

Anticipating outcomes for patients with COVID-19 and identifying prognosis patterns



Since its first description, SARS-CoV-2 has been the subject of more than 59 000 publications worldwide. Although SARS-CoV-2 infection mainly results in mild disease, during the first COVID-19 wave in France, up to 3% of patients required admission to hospital, 0.8% required intensive care unit admission, and overall mortality was reported to be around 0.5%.¹ The ability to predict disease severity and subsequent course might help with triaging patients, optimising resource management, and understanding modifiable and non-modifiable factors involved in patient outcomes.

In *The Lancet Infectious Diseases*, Belén Gutiérrez-Gutiérrez and colleagues² aimed to identify clinical phenotypes of COVID-19 among patients who required admission to hospital. In this large, multicentre, retrospective cohort study, the authors report the outcomes of 4035 patients with COVID-19 admitted to 127 Spanish hospitals between Feb 2 and March 17, 2020. The authors did a two-step cluster analysis to identify clinical characteristics associated with patient outcomes, and identified three phenotypes with adequate performance in predicting 30-day patient mortality in derivation, internal validation, and external validation cohorts.

Similar to previous studies,^{3,4} severity of COVID-19 was associated with older age, male sex, more comorbidities, and increased body-mass index, and both respiratory failure and extra-pulmonary organ failure were associated with more severe COVID-19. The three phenotypes identified by Gutiérrez-Gutiérrez and colleagues are clinically relevant and in line with criteria usually used in clinical practice. The authors identified a specific phenotype that comprised younger patients without respiratory involvement, who were mainly women and had good patient outcomes. By contrast, another phenotype was identified to be associated with poor outcomes, and comprised older patients, who were generally men with comorbidities and obesity, and who had frequent and severe respiratory involvement and extrapulmonary organ dysfunction. The third phenotype was intermediate, between the other two. Gutiérrez-Gutiérrez and colleagues' study² allows us to appreciate the characteristics of patients with COVID-19, and the

authors should be commended for their thorough analysis and careful interpretation.

However, whether the model and derived calculator might be helpful in clinical practice is unknown. Hence, model calibration—in other words, the ability of the population prediction to apply to individuals—remains uncertain. Confirming that the model is adequate in patients with a high probability of poor outcomes, avoiding underestimation of risk in patients with a low probability of poor outcomes and overestimation of risk in patients with a high probability of poor outcomes, seems mandatory should this model be used for decision making.⁵ The developed model appears to provide an adequate estimate of patient outcomes at a population level, and could be a useful tool to stratify patients in future research, but might be insufficient to be used to estimate individual outcomes. This issue might be further exacerbated by the vast heterogeneity of the studied population, which could have overestimated the input of the predictive model.⁶ Consequently, the model seems to allow identification of high-risk patients, but could have unclear performance and relevance for patients of uncertain outcome, for whom a decision-making tool might be required.⁶

The quality of this study and analysis should not mask further limits to implementation of this model in clinical practice. Thus, the timeframe of the study and restricted access to confounding factors involved in disease severity and clinical presentation must be acknowledged. Ethnicity, deprivation, genetic susceptibility to severe disease,⁷ time since onset of symptoms,³ and distinct immunophenotypes⁸ have been associated with disease severity and might explain within-cluster heterogeneity. Additionally, morbidity and mortality might vary over time,⁴ either as consequences of intensive care unit strain in a specific geographical area⁹ or change in disease management. Finally, more newly described SARS-CoV-2 variants might affect patient presentation, clinical course, and patient phenotypes.¹⁰

Despite these limitations, this study asks important questions concerning the management of patients with COVID-19. Identification of these three phenotypes could be an important step to anticipate patient clinical

Lancet Infect Dis 2021

Published Online
February 23, 2021
[https://doi.org/10.1016/S1473-3099\(21\)00073-6](https://doi.org/10.1016/S1473-3099(21)00073-6)
See Online/Articles
[https://doi.org/10.1016/S1473-3099\(21\)00019-0](https://doi.org/10.1016/S1473-3099(21)00019-0)

course during an era in which physicians and health systems around the world are facing a new surge and emergence of new SARS-CoV-2 variants. Establishing whether these identified phenotypes could be helpful in clinical practice and how they could help us promote adequate management strategies in a rapidly changing epidemic will undoubtedly be the next important step.

MD reports grants and personal fees from MSD, and personal fees from Astelas and Gilead-Kite, outside the submitted work. GD declares no competing interests.

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