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.

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

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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 colleagues[2] 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,[1,3,4] 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' study[2] 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 immunophenotypes[8] 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 area[9] 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

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.

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*Michael Darmon, Guillaume Dumas
michael.darmon@aphp.fr

APHP, Service de médecine intensive et de réanimation, Hôpital Saint-Louis, 75010 Paris, France (MD, GD); Université de Paris, ECSTRA team, UMR 1153, Center of Epidemiology and Biostatistics, INSERM, Paris, France (MD, GD)

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Risking further COVID-19 waves despite vaccination

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The sudden outbreak and global spread of COVID-19 took the world by surprise. Policy makers started to work side-by-side with theoreticians, as there were and still are many unknowns, especially regarding properties of virus variants, and the subsequent future development of the pandemic. In times of uncertainty, mathematical models have shed light on the evolution of the pandemic to the best of current scientific knowledge. In *The Lancet Infectious Diseases*, Sam Moore and colleagues[1] present a model to explore the effects of vaccination and the potential danger of lifting restrictions too early in the UK.

With vaccination progressing, we all want restrictions to be lifted as soon as possible. Lifting them only slowly is like being forced to eat a chocolate cake slowly, after not having any for months. So why should one be cautious? It is intuitively clear that if restrictions are lifted too early then another pandemic wave might strike and affect those who have not yet been vaccinated. Furthermore, even some of those individuals recently vaccinated might not yet be immunised by the time of lifting restrictions and thus remain partly susceptible. Risking the health and lives of such individuals would be unethical.

Can Moore and colleagues tell us when precisely we can have the chocolate cake? Unfortunately, no. There are too many unknown factors that might affect the transmission dynamics of SARS-CoV-2 during the vaccination campaign and thereafter. Including such uncertainties is at the heart of designing a good epidemiological model. Moore and colleagues found that the still unknown level of vaccine-induced protection against infection is crucial to the timing and effect of further waves on viral spread. Furthermore, they quantify how low vaccine uptake, together with a lifting of non-pharmaceutical interventions (NPIs), will induce further waves of hospitalisations and deaths, most of which could be prevented. They also show that only in a best-case scenario of high vaccine uptake (85% protection against infection and high efficacy against severe symptoms) could a gradual relaxation of NPIs be allowed without deaths surging over 500 per day.

Moore and colleagues did not explicitly include variants that escape the immune response (either post-infection or induced by vaccines).[1] This approach does not change their general findings and is straightforward to discuss. Escape variants[2] might have a devastating effect; at worst, they could force us to start the vaccination programme from scratch, including the necessity to re-enforce strong restrictions. If escape