

## Introduction

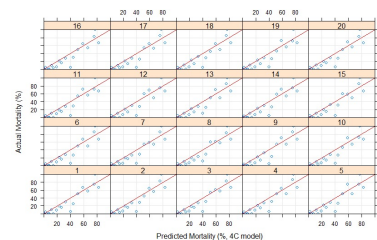
- The management of patients with COVID-19 is challenging for front-line healthcare providers given limited validated, evidence-based clinical decision support. Determining patient mortality risk is critical for effective triage, management, and discharge decision making.
- Numerous COVID-19 risk prediction models have been created, though the robustness of these models varies. The 4C Mortality Score, created by the International Severe Acute Respiratory and emerging Infections Consortium (ISARIC) in Great Britain, is one of the largest-scale, high-performing predictive models published to date.<sup>1</sup> The 4C Score uses 8 weighted variables to predict risk of 30-day mortality: age, sex, select comorbidities, respiratory rate, peripheral oxygen saturation, Glasgow Coma Scale (GCS), blood urea nitrogen (BUN), and C-reactive protein (CRP).
- The 4C Mortality Score has been externally validated in cohorts from England, Holland, Italy, Brazil and Spain; however, this model has not yet been validated in a United States (U.S.) population.<sup>2-5</sup>
- For U.S. clinicians to confidently utilize the 4C Mortality Score, the model must be validated in a population similar to its intended implementation. The objective of this study is to determine whether the 4C Mortality Score is a valid model to predict hospital mortality in United States patients with COVID-19.

## Methods

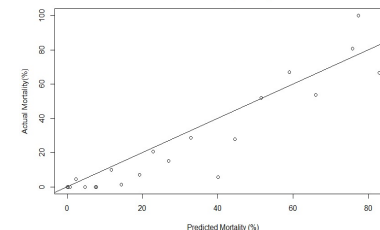
- Patients (n=426) were admitted with a positive SARS-CoV-2 PCR to Thomas Jefferson University Hospital (TJUH) (Philadelphia, PA) between March 1st and June 6th, 2020. (IRB #20E.737)
- Comorbidities were extracted from electronic health records (EHR) by two separate chart reviewers through manual chart review from the discharge summary, the emergency department note, the admission history and physical, the EHR "Past Medical History" and/or "Active Problems" sections. An independent reviewer adjudicated reviewer discrepancies.
- Quantitative data (respiratory rate, oxygen saturation, CRP, BUN, GCS) from the first 24 hours of admission was digitally extracted.
- Twenty imputed datasets were created to account for missing data, using predictive mean matching for numerical variables (e.g., CRP) and logistic regression for binary variables (e.g., obesity). Data was missing for less than 1.4% of variables.
- Receiver operating characteristic curves were calculated for each imputed dataset comparing the predicted 4C Score and actual mortality for each record, and areas under the curve (AUC) were calculated for each curve. A pooled AUC (and corresponding 95% CI) was calculated by pooling all 20 results using Rubin's rule.

## Results

The area under the receiver operator curve of the pooled dataset was 0.85 (95% CI, 0.79-0.89). Figure 1 shows the observed vs. predicted mortality for each imputation (Fig 1A) and the pooled dataset (Fig. 1B)



**Figure 1A.** Observed vs. predicted mortality for 4C Mortality score in the imputed datasets.



**Figure 1B.** Observed vs. predicted mortality of the 4C Mortality score in the pooled dataset.

## Discussions and Conclusion

- With an AUC of 0.85 (95% CI, 0.79-0.89), the 4C Mortality Score performed well in a United States urban population. These findings are consistent with the results of external validation studies in other countries.
- The 4C Mortality Score overpredicts mortality, particularly in the 4C scores <15. This over-prediction may occur more notably in current patient populations given increased availability of effective outpatient and inpatient treatments relative to the study population (prior to June 7, 2020).
- This validation supports the use of the 4C Score in U.S. populations; clinicians should apply carefully accounting for the mentioned limitations.

## References

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