Author’s response to reviews

Title: Population-Based Cohort Study of Outpatients with Pneumonia: Rationale, Design and Baseline Characteristics

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Author’s response to reviews: see over
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Jigisha Patel, MRCP, PhD
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Dear Dr Patel

Thank you for the opportunity to revise and resubmit our manuscript entitled “Population-Based Cohort Study of Outpatients with Pneumonia: Rationale, Design and Baseline Characteristics.” We have addressed the comments in the revised manuscript and have provided a point-by-point response to the concerns. We look forward to your decision.

Reviewer 1: No issues to address

Reviewer 2:

C1. I am interested that the IRB allowed telephone contact of patients and collection of data beyond clinical needs without individual informed consent. However, this has been an evolving area and it appears that a dozen years ago this was deemed acceptable. It appears that the lack of individual informed consent makes specific clinical follow up data unavailable to the research team. While this may not be feasible or allowed currently by the IRB, it would strengthen the study if patient consent could now be obtained so that detailed subsequent clinical information could be accessed.

R1. We appreciate the comment. This information was collected as part of a quality improvement project within the health region. As a result, we did not require individual level consent; however, as we did not receive individual consent at the time, we are also precluded from re-contacting participants.

Major compulsory revisions.

C2. Whether treating physician radiographic interpretations are adequate for defining pneumonia is debatable, but researchers have usually required either a radiologist’s interpretation, or interpretation by the study investigators. Using the more strict methodology, only 53% of the study group actually meet the case definition per the 2007 IDSA-ATS guidelines of having a confirmatory radiographic study. As a minimum, suggest that the patients with and without radiologist’s confirmation of disease be compared and contrasted.

R2. Thank-you for the comment. We have added the following (pg 11): “Overall, patients with abnormal chest radiographs were very similar compared to those with
normal chest radiographs, although the PSI score suggests they may have had slightly more severe pneumonia (Table 3).”

We have added a Table 3 outlining differences between normal and abnormal chest radiographs.

Results pg 12: Overall, 35 (1%) patients died within 30 days of discharge with the majority in those with chest radiograph confirmation of pneumonia (27 vs 8 with normal radiograph, p=0.004).

C3. While PSI was prospectively scored, it would appear to me that the absence of prospective, specific data acquisition will make it difficult for this study to evaluate CURB-65 or A-DROP severity systems among outpatients. Therefore I am uncertain about the statement that they will be able to investigate severity scoring systems other than the PSI.

R3. Our data is currently sufficiently detailed to allow for the calculation of several indices to gauge pneumonia severity including the PSI, CORB, CURB-65, CURB-AGE, and A-DROP. With respect to the CURB calculations, we did not employ the ATM to estimate confusion but have assessed confusion using alternative measures.

C4. The drop out rate among study subjects is not stated here, likely because the investigators do not yet have these data. Presumably, some of the 3000 patients initially enrolled will have moved away from the Edmonton region during the follow up period. This should be stated more clearly as a limitation in this manuscript, and enumerated in the future report.

R4. As our information is linked to the administrative databases, patients can freely move into and out of the region without being lost to follow-up provided they remain within the province of Alberta. Our data currently indicates that we have no losses to follow-up within the first 30 days. As the author indicates, we have not assessed longer-term losses at this time and have added this as a potential limitation.

Pg 13 now reads: “Moreover, it is possible some patients may be lost to follow-up due to out migration from the province and subsequently the administrative datasets.”

Discretionary revisions
C5. Statistical methods – power calculation. In addition to % change and hazards ratios, power calculations depend on the baseline frequency of the outcome, and the number of events observed. For example, if the mortality rate is only 1%, it will hard to validate mortality based severity systems or observe therapy associated differences in mortality. This is addressed in the discussion under limitations. In addition, I worry whether the investigators will “be able to fully examine the impact of an episode of pneumonia on longterm sequelae, health care resources use, and prognostic factors associated with improved or adverse
outcomes including recurrent episodes of pneumonia” - this may require matched controls, a methodology not described in this publication.

R5. We agree that statistical power may be an issue for rare events; however, even for mortality of 1% we have already observed statistical differences with respect to PSI scores, as well as in chest radiographs). As a result, we do feel the cohort will provide important information in a group of CAP patients who have been relatively understudied.

We have added the following to our statistical limitation (pg 12, last paragraph) “For example, the evaluation of specific therapies on short term mortality may be problematic due to low short-term mortality rates.”

We also agree that matched controls would enhance our proposed work; however, we currently do not have data pertaining to matched controls. However, given our datasets, we will still be able to fully evaluate the long term consequences of patients with pneumonia managed on an outpatient setting.

Minor essential revision:
C6. “need for hospitalization” should be changed to language indicating just that the patients were hospitalized. No data in regards to actual need or necessity of hospitalization is presented.

R6. Corrected