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# Decoding the next SARS-CoV-2 variant

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What will the next SARS-CoV-2 variant bring to the world? Much mental horsepower has been dedicated to this question, ever since it became apparent in mid-2020 that the virus was far from settled into a stable evolutionary niche. The selection pressure on a virus is to generate as many onward infections as possible, whether through changes in its intrinsic transmissibility or through immune evasion. Sure enough, subsequent variants of concern have increased one or both parameters, with more recent variants being both more contagious and far better at evading antibody-driven responses from vaccines and earlier infection waves.[1–3] The process has shown little evidence of slowing either, leading commentators to wonder aloud about the prudence of choosing the Greek alphabet, which contains only 24 letters, to name variants.

A rapid uptick in COVID-19 cases in southern Africa in November, 2021—caused by the variant B.1.1.529, subsequently named omicron by WHO—in turn drove a rapid global surge in cases. The race was then on to work out what the clinical impact of the new variant was likely to be. Virulence is not a primary focus of natural selection, just its by-product, and is thus complex to predict. SARS-CoV-2 had already disproven the comforting, but evolutionary naive, myth that respiratory viruses inevitably evolve towards lesser virulence—the alpha (B.1.1.7), beta (B.1.351), and delta (B.1.617.2) variants had instead proven to be a ghastly sequence of ever-worsening intrinsic virulence.[4] What would omicron bring?

In *The Lancet Global Health*, Waasila Jassat and colleagues[5] describe the clinical severity of the omicron-driven wave in South Africa from Nov 21, 2021, to Jan 22, 2022, comparing it with the country's previous three waves that were each dominated, in order, by the ancestral strain with an Asp614Gly mutation, the beta variant, and the delta variant. The authors have fused elements of South Africa's impressive COVID-19 surveillance network: a national database of all positive COVID-19 tests, a national surveillance programme of all patients admitted to hospital with COVID-19, and the national COVID-19 genomic sequencing data.

335 219 COVID-19 hospital admissions were analysed, and the results support the preliminary data suggesting that the omicron-fuelled wave was considerably less severe than previous waves had been. In the omicron-driven wave, a lower proportion of patients (52 038 [8·3%] of 629 617) were admitted to hospital than in the preceding waves (71 411 [12·9%] of 553 530 in the Asp614Gly wave, 91 843 [12·6%] of 726 772 in the beta wave, and 131 083 [10·0%] of 1 306 260 in the delta wave; p<0·001). Of patients who were admitted to hospital in the omicron-driven wave, far fewer had severe disease, required oxygen, or died than in the other three waves. Overall, adjusting for age, sex, race, comorbidities, and other plausible confounders, patients were twice as likely to develop severe disease if infected during the ancestral Asp614Gly wave, and 3·5-times more likely to develop severe disease if infected during the beta or delta waves. The verdict is in. But what proportion of this lower overall severity can be attributable to intrinsic changes in omicron itself, rather than to increasing population immunity? Jassat and colleagues convincingly argue that decreased intrinsic virulence, increased reinfections due to immune evasion (with the pre-existing immunity shielding individuals from severe disease), and increased vaccination probably all contributed to this lower severity, although the relative proportions were hard to disentangle.

Two things stand out from this impressive study. First is the incredible importance of having robust surveillance systems in place to rapidly establish the clinical characteristics of new variants as quickly as possible after they arise. South Africa punches above its weight in this regard in most aspects, although its ability to answer these clinical questions was hampered by its Government's ongoing inexplicable refusal to allow linkage to vaccination data, which are collected on a separate electronic database. This will need to be remedied in advance of future waves.

The other salient point is how consistent these data are with earlier results from other scientists in southern Africa. Omicron's markedly lesser clinical severity compared with preceding variants was noticed and robustly reported by them within weeks of the outbreak occurring.[6–9] Yet, the message took frustratingly long to be accepted by large swathes of the international community.[10] This point isn't merely academic: economically devastating travel bans were quickly slapped on the region after the discovery of omicron,

despite the ban's illogicality and epidemiological futility.[11]

For reasons that are still opaque, both beta and omicron variants appear to have arisen in southern Africa. Predicting the future might be a fool's errand, but it seems equally unwise to bet against another variant of concern arising from the same area. If it does, one hopes that the lessons will be more quickly heeded next time.

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