Author's response to reviews

Title: A predictive model for the early identification of patients at risk for a prolonged intensive care unit length of stay

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Author's response to reviews: see over
Cover Letter

MS: 9301988483401114 – A predictive model for the early identification of patients at risk for a prolonged intensive care unit length of stay

Dear Dr. Koutsos,

We have addressed the comments of the reviewers in our revised manuscript and provide a point-by-point response to their comments below. We thank the reviewers for their helpful comments.

Sincerely,

Andrew A. Kramer, PhD
Jack E. Zimmerman, MD, FCCM

Responses to Reviewer # 1: Elisa Estessoro

General Comments:

We thank Dr. Estessoro for her suggestions and the positive comments about our study.

Major Compulsory Revisions:

1. You are correct about the limitations imposed by a database. This is probably why length of stay predictive models only attain modest correlation coefficients. We acknowledged the lack of information about ICU-acquired infections, which includes ventilation-associated pneumonia. Our database does not include information about ICU-acquired paralysis, ICU sedation practices, or shock on admission. The latter, however, is reflected by the coefficients for several ICU admission diagnoses, and physiological measures included in the acute physiology score. Our revised manuscript acknowledges the lack of information about ICU-acquired paralysis and ICU sedation practices with appropriate references. Thank you.

2. “Eliminating patients with an ICU stay > 30 days removed 3,435 (1%) of the 343,555 patients in this study.” In fact we did not eliminate these patients, but truncated their ICU stay to 30 days. We did this because the small proportion of patients with a length of stay > 30 days has such extreme and variable values that without truncation these outliers would greatly influence model development. In addition, without truncation these outlier values would affect calculation of...
mean length of stay, as well as artificially reduce the proportion of patient-days for the 99% of study patients with an ICU stay that is less than 30 days.

In our methods section we justified this decision based on data presented by reference 4, which shows that truncating ICU stay to 30 days reduces the impact of these extreme outliers on length of stay calculations and the proportion of patient days used by the majority of patients. We also cited studies used to develop other ICU length stay models that have truncated ICU stay at 30 days. Because this issue is complex and was of concern to both reviewers we have added more information that justifies truncating ICU stay to 30 days and cited multiple studies that have used identical truncation. A model that could predict ICU stay for extreme outliers would be valuable, and is certainly worth considering for future research.

We are aware that LTACs are not widely available in Europe and Latin America, which could result in an even greater proportion of extreme outliers (patients with an LOS ≥ 30 days). LTAC availability, however, had little influence on ICU length of stay in our database. Only 25 (0.2%) of these patients were discharged to LTACs. We acknowledge that a greater proportion of patients may have a prolonged ICU stay in Europe and Latin America, but have clearly stated that the usefulness of our model is probably limited to the U.S.

3. The APACHE IV models for predicting hospital mortality and ICU length of stay were placed in the public domain in 2006 [see references 10 & 20]. We believe that the infrequent use of these tools is primarily a consequence of hospitals maintaining non-digital health information technology systems.

4. We used a backwards elimination approach with p<0.05 necessary to remain in the model. This should have been mentioned in our manuscript and we have inserted this text into the revision. Thus inability to assess GCS due to sedation/paralysis, as well as PaO2:FiO2 still add significantly to the model, even with ventilation at day 5 included. Clinically, it does make sense to include inability to assess GCS due to sedation/paralysis, PaO2:FiO2, and mechanical ventilation on day 5. Although all of these patients are receiving mechanical ventilation, not all will be sedated/paralyzed (e.g. those with neuromuscular respiratory failure), or have an abnormally high PaO2:FiO2 (e.g. those with emphysema). “Other physiological variables” refers to “other day 5 physiologic variables included in the APS”. We have clarified this in our revised manuscript. Thank you.

5. “I would like to see a Kaplan-Meier survival curve of both groups”. By “both groups” we assume that the reviewer means admissions with normal ICU stay vs. admissions with prolonged ICU stay. As a survival analysis technique Kaplan-Meier evaluates time to an event. Since the two groups have predefined limits on their length of stay, comparing survival curves would be inherently biased.

