

Article details: 2020-0250	
Title	<b>Characteristics and outcomes of hospitalized and critically ill COVID-19 patients in the first phase of the pandemic in Canada: A National Cohort Study</b>
Authors	For the SPRINT-SARI Canada Investigators and the Canadian Critical Care Trials Group
Reviewer 1	Claudio Martin
Institution	London Health Sciences Centre, Critical Care
General comments and author response	<p>The authors report on a cohort of hospitalized patients in Canada with COVID-19 disease. The project is based on an ongoing international registry for acute respiratory disease. This project clearly represents a huge effort by a large number of collaborators with apparently limited resources, which were likely stressed further by this pandemic. While the results are interesting, I think they are not terribly surprising and by now most readers will be aware that early reports of high mortality were not likely generalizable. Given that this paper is based on an international registry, I would expect that the larger group would perform a more detailed analysis and comparison.</p> <p><i>This is true; yet, we feel there is value in having a Canadian specific dataset for Canadian readers. The larger analysis will not report country-specific variables and outcomes, in the interest of privacy and fear of highlighting poor outcomes in specific countries.</i></p> <p>The conclusion is quite vague - the authors should state what specific data is crucial to maintain and expand and how will it be useful?  <i>This has been updated in the manuscript, including the requirement for risk-stratification variables to ensure standardized comparability across regions. How does the comparison to international and temporal data in this paper make that point? In fact, as they point out themselves, the data lacks granularity to perform the more nuanced analysis required to understand even how we use mechanical ventilation, which is fundamental to the support of patients with acute respiratory disease in the ICU. The conclusion could be that this attempt actually failed and we need more detailed data to answer the necessary questions, which of course requires funding and perhaps a different approach such as integrated electronic health databases.</i></p> <p><i>We agree! Hopefully we have highlighted the need for a more robust data infrastructure in place across Canadian regions, but have emphasized this point in the Discussion.</i></p> <p>Other comments:</p> <ol style="list-style-type: none"> <li>1. Is the sample representative of provinces and hospitals? Reference 8 (in CMAJ) is Vancouver area experience - that should be highlighted and specify whether this report includes those cases (117 ICU cases).  <i>This dataset is inclusive of some of those patients, and this has been highlighted.</i></li> <li>2. How do these data compare with other respiratory infections, since a point of discussion is whether COVID-19 is different in presentation and management from</li> </ol>

other viral pneumonias, all pneumonias or sepsis in general  
*References and discussions added*

3.  
Please specify how COVID-19 diagnosis was confirmed.  
*This was specified in the Methods, and left to local practice to guide*

4.  
How did sampling of non-ICU patients impact results (first 60 per hospital rather than random sampling). And did 1st 60 include ICU patients? Or was it 60 non-ICU from each hospital plus all ICU cases? Did all hospitals reach that number? Could there be a "learning" curve? Hospitals with high case loads could do better with experience, or worse if capacity was strained. This should be reported and discussed.  
*Added comments to this point in the Methods.*

5.  
The outcomes listed as secondary are actually subgroup analyses.  
*Clarified in the Methods*

6.  
Were patients enrolled up to July 7 2020? Some detail about the 20 (2.4%) patients not yet discharged should be provided (were they enrolled at the end, ICU long stay? Mostly ICU patients since only first 60 non-ICU were captured?  
*This was clarified in the Methods, as to the sampling strategy*

7.  
Results are hard to follow and understand with flipping between the full cohort and the ICU subgroup. Either discuss them separately or be clearer when stating results.  
*Re-organized the Results section*

8.  
Tables - should show non-ICU patients as own column, e.g. by doing the arithmetic I infer that mortality is  $80/483 = 17\%$ ; oxygen was received by 57% on non-ICU patients (see point #7)  
*The Table 2 has been updated accordingly; given the demographics being relevant to include all hospitalized patients, have kept that table as is, but would be happy to change accordingly.*

9.  
Survival curve flat after 60 days - how many in sample at that time point?  
*Bulk were discharged, so limited numbers remain in hospital.*

10.  
Discussion, p9 2nd para (lines 8-15) can be deleted since not relevant to current data.

*Deleted.*

11.

