Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Letter to the Editor

Predicting critical illness on initial diagnosis of COVID-19 based on easily-obtained clinical variables: author's response

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To the editor,

We thank Moretto et al. for their thoughtful comments pointing out some aspects of our original article [1] that may be worth discussing in more detail, and we appreciate the opportunity to respond.

In our study, we developed and validated a prediction model called PRIORITY to estimate the risk of critical illness in patients with coronavirus disease 2019 (COVID-19). However, unlike most of the available COVID-19 risk models, our approach was focused on developing a tool that could also be used in resource-limited or out-of-hospital settings. Thus, we only considered simple clinical features available on initial assessment, excluding any other additional test (e.g. imaging or laboratory). When developing our prediction model, we built on previous literature and expert opinion to select the predictors, rather than using a data-driven approach, to avoid biases that have affected previous studies [2]. Moreover, we assumed a number of design requirements (e.g. inclusion/exclusion criteria, merging, and number of predictors) that may limit the discriminative ability of the model, but we met our ultimate purpose of maximizing the applicability of the model in the scenarios for which it was developed.

In our model, age has a relevant impact on risk prediction and is included in the subset of the nine best predictors of critical illness. However, of note, we used fractional polynomials to better model the nonlinear relationships between the outcome and continuous predictors (e.g. age and blood pressure). Thus, the interpretation of their ORs should be carefully considered [3] because the risk does not increase linearly across the entire range of the predictor. Therefore, we advise against interpreting the OR for the age-related term as 14.339 for every 10-year increment, because this OR refers to a 1-unit increment in the quadratic term $(age/100)^2$. We acknowledge that the interpretation of ORs for nonlinear terms can be challenging, so we included in the manuscript the (a) footnote under Table 2, in which we provided linear approximations of ORs for ranges of clinical relevance. For example, the OR for a 10-year increment in age from 40 to 50 years would be around 1.3, whereas for the same increment between 80 and 90 years, the OR would increase to 1.6.

Regarding the possibility of considering therapeutic limitations as a covariate in the predictive model, several points should be addressed. First, as previously mentioned, our model is mostly intended to be applied in a number of settings where it would be difficult to assess at presentation whether the patient would be a candidate for a complete therapeutic escalation (mainly intensive care unit and mechanical ventilation). Likewise, therapeutic limitation criteria could vary across different pandemic scenarios and health care systems. Furthermore, increasing risk due to therapeutic limitation may be especially relevant in elderly patients. As discussed in detail earlier, we modeled the relationship between age and the outcome as a quadratic term to take into account a steep increase in risk for advanced age. Finally, the overall effect of therapeutic limitation on risk may be partially explained by the predictors already included in the model, such as age, comorbidities, or dependency.

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The National Early Warning Score (NEWS) 2 is a standardized and widespread tool used to help prioritize severity, especially in emergency departments. NEWS2 includes as predictors easily obtainable variables, some of which are also included in the PRIORITY model. As noted by Moretto et al., several studies have assessed NEWS2 for predicting critical outcomes in patients hospitalized with COVID-19. Although promising, their findings should be considered in light of some limitations, mainly due to small sample sizes, which may lead to lower performance on different cohorts [2]. Of note, Knight et al. [4] compared in a large external validation cohort the 4C Mortality Score against NEWS, reporting a C-statistic of 0.774 for the 4C Mortality Score vs. 0.654 for NEWS in predicting in-hospital mortality. Additionally, Maves et al. [5] showed that the simple addition of age to NEWS appeared to improve the score's ability to predict progression to invasive ventilation or death among patients hospitalized with COVID-19. In summary, we agree that the comparison of PRIORITY and NEWS2 could be interesting due to their similarities, and the prognostic value of predictors not included in NEWS2, such as age or previous comorbidities, should be considered.

Finally, as extensively discussed elsewhere, although including imaging or laboratory tests may certainly improve the discriminative capacity of the model, it was beyond our objectives as it would limit the model's applicability. Notwithstanding, we appreciate for the suggestion regarding the added prognostic value of CT scans as an interesting approach for further research.

Transparency declaration

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Author contributions

Writing of original draft, review, and editing by AV, MM, MF, and LM.

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