

BA.2 subvariant of Omicron in more than 40 countries across the globe

Benjamin Mateus
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During his opening remarks at the 150th session of the World Health Organization (WHO) executive board, Director-General Tedros Adhanom Ghebreyesus warned that conditions were ideal for new variants to emerge and that countries, if acting collectively, had the power to change the trajectory of the pandemic.

The Director-General's comments this week come in the wake of approximately 8,000 new cases of an Omicron subvariant designated BA.2 being detected in more than 40 countries. Some scientists have also nicknamed it the “stealth omicron” because it can only be confirmed as BA.2 by gene sequencing. As a result, the exact incidence remains speculative, but it is considered still very low. It was first reported on in November when the BA.1 subvariant was exploding in South Africa. Its precise geographic origin remains unknown, but it was also first detected in South Africa.

The Omicron strain (BA.1), also designated by B.1.1.529, has an S gene dropout or S gene target failure. A widely used PCR test is unable to detect this one gene of three target genes, meaning that if the PCR tests lack this target when an infection has resulted, assumptions are made that is the Omicron variant causing the infection. The Alpha variant that came to dominate the UK in December 2020 shared this characteristic, and the S gene failure was used to track its spread with PCR testing. The BA.2 subvariant lacks this S gene dropout, making it more difficult to track.

According to a recent statement from Statens Serum Institute (SSI), Denmark's leading public health academy, BA.2 is spreading 1.5 times faster than the BA.1. “Preliminary calculations indicate BA.2 is effectively well over one and half times more contagious than BA.1,” it wrote, with the spread fastest among children.

Omicron has already hit children with ferocity. A

recent report out of South Africa had shown pediatric hospitalizations were almost 50 percent higher than with the Delta wave. Children under five were being admitted at rates higher than the elderly. In the UK, hospitalizations among children 6–17 were 2.3 times last winter's record.

Like BA.1, the new subvariant does not appear to have the same clinical impact as Delta on those infected, though extensive previous infections and high population vaccination appear to diminish the virulence of these subvariants. Still, virulence and vaccine efficacy data still need to be evaluated before true comparisons can be made.

Dr. Tyra Grove Krause, epidemiologist and a specialist in public health medicine at the SSI, said, “It is the Omicron variant that is driving the epidemic right now. We estimate that more than 99 percent of all COVID-19 cases in week three [of January 2022] are due to Omicron, and data show that it spreads faster, but gives a lower risk of serious disease outbreaks compared to Delta. At the same time, we can see a marked difference in the risk of being admitted between vaccinated and unvaccinated. The vaccinated are better protected against being hospitalized—even if they are infected by the Omicron variant.”

The present seven-day average in hospitalizations in Denmark is approaching pandemic highs at 822, but ICU admissions have been trending downward since early January. However, just counting ICU admissions may confound the real picture, as Denmark relies on long-term care nursing homes, according to Dr. Eric Feigl-Ding. New infections are at pandemic highs with 43,719 cases on January 26, 2022. Daily deaths, though remaining low in general, turned upwards before the Christmas holidays and have now exceeded the first wave in April 2020.

With the more contagious BA.2 dominant in Denmark, the current wave may extend well into February. However, it remains to be seen if BA.2 will supplant BA.1, which is currently responsible for 98 percent of infections worldwide. It is also spreading into the UK, Singapore, India, and the Philippines, where it is beginning to edge out the original strain.

In total, there are three sub-lineages of the Omicron variant. BA.3 has remained dormant with only a few hundred cases detected. However, what distinguished these three is that the number of unique mutations they possess, which sets them apart as much as Alpha, Beta, Gamma, and Delta, are different from one another.

Looking at the evolution of the wild-type strain that first emerged in Wuhan, China, in December 2019, a precursor variant denoted as the Omicron parent most likely arose sometime in March 2021. It remains unknown why Omicron then surfaced in November 2021. These events underscore the warnings made by the WHO Director-General. As Dr. William Haseltine, science contributor to *Forbes*, wrote, “One thing is clear: SARS-CoV-2 has an enormous capacity not only to continue to produce new variants, but variants that surprise us both in their number and their biological properties.”

Regarding the three sub-lineages, Dr. Haseltine explained, “The three share 39 mutations, which we include as the presumptive ‘Omicron parent.’ The Omicron parent diverged into the Omicron Family: BA.1, which contains an additional 20 mutations (13 unique); BA.2, which includes an additional 27 (ten unique); and BA.3, which consists of an additional 13 (one unique). Remarkably, all the family members were detected simultaneously in South Africa, although they likely diverged from a single variant several months previously. This is a unique example of such highly divergent strains appearing in a population simultaneously.”

Most of the mutations are located on the spike protein of the virus, which it uses to attach to the human ACE2 receptor and enter the cell so that it can reproduce itself. These mutations on the spike determine, to a large extent, its transmissibility and immune-evasive properties. For instance, BA.1 has proven to be three time more transmissible than Delta and its vaccine-evasive capacity has deemed the importance of obtaining a booster. The additional and unique

mutations of BA.2 will need further study in the real-world setting.

Despite the continued tsunami of Omicron cases across the US, according to the GISAID virus database, the BA.2 subvariant is now present in 22 states across the country, including Arizona, Texas, California, New York, and Washington. Scientists are speculating that given the high rates of reinfection with Omicron, it could mean that BA.2 may be a second wave that quickly follows.

Dr. Anders Fomsgaard, chief physician and virus researcher at the SSI, said, “It is possible that you can be infected with BA.1 Omicron first and then shortly after with BA.2.” Several cases in Norway have confirmed this. He added, “The eyes of the world are resting on us to find out what is happening with BA.2. There is no explanation as to why it has come to Denmark and is spreading so much right here.” Aside from being more contagious, Fomsgaard cautioned, “It may also be that it is more resistant to the immunity that is in the population, which allows it to infect better. We do not know yet.”



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