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Omicron variant and booster COVID-19 vaccines

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Published Online
December 17, 2021
https://doi.org/10.1016/S2213-2600(21)00559-2

On Dec 13, 2021, the UK Health Security Agency (UKHSA) confirmed that a patient in England had died after contracting the omicron variant of SARS-CoV-2. The previous day, prime minister Boris Johnson launched a drive to offer all adults in the UK a third dose of the COVID-19 vaccine by the end of the year. "We are now facing an emergency", stated Johnson. "There is a tidal wave of omicron coming and I am afraid it is now clear that two doses of vaccine are simply not enough." WHO categorises the risk associated with omicron as very high. The new variant, which is also known as B.1.1.529, was identified in November, 2021. It has since been detected in more than 60 countries. As *The Lancet Respiratory Medicine* went to press, the UK had registered 10 017 cases of omicron. The true caseload is likely to be considerably larger. On Dec 15, 2021, 78 610 people tested positive for SARS-CoV-2 in the UK. "There will be an increasing number of omicron patients going into the NHS, going into hospital, going into intensive cares", cautioned Chris Whitty, England's Chief Medical Officer. "That will begin to become apparent, in my view, fairly soon after Christmas."In the week ending Dec 12, Africa recorded 196 000 cases of COVID-19, an increase of 86% on the previous week. Cases of COVID-19 rose by 66% in South Africa, where omicron was first detected. But bed occupancy rates in the country's intensive care units remain low.

The original strain of SARS-CoV-2 has an R0 of 2·5, while the delta variant (B.1.617.2) has an R0 of just under 7. Martin Hibberd, professor of emerging infectious diseases at London School of Hygiene & Tropical Medicine (London, UK), reckons omicron's R0 could be as high as 10. In the UK, cases of omicron are doubling every 2–3 days, which puts it on track to supplant delta as the dominant variant in the country by mid-December. It also complicates control efforts. "Contact tracing works well if you have about a week between one infection and the next", explained Hibberd, "But it is almost impossible to make it work if you only have 2 or 3 days between infections. We may have to rely on other measures, like daily testing."

It is too soon to know the exact extent to which vaccination or previous infection with SARS-CoV-2 protects against infection with omicron. The early signs are worrying. 70% of the UK population have had two doses of the COVID-19 vaccine, while the proportion of the population who harbour antibodies against SARS-CoV-2 exceeds 90%. Although vaccination rates are considerably lower in South Africa, infection rates with SARS-CoV-2 are thought to have been extremely high over the course of the pandemic. Yet omicron is spreading rapidly in both nations. The UKHSA has suggested that protection against symptomatic disease at 25 weeks after two doses of the COVID-19 vaccine could be less than 10% for the omicron variant, compared with 40% for the delta variant.

"It certainly looks like a three-shot vaccination schedule will be needed against omicron", commented Susanna Dunachie, professor in infectious diseases at the University of Oxford (Oxford, UK). In which case, the term booster might need to be retired. As of Dec 11, 34% of the UK population had received three doses of the COVID-19 vaccine; if this is now regarded as the equivalent of full vaccination, the country is back to where it was in the fourth week of May, 2021.

Pfizer-BioNTech and Moderna, the manufacturers of the two mRNA vaccines that have been approved for COVID-19, have stated that they could produce vaccines specific to omicron within 100 days. "It might be the right time to consider changing the vaccine", said Hibberd. "The current vaccines are based on the Wuhan strain of SARS-CoV-2, but that is not what the virus looks like anymore." A vaccine based on omicron would presumably require only two doses. "There are a lot of mutations in omicron that are similar to the other variants of concern that we have seen so far, so there is no reason to think you would not get strong cross-protection from a vaccine based on omicron", added Hibberd. "The major issue is that we risk creating a two-tier system, with poorer countries stuck with out-of-date vaccines."

Much will depend on the scale and severity of the breakthrough infections associated with omicron. Currently, researchers are heavily reliant on the sequencing data for omicron, which reveals more than 30 mutations in the spike protein upon which the COVID-19 vaccines are based, and neutralising antibody data, which shows that the variant has partial but not complete resistance to pre-existing immunity. But vaccine effectiveness is also determined by binding antibodies, which prevent SARS-CoV-2 from getting into the cells, and T-cells, which attack infected cells and help with antibody production.

"T-cells respond to the whole of the spike protein, so they are less likely to be bothered by a few mutations", points out Dunachie. "They probably play a part in preventing severe disease, though we do not yet know how big a part." When it eventually emerges, the vaccine effectiveness data might indicate that Omicron does not significantly increase the risk of severe disease or death in vaccinated populations. But billions of people around the world are not part of a vaccinated population. Just 7% of Africans have received two jabs with the COVID-19 vaccines. How omicron will interact with populations with low immunity against COVID-19 remains to be seen.

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