must be some mistakes in preparation of the manuscript.*

Please see our response to Reviewer 3, Comment #6.

2. *Page 7, in “Mortality Rates” section, the authors described that they calculate weekly age- and sex-specific mortality rate. But there was no any sex-specific mortality rate data shown in the results.*

We have corrected this error by eliminating all references to sex-specific mortality rates.

We hope that these revisions meet with the approval of the editors and the reviewers. Thank you.

Sincerely yours,

Stephen Hwang, MD, MPH