Author's response to reviews

Title: Acute Kidney Injury Among Critically Ill Patients with Pandemic H1N1 Influenza A in Canada

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Author's response to reviews: see over
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Hayley Henderson
Executive Editor, *BMC Nephrology*

Dear Dr. Henderson,

Re: Resubmission of MS: 3773987698747864 entitled “Acute Kidney Injury Among Critically Ill Patients with Pandemic H1N1 Influenza A in Canada”

Thank you for the opportunity to revise and resubmit our manuscript to *BMC Nephrology*. We have reviewed your letter of 16 May 2013 and have provided itemized responses to the reviewers’ comments below.

**Response to Reviewer 1 Comments**

The Tables are too full of data. In particular Table 1 may be limited to data of Day 1 physiology and laboratory parameters. Table 2 may start from Age including the following data until the end. In Table 3 the note n.3 is not mentioned within the Table.

We appreciate the Reviewer’s comments and feedback. We have left Table 1 as is, since it provides data comparing included vs. excluded patients. If the reviewer or editor believes that this Table is better suited to an online appendix, we will move it. We have split Table 2 into two tables – demographics (Table 2), and day 1 values and outcomes (Table 3). We have renumbered the remaining tables. We have clarified the footnote for Table 3.

**Response to Reviewer 2 Comments**

The manuscript BMC-2013 by Bagshaw et al. “Acute kidney injury among critically ill patients with pandemic H1N1 influenza A in Canada: cohort study.” is confirmatory by nature. Authors argue that “There have been few larger scale prospective multi-center cohorts [19,23,26], none of which described the Canadian pandemic. This is the reason why they worked on a multi-centre Canadian cohort”. But, this is a secondary analysis of the reference 27. And comparing to previous publications (see references 13 to 28), the reason why this study is original is not clear.

We appreciate the Reviewer’s comment. To clarify, this study was a prospective observational (non-interventional) cohort study of all confirmed and probable cases of pH1N1-infected patients admitted to 51 intensive care units from across Canada, out of 286 that provide mechanical ventilation (R. Fowler, personal communication). The sample included all available ICUs that were capable of participating in a study focused on capturing pH1N1-related critical illness during the pandemic. Accordingly, this study focused on the epidemiology of AKI and RRT utilization in this cohort. This study was not a secondary analysis of Reference 27, but rather was a substudy of a Canada-wide prospective registry of pH1N1-related critically ill patients that was published in
We believe that reporting of observational data from multiple jurisdiction is valuable, because even if the research question is not novel, the data themselves are novel and provide support for a common clinical experience with AKI in pandemic H1N1 patients. Of the previous publications cited by the reviewer, only 3 are multicentre cohort studies like ours, as we point out in the introduction. We believe that our data have been the most rigorously analyzed and reported to date.

45 values of serum creatinine are missing. How was it possible in a prospective study in ICU? The prospective design of the study is quite unclear.

We appreciate the Reviewer’s comment. The simple explanation for these missing values is that our study, while relatively comprehensive and prospective, was non-interventional in nature. As such, the study did not mandate specific blood tests at selected time points to be performed in pH1N1 patients. Instead, data capture focused on what was available in the patient medical record based on the site-specific ICU standards of care. We have clarified the study design in the Methods (page 4).

First paragraph of discussion: why “Canada wide” when the study setting is limited to a sample of ICU? Did all Canadian ICU units be enrolled in the study? If not, please do not use the substantive: incidence, for AKI case, because of lack of wholeness.

We appreciate the Reviewer’s comment. In response, this study captured pH1N1-related admissions to 51 ICUs from across Canada, out of 286 ICUs that provide mechanical ventilation (R. Fowler, personal communication). A true nationwide population-based inception cohort study of all pH1N1-related ICU admissions occurring during a pandemic would not have been feasible. However, this is a very large sampling of all ICUs in the country and is broadly representative and generalizable. This would be similar, if not more comprehensive, in scope to prior larger-scale prospective cohort studies performed in other jurisdictions (i.e. Mexico, Australia, Spain, and Argentina). Accordingly, we believe, from an epidemiologic perspective, that the estimates of the incidence of AKI among this cohort are representative of the burden of AKI among pH1N1 patients receiving critical care services in Canada. We have clarified in the Discussion section that this study is a sample of all ICUs from across Canada (page 9).

Authors’ conclusion is that the exact balance between needs and resources is difficult to establish. This is not new and the study did not bring solutions. In a prospective study, it would have been more valuable to identify fatal cases that might have benefit from RRT.

We appreciate the Reviewer’s perspective; however, in our study, estimating the potential incremental benefit on survival of the provision of RRT among patients dying with or without AKI was not possible.

If you require any additional information, please contact us as necessary. We appreciate your consideration of our manuscript for possible publication in *BMC Nephrology* and look forward to your review.

Yours sincerely,

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