Author's response to reviews

Title: The impact of performance status and comorbidities on the short-term prognosis of very elderly patients admitted to the ICU

Authors:

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Author's response to reviews: see over
We would like to thank the reviewers once again for their comments on our manuscript. We provide below, in bold, a point-by-point answer to the reviewer’s queries. Changes in the manuscript have been highlighted in red. Please note that previous changes addressed on the formerly revised version are no longer highlighted in the manuscript.

**Reviewer 1:**

Zampieri and Colombari have done a very complete job in responding to both my concerns and those of my co-reviewer. I have two remaining comments:

We are glad that we were able to respond to most of the reviewer’s previous comments in our revised version. We believe that the peer review process was crucial to improve our manuscript and make it more useful at the bedside.

Regarding the reviewer’s remaining comments, we present our answer below:

1. I worry that comparing the calibration, goodness of fit, and discrimination of the new model (including PS, comorbidities, code status, and SAPS) to that of SAPS in this dataset is potentially flawed. The new model was constructed on this data set but the SAPS score was not. The fit of the new model will, almost by definition, I believe, be better on this dataset, therefore. The more “correct” way to compare the fitness characteristics of the new model and the SAPS score would be to compare them both using a third, entirely independent, dataset. I would ask that the authors at the least address this issue in the limitations section of the discussion section.
The reviewer highlights an important point: A newer model based on a dataset may be more accurate and calibrated than a model built on another sample due to statistical reasons. The model reflects the sample in which it was built. We agree that using a third database would be the “gold-standard” method for this. We tried to overcome this limitation using bootstrap analysis (to evaluate overfitting), but we are aware that even so there may be bias in the analysis. We added, as requested, this limitation to the limitations section of the manuscript, as follows:

“Finally, most customizations of prognostic scores validated on a single sample display better calibration and discrimination capabilities than general prognostic scores that were developed on larger, different samples, since they tend to reflect the sample in which they were built. The most appropriate way to solve this bias would be through the validation of our model on a different, third sample unrelated to ours. We tried to minimize this bias by using a robust statistical analysis with bootstrapping and Monte Carlo replications in order to discard the presence of model overfitting; nevertheless, an independent validation of our results on other settings should be performed”

2. In the last paragraph of the results section, the authors provide the results of the sensitivity analysis suggested by my co-reviewer excluding patients with non-full code status. The plan to conduct this sensitivity analysis should be mentioned in the methods section.

Thank you for bringing this to our attention. This was changed in the manuscript as requested.
Reviewer 2:

During a previous review, I included the following suggestions for revisions (see below). The authors have responded to the suggestions thoroughly and appropriately. My only further revision is as follows:

Thank you for once again reviewing our manuscript. We are pleased to see that we have addressed all your previous comments thoroughly. An answer to your query is shown below.

Minor Essential Revision:

Please further clarify for the readers how the point system for the EPCP was developed as it is not clear from the text in the methods (“we used the rounded values of the beta…” paragraph 5)

Thank you for your comment. We rebuilt the sentence describing how points were attributed to the EPCP score and provided an example in the manuscript. It was indeed not clear in the manuscript and we would like to thank the reviewer for his comments.

Once more, we would like to thank the reviewers for his comments and concerns.

We hope that all queries were addressed.

Best regards,

Fernando Zampieri