	<p>Supp Figure 1 - what do grey bars represent (I believe there was no ear pain reported at all - remove or clarify in legend) <i>Updated figure legend</i></p> <p>12. Supp Figure ? (LOS by age group) - legend is redundant since X axis is labelled.</p>
<b>Reviewer 2</b>	Name withheld
Institution	USA
General comments and author response	<p>Comments to the Author</p> <p>This cohort study describes 811 hospitalized patients with COVID-19 at 32 sites in Canada, including 328 who were critically ill. Basic info on demographics, symptoms, and comorbidities are provided, along with limited data on interventions (e.g., medications and organ support) and outcomes (e.g., hospital length of stay and mortality). Notably absent are data on vital signs, physiologic parameters, and laboratory values. Inclusion of data from 32 sites is a strength, but the limited granularity of data is a major weakness. At this point in the pandemic, a sample size of 328 critically ill patients is quite modest (similarly conducted studies from other countries, for example, had sample sizes &gt;10-fold higher).</p> <p>I also did not see any attempt to examine interhospital variation in outcomes, which would have been of interest. <i>Due to limited numbers in many hospitals, these inter-hospital variability determinations were too unstable to report. Additionally, due to privacy concerns, and the possibility for re-identification of sites, this was decided to not include in a public analysis. The small numbers overall are a good thing for Canada, and represent a good proportion of our national ICU population. That being said, we fully agree that it is comparably small to our international cohorts, and hence, does not add much in terms of risk prediction scores or inferential statistics. Hence, the aim to describe the population for the Canadian context, primarily.</i></p> <p>I have the following additional comments:</p> <p>Major</p> <p>It is unclear to me why the authors did not collect more granular data on acute severity of illness on admission to the hospital/ICU, such as SOFA score, PaO<sub>2</sub>/FiO<sub>2</sub> ratio, urine output, etc. Even “inotropes/vasopressors”, as shown in Table 2, appears to be dichotomized as “yes/no” rather than number of agents used. It is also unclear in Table 2 when these interventions were administered. At any point during the hospital/ICU stay? Did the authors not collect data on the timing of these interventions? <i>I would love to have granular data to calculate SOFA for risk stratification! Our tiered data collection tools had this data, but were only used for a subset of the cohort, making comparisons difficult.</i></p> <p>Unclear definitions in various places. For example, “malignant neoplasm” and “chronic renal disease” (page 8). How were these defined? If the authors can provide the case report form, that would be helpful. <i>Self-defined. A link to the Case-report form (open-access) is provided</i></p> <p>Unclear why there was no attempt to perform multivariable analyses. <i>Edits made, and see above.</i></p>

<b>Reviewer 3</b>	Withheld
Institution	Withheld
Author responses	<p><i>Have provided a preliminary MV analysis, adjusted for age and sex. Given the selected patient population and the main aim as to describe Canadian hospitalized patients, we elected to not provide overly inferential analyses for this cohort. While we have adequate numbers to perform more advanced LASSO analyses and fall within best practices for logistic regression, the use of this for the reader remains debatable.</i></p> <p><i>Updated [added some more recent references].</i></p> <p><i>[Did] Not [analyze or collect the time on mechanical ventilation/ NIV/ high flow] in this analysis. With larger numbers in a global cohort, we will be able to provide more accurate descriptions for inpatient journeys. We do report duration of</i></p> <p><i>We hesitate to provide an analysis of the association of interventions (ie medications or therapies) and outcomes, given the inability to provide any degree of causal inference in this regard. We provide some demographic and care-related variables, but linking any medication or therapy to outcomes is fraught with confounders that would be impossible to correct for.</i></p> <p><i>[... only 10 tracheostomies in a population of 291 mechanically ventilated patients with a length of stay of roughly 16 (22) days] was noted, and not commented upon in the Discussion. It may be due to a general hesitation to tracheostomize these patients, given the risk for nosocomial infection and health-care worker</i></p>