



Omicron severity: milder but not mild

Published Online
January 19, 2022
[https://doi.org/10.1016/S0140-6736\(22\)00056-3](https://doi.org/10.1016/S0140-6736(22)00056-3)
See [Articles](#) page 437

In *The Lancet*, Nicole Wolter and colleagues¹ report data from more than 11 000 individuals (>80·0% aged 19–59 years; 55·9% women) with COVID-19 in South Africa indicative of significantly reduced odds of hospital admission for patients infected with the omicron SARS-CoV-2 variant of concern (B.1.1.529) versus other SARS-CoV-2 variants during the same period (Oct 1–Nov 30, 2021; adjusted odds ratio [aOR] 0·2, 95% CI 0·1–0·3) and significantly reduced odds of severe disease among patients infected by the omicron variant than among patients infected with the delta variant (B.1.617.2) in earlier epidemic waves (aOR 0·3, 0·2–0·5). These useful findings—derived from national-level COVID-19 hospital surveillance data linked with case, laboratory, and genomic data—represent a reassuring confirmation of early indicators that the omicron variant might lead to less severe disease and societal disruption, and have a reduced effect on hospital resources, than variants that dominated earlier pandemic waves. In the absence of widespread genotyping of confirmed SARS-CoV-2 infections, Wolter and colleagues¹ used amplification failure of the spike gene (S gene target failure [SGTF]) on the TaqPath PCR assay as a proxy for the omicron variant. SGTF is a reasonable marker for the omicron variant given that other circulating variants did not have this characteristic during the period of study.¹ In the context of expanding omicron variant epidemics, the level of generalisability of these South African data

to other jurisdictions and timepoints is of paramount global importance.

If this reduction in the risk of severe disease with the omicron variant, similar to that observed in England,² could be attributed to lower intrinsic virulence, it would provide reassurance to the public and health authorities that the recent alarming spike in COVID-19 case numbers observed globally would not translate to unmanageable increases in hospitalisations, with implications for the tightening or relaxation of disease control policies. However, South Africa has had repeated waves of infection and the extent to which this factor could explain the reduced effect of SGTF infections in late 2021 is unclear. SARS-CoV-2 reinfections are milder on average than primary infections,³ and, by December, 2021, more than 70% of South Africans had existing anti-SARS-CoV-2 antibodies as a consequence of either natural infection or vaccination.⁴ In the study by Wolter and colleagues,¹ the odds of previous infection were around 23-times higher in SGTF-infected versus delta variant-infected patients, which could be due to the omicron variant's capacity for immune escape that could increase the proportion of milder reinfections.⁵ The possibility of some patients being hospitalised with, rather than for, SARS-CoV-2 infection could also affect severity analyses given near universal, pre-hospitalisation COVID-19 testing and the increasing population prevalence of infection.⁶

In an attempt to disentangle intrinsic severity from population immunity, Wolter and colleagues¹ analysed disease severity by comparing contemporaneous, hospitalised individuals with the omicron (SGTF) versus other variants (non-SGTF) using a composite measure of severity, which included admission to an intensive care unit, acute respiratory distress, oxygen treatment, and death.¹ This analysis was inconclusive, possibly due to the small number of severe outcomes; however, there is biological plausibility for some reduction in the intrinsic severity of omicron infections, as indicated by laboratory studies that report reduced pathogenesis in an animal model⁷ and lower replication competence in human lung cells for omicron versus other variants.⁸

Knowing how frequently omicron causes severe disease is important. But even a milder average clinical



Bloomberg/Getty Images

presentation could be offset by an increased incidence of infection with the omicron variant, with the potential for considerable societal disruption through sickness, lost productivity, and distress, and the exertion of additional pressure on health-care systems due to staff absences. For example, on Jan 6, 2022, it was estimated that one in 25 individuals in the UK had symptomatic COVID-19.⁹ Self-isolation of cases, and either voluntary or mandatory quarantine of their contacts, can consequently impact large numbers of individuals.

