



Letter to the Editor

Reply-Letter to the Editor – Methodological issues on prediction of early- and long-term mortality in adult patients acutely admitted to internal medicine

Dear Editor,

We would like to thank Drs. Abbasi and Naderi for their interest in our study and for their comments on our recent article [1]. Their letter offers us the opportunity to explain better the underlined methodological issues and to integrate our analysis in order to validate our developed prediction models.

The study aim was to explore the ability and the relative weight of NRS-2002 screening tool to predict in-hospital and post-discharge (up to 1 year) mortality. Logistic regression models were fitted to evaluate the independent, adjusted predictive power of NRS-2002 on mortality at different time intervals. Furthermore, through the logistic regression models we aimed at predicting the probability of the occurrence of our binary outcome (i.e. mortality) based on a specific combination of covariates as this method is used in biomedical research when the interest is to predict the prognosis of individual patients [2]. On this basis we assessed the performance of the regression models in terms of their discriminative ability in predicting mortality (i.e., the probability that a randomly selected patient who died had a score greater than a similarly selected one who survived) by using the *c*-statistic, equivalent to the area under the ROC curve (AUC) [3,4]. As described in the Methods paragraph, the closer to 1 the *c*-statistics (AUC) value is, the better the model discriminates. In this step, we checked also for potential interactions between covariates. No interaction among the explored risk scores with respect to the mortality risk was expected from clinical perspective. We tested for interaction between

sex and risk scores, and between age and risk scores (for each outcome) and no significant interaction was found.

Having clarified that, we completely agree with Drs. Abbasi and Naderi on the fact that, if the models were not validated, we could have gotten misleading results, with the risk of overestimating the performance of the developed predictive models. Therefore, as suggested, we tested the possible 'over-optimism' in the performance of the final models by bootstrapping technique. This analysis has been proven as the most accurate for estimating internal validity of predictive logistic regression models, providing a bias close to zero [5,6]. According to bootstrapping, for each model one-thousand replications of random sampling with replacement by drawing same size samples from the original data set were performed. The difference between the bootstrap and the original AUC represented the optimism in model performance measures. Optimism-corrected performances and 95% bootstrap confidence intervals were determined (Table 1). The bootstrap optimism estimates ranged from 0 to 0.002, showing an overall good internal validity for the proposed predictive models.

Conversely, as reported in the manuscript, the external validity of the models was not assessed, so that the research findings should be confirmed by testing the predictive models in similar large populations.

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Table 1

Bootstrapping analysis for validation of performance of regression models in predicting mortality [1].

Outcome	Original AUC (95% CI)	Corrected AUC (95% CI)
Hospital mortality	0.843 (0.816–0.871)	0.843 (0.816–0.871)
30-days mortality	0.824 (0.803–0.844)	0.823 (0.802–0.844)
90-days mortality	0.809 (0.792–0.826)	0.807 (0.791–0.826)
180-days mortality	0.790 (0.774–0.806)	0.789 (0.773–0.807)
365-days mortality	0.769 (0.754–0.785)	0.769 (0.753–0.785)

AUC: area under the ROC curve.

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Gianfranco Sanson

School of Nursing, Dept. of Medicine, Surgery and Health Sciences,
University of Trieste, Piazzale Valmaura, 9, 34100, Trieste, Italy

Giulia Barbati
*Biostatistics Unit, Department of Medical Surgical and Health
Sciences, University of Trieste, Strada di Fiume 447, 34100, Trieste,
Italy*

Michela Zanetti*
*Internal Medicine Department, University Hospital, Strada di Fiume
447, 34149, Trieste, Italy*

* Corresponding author.
E-mail address: zanetti@units.it (M. Zanetti).

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