



The Omicron variant: what do we know so far

- Variants are discovered via phylogenetic sequencing which focuses on the evolutionary relationships of organisms and viruses
- B.1.1.529 was discovered using such sequencing techniques on November 11 in Botswana. Other cases soon followed in South Africa, Belgium, Israel and Hong Kong (where infected individuals had been Pfizer-vaccinated in May/June). Some people thought the new variant would be called “Nu”, but the WHO called it “Omicron” which is what we will use
- The Omicron variant has 32 mutations of the spike protein alone, compared to the Delta variant which had only 9. This is a very large degree of mutation; as a reminder, vaccines target the spike protein based on its three dimensional shape, so the more severe the topographic mutation of the spike protein, the greater the risk of lower efficacy for any vaccine developed vs a prior variant. Importantly, the Omicron variant is NOT genetically descended from the Delta variant, suggesting it probably mutated over time in a single immunocompromised person. The tens of millions of immunocompromised people around the world serve as incubators for mutations since existing vaccines are less effective in such people, and they can remain infectious for several months
- The Omicron variant could be a serious risk to global health: 9 of its mutations have been seen in other variants of concern; 8 have not been seen before but lab data suggest they are a threat; and some of the other mutations are unknown and still need to be examined
- Some Omicron mutations have properties that signify potential resistance to antibodies derived from existing vaccines. Other Omicron mutations show potential for increased transmissibility (speed with which viruses pass from one organism to another) and increased infectivity (the ability of a pathogen to establish an infection)
- The increase in the positive testing rate in the Johannesburg region rose from 1% to 30% in one week as Omicron outcompeted the Delta variant. This suggests a high degree of contagiousness, and South African cases are now increasing at an exponential rate (from very low levels). Disease modeling scientists estimated that Omicron is several times more transmissible than the original Wuhan variant, while the Delta variant was only 70% more transmissible
- It is important to point out that vaccination rates are only (24% full, 28% partial) in South Africa, so we do not have information yet on what Omicron spread might look like in places with higher vaccination levels, nor do we have any information on Omicron disease severity
- It will take time for the scientific community to figure out the implications of all of these new mutations. Pfizer announced that it may take up to two weeks to determine if their existing vaccine prevents or inhibits virus replication in vitro
- The “good” news about Omicron: unlike other variants, it can be tracked via a simple PCR test (like the Alpha variant) and will not require genomic sequencing to identify. In the chart on the next page, the Omicron variant was tracked in South Africa using a simplified approach that identifies when genes are deleted from their expected positions
- mRNA vaccines are relatively easy to alter compared to other vaccine types. Once the change is made to recognize the new spike protein, only 2 dozen people need to enroll in a trial to make sure the updated vaccine works after which it can be distributed (i.e., no need for Phase III trials and/or regulatory approval). This process could take 4-6 weeks. But as you can imagine, the process of revaccinating everyone for a new variant would be logistically challenging if required



- Oral polymerase inhibitor/protease inhibitors from Merck and Pfizer may hold up well against the new Omicron variant given their different mechanism of action. They're not a substitute for vaccines, but could help mitigate the severity of the disease in people who get it. Note: they are not FDA approved yet, and earlier today some news came out from Merck indicating a more disappointing efficacy rate against hospitalization and death for high risk people of just 30% compared to earlier estimates of 50%. Pfizer's reported antiviral efficacy numbers are higher: 89% vs hospitalization and death. As a reminder, these pills have to be taken within 5 days of infection onset
- One of the most important things to track right now: hospitalization rates in the Gauteng province of South Africa where the Omicron outbreak is occurring. So far, there has been no increase in hospital or ICU admissions, but given how recent the outbreak has been it's too soon for that. By mid-December, we should have a better read on in vitro vaccine efficacy and Omicron disease severity
- While we don't know how far efficacy will decline in vaccinated people if this variant spreads, it's fair to say that for unvaccinated people, the risks of infection and other severe outcomes may have just risen again. The most recent data already show a very large gap between hospitalization and mortality rates for vaccinated and unvaccinated people, which we illustrate in Section 1 of our COVID web portal

If I learn anything else, I will let you all know.

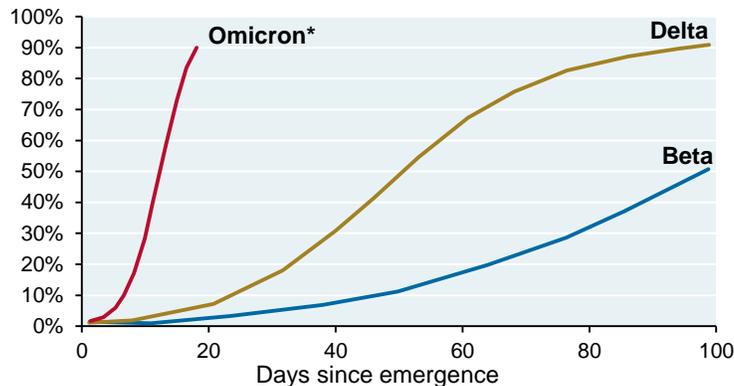
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Sources: Jeffrey Barrett, UK Sanger Institute and former Chief Science Officer at Genomics; South African Health Ministry; Katelyn Jetelina, University of Texas Health Science Center/Houston; David Fisman, University of Toronto Dalla Lana School of Public Health; Otello Stampacchia, Timmerman Report; New York Times (on Merck/Pfizer antiviral efficacy levels); ThermoFisher Scientific

Speed of COVID variant outbreaks

%, share of all sequenced cases in South Africa



Source: FT, GISAIID, South African Health Lab Service. Nov 25, 2021.

*Tracked via S-gene target failure.

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