Community epidemics of the omicron variant will probably have less of an impact on health compared with previous COVID-19 waves in most locations because of increased levels of population immunity and the possible reduced intrinsic severity of omicron infections. Nonetheless, in this generally young South African population, 21% of hospitalised patients infected with the SARS-CoV-2 omicron variant had a severe clinical outcome,¹ a proportion that might increase and cause substantial impact during outbreaks in populations with different demographics and lower levels of infection-derived or vaccine-derived immunity. This report of typically milder disease following infection with the omicron versus delta variant in South Africa is encouraging, but we should not assume that omicron variant epidemics will have such a low health effect elsewhere.

BJC reports honoraria from AstraZeneca, GSK, Moderna, Roche, and Sanofi, outside the area of work commented on here. JN was previously employed by,

and owns shares in, Sanofi, outside the area of work commented on here. We thank Julie Au for technical assistance.

Joshua Nealon, *Benjamin J Cowling
bcowling@hku.hk

WHO Collaborating Centre for Infectious Disease Epidemiology and Control, School of Public Health, Li Ka Shing Faculty of Medicine, The University of Hong Kong, Hong Kong Special Administrative Region, China (JN, BJC); Laboratory of Data Discovery for Health Limited, Hong Kong Science and Technology Park, Hong Kong Special Administrative Region, China (BJC)

- 1 Wolter N, Jassat W, Walaza S, et al. Early assessment of the clinical severity of the SARS-CoV-2 omicron variant in South Africa: a data linkage study. *Lancet* 2022; published online Jan 19. [https://doi.org/10.1016/S0140-6736\(22\)00017-4](https://doi.org/10.1016/S0140-6736(22)00017-4).
- 2 UK Health Security Agency. SARS-CoV-2 variants of concern and variants under investigation in England. Technical briefing: update on hospitalisation and vaccine effectiveness for omicron VOC-21NOV-01 (B.1.1.529). Dec 31, 2021. https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1044481/Technical-Briefing-31-Dec-2021-Omicron_severity_update.pdf (accessed Jan 9, 2022).
- 3 Abu-Raddad LJ, Chemaitelly H, Bertollini R. Severity of SARS-CoV-2 reinfections as compared with primary infections. *N Engl J Med* 2021; **385**: 2487–89.
- 4 Madhi SA, Kwatra G, Myers JE, et al. South African population immunity and severe Covid-19 with omicron variant. *medRxiv* 2021; published online Dec 21. <https://doi.org/10.1101/2021.12.20.21268096> (preprint).
- 5 Cao Y, Wang J, Jian F, et al. Omicron escapes the majority of existing SARS-CoV-2 neutralizing antibodies. *Nature* 2021; published online Dec 23. <https://doi.org/10.1038/s41586-021-04385-3>.
- 6 Sastry SR, Pryor R, Raybould JE, et al. Universal screening for the SARS-CoV-2 virus on hospital admission in an area with low COVID-19 prevalence. *Infect Control Hosp Epidemiol* 2020; **41**: 1231–33.
- 7 Diamond M, Halfmann P, Maemura T, et al. The SARS-CoV-2 B.1.1.529 omicron virus causes attenuated infection and disease in mice and hamsters. *In Review Nature Portfolio* 2021; published online Dec 29. <https://doi.org/10.21203/rs.3.rs-1211792/v1> (preprint).
- 8 Chan MCW, Hui KPY, Ho J, et al. SARS-CoV-2 omicron variant replication in human respiratory tract ex vivo. 2021. <https://doi.org/10.21203/rs.3.rs-1189219/v1> (preprint).
- 9 ZOE COVID Study. Data press release. Omicron spread slows but cases hit vulnerable over 75s. Jan 6, 2022. <https://covid.joinzoe.com/post/omicron-spread-slows-but-cases-hit-vulnerable-over-75s> (accessed Jan 9, 2022).