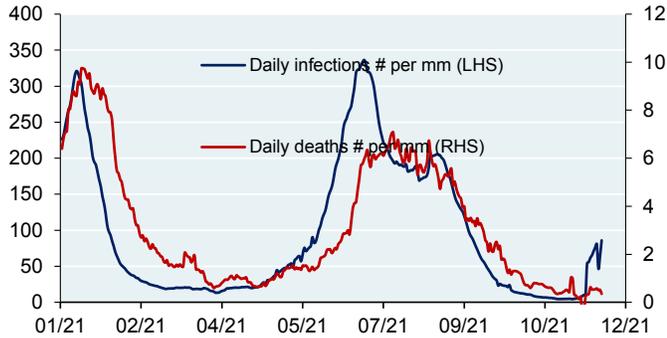




**The Omicron variant: what we know so far**

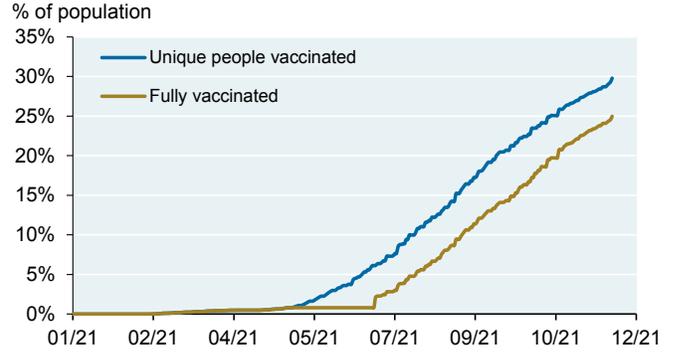
- Omicron discussion follows the six charts

**South Africa: infections, hosp and mortality**



Source: JHU, IMF, JPMAM. Dec 2, 2021. 7 day smoothing.

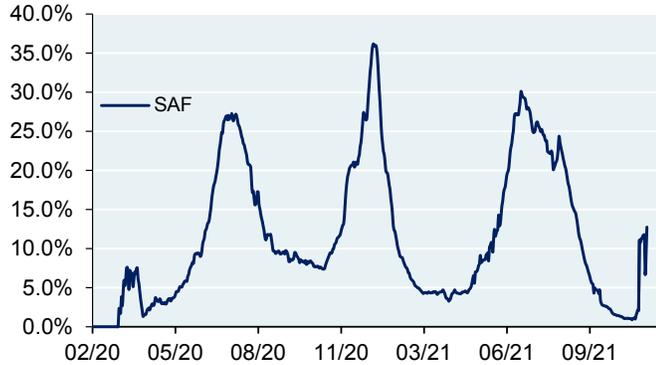
**South Africa: vaccination**



Source: OWID, JPMAM. Dec 2, 2021.

**South Africa positive testing rate**

Daily infections, % of total tests, smoothing = 7 days



Source: Johns Hopkins University, JPMAM. Dec 2, 2021.

**Gauteng COVID hospitalizations**

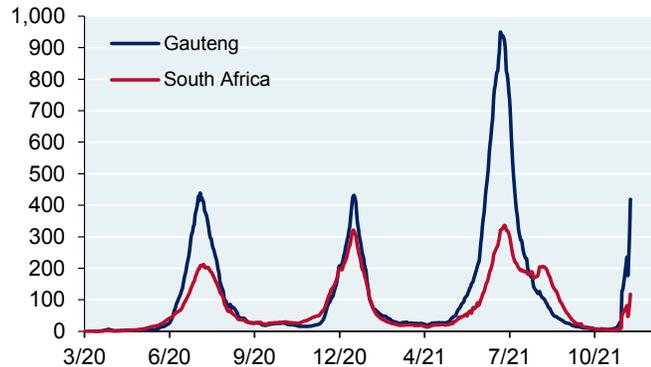
Current hospitalizations



Source: National Institute for Communicable Diseases, JPMAM. Dec 2, 2021.

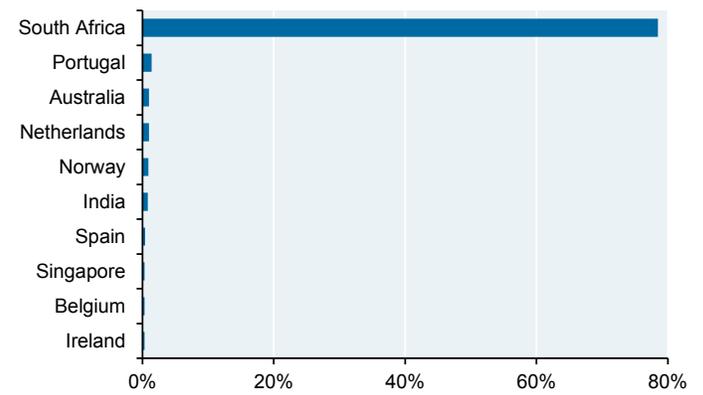
**South Africa daily infections**

Daily infections, # per mm, smoothing = 7 days



Source: JHU, IMF, NICD, JPMAM. Dec 3, 2021.

**Omicron variant prevalence**



Source: GISAID. December 4, 2021.



## Omicron: what 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)
- 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 might have mutated over time in an 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. In addition, some Omicron mutations have properties that can 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)
- In an early non-peer reviewed piece from Stellenbosch University in South Africa, researchers found a much higher rate of reinfection amongst unvaccinated survivors in South Africa than they did during the Delta and Beta waves. In other words, Omicron is demonstrating the ability to evade natural immunity
- There is limited data so far on Omicron's ability to evade vaccine (acquired) immunity; in South Africa, most infections and hospitalizations are occurring among younger people, who happen to be less vaccinated. Many scientists are assuming a decline in vaccine efficacy against the Omicron variant, although its extent would have to be determined through observed field data
- Also limited information so far on Omicron disease severity, and whether increased transmissibility is associated with less severity (which is sometimes the case)
- The increase in the positive testing rate in the Johannesburg region reportedly 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). While some disease modeling scientists estimate that Omicron is much more transmissible than Delta, there is still uncertainty as to the exact timing of the initial Omicron cases in which case speed of transmission is still to be determined
- Full vaccination rates are still just 24% in South Africa, so we do not have information yet on what Omicron spread might look like in places with higher vaccination levels
- Pfizer announced that it may take up to two weeks to determine if their existing vaccine prevents or inhibits virus replication in vitro. 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
- The "good" news about Omicron: unlike other variants, it can be tracked via a simple PCR test (like the Alpha variant) with subsequent genomic sequencing to confirm its presence. Both Alpha and Omicron have a specific spike protein deletion at positions 69/70 which causes one of the three PCR assay tests (the S-gene test) to fail. A similar proxy for Omicron has been identified in three large UK labs in a nationwide UK infection survey
- Oral polymerase inhibitor/protease inhibitors from 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 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. Hospitalizations have been rising; so far, they are rising more quickly in public hospitals with younger less vaccinated patients, so it's too soon to draw conclusions on vaccine efficacy vs Omicron. By mid-December, we should have a better read on 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

**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; Shane Crotty, La Jolla Institute of Immunology; Stellenbosch University South Africa

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