6. The length of the Discussion section is always equivocal. While Reviewer #1 feels the discussion should be shortened, Reviewer #2 found the manuscript “well written and concise”. We believe that our Discussion addresses all pertinent topics succinctly.
7. We’ve added the median and IQR for hospital LOS and duration of mechanical ventilation to Table 5.

8. The diagnoses in Figure 3 were selected according to both frequency and the extent to which their LOS distribution was skewed. We did this to emphasize the differences in skewed distribution rather than just frequency among diagnoses.

**Minor Essential Revisions**

1. APACHE refers to the Acute Physiology and Chronic Health Evaluation system. APACHE IV refers to the fourth generation version of APACHE. Thus, these terms are used correctly in the manuscript.

2. The term “rescaled Glasgow coma score” is defined in Table 1 as “12 – Glasgow Coma Score”.

3. In Table 3, the term “visit” refers to the number of ICU admissions. We have substituted this text in our revision.

4. We have corrected typing errors.

**Responses to Reviewer # 2: Graeme K Hart**

**General Comments**

We thank Dr Hart for his expertise and extremely positive comments.

In regard to long stay ventilation units. We are aware that long-term acute care facilities (LTACs) are not widely available in Europe and Latin America, and Australia and that this could result in an even greater proportion of extreme outliers (patients with an LOS > 30 days). LTAC availability, however, had little influence on ICU length of stay in our database. Only 25 (0.2%) of these patients were discharged to LTACS. None-the-less, a greater proportion of patients have a prolonged ICU stay in Europe and Latin America, which limits the usefulness of our model to the U.S.

**Minor Essential Revisions**

Regarding Coronary Care Units (CCUs).

We believe that their inclusion enhances the usefulness of our model. In the U.S. (and in our database) patients with diagnoses commonly treated in CCUs are also treated in mixed medical-surgical ICUs in smaller hospitals. Most patients admitted to CCUs and mixed ICUs have chest pain, unstable angina, acute MI and have a short length of stay. Our ICU day 1 model was shown to accurately predict length of stay for these patents. Few of these patients reach our day 5 threshold for concern about a prolonged ICU stay.
But patients with other cardiac diagnoses such as cardiac arrest, cardiogenic shock, congestive heart failure, and rhythm disturbances (see Table 4) often remain in an ICU or CCU on day 5. For these patients a prolonged ICU stay is of concern and our model generates coefficients for each of these diagnoses.

2. We did this because the small proportion of patients with a length of stay > 30 days has such extreme and variable values that without truncation these outliers would greatly influence model development. In addition, without truncation these outlier values would affect calculation of mean length of stay, as well as artificially reduce the proportion of patient-days for the 99% of study patients with an ICU stay that is less than 30 days.

In our methods section we justified this decision based on data presented by reference 4, which shows that truncating ICU stay to < 30 days reduces the impact of these extreme outliers on length of stay calculations and the proportion of patient days used by the majority of patients. We also cited studies used to develop other ICU length stay models that have truncated ICU stay at 30 days. Because this issue is complex and was of concern to both reviewers we have added more information that justifies truncating ICU stay to 30 days and cited multiple studies that have used identical truncation.

3. You are correct, as we probably extended our 1991 IRB approval beyond its “use by” date. However Cerner has contracts with each hospital that allows for the use of their data in aggregate for research purposes. Without these agreements the APACHE predictive models could not be updated. All data are stripped of patient identifiers and conform to guidelines set forth in the US Health Information and Portability Act (HIPAA).

4. Thank you for pointing out this potentially confusing text. “Reference Group” only pertains to non-continuous variables. By “Reference Group” we mean the specific level of a discrete variable that serves as the reference group in our multivariate model. For example, ICU Admission Source: there are indicator variables for all of the potential choices except for “Direct Admission”. So those patients aren’t excluded, but serve as the default level. We’ve added some text to Table 1 to more clearly make this point.