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How Virulent Is Omicron?

Richard Simoneaux

Steven L. Shafer, MD, FASA
Editor-in-Chief

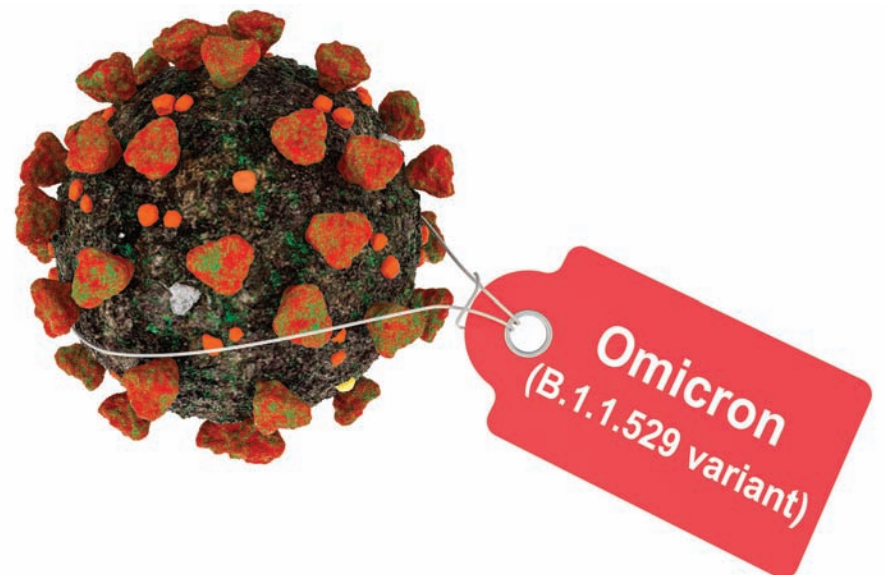
Danny (not his real name) is a 29-year-old medical student in London and a good friend of one of the authors (SLS). Danny is triple vaccinated with the Pfizer BNT162b2 mRNA vaccine, has no chronic health problems, and exercises regularly. When we spoke last weekend, Danny told me (SLS) that COVID finally caught up with him. His roommate, a teacher, brought Omicron home from the classroom. The roommate had only mild symptoms. Danny had a temperature of 104.5 despite taking ibuprofen and paracetamol. He also had

severe neck pain, sounding suspiciously like inflammatory meningitis. Danny was incapacitated for almost a week. Having received my COVID-19 updates for the past year,* Danny called with a specific question: "I'm young, healthy, and triple vaccinated. If Omicron does this to me, how does someone who isn't vaccinated, is immunocompromised, or is frail survive this?" My answer was short: some don't.

South Africa

We are still learning about the virulence of Omicron. We know a great deal from

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A Spotlight on Female Leaders in Anesthesiology

Catlin Nalley

As the field of anesthesiology evolves and grows, so does the important role women play in its ongoing success and development. The ASA Monitor had the privilege of speaking with three women whose leadership and expertise have had – and continue to have – a positive impact on anesthesiology and medicine as a whole.

Margaret Wood, MBChB, FRCA, is the Emanuel M. Papper Emerita Professor of Anesthesiology and Department of Anes-

esthesiology Emerita Chair, College of Physicians and Surgeons, Columbia University. Throughout her career, Dr. Wood has conducted extensive research in anesthesiology, publishing more than 140 articles and book chapters. She was the first woman to chair a clinical department at Columbia University, a position that she held until June 30, 2016. Dr. Wood was also the first woman to be elected as president of the Association of University Anesthesiologists (AUA).

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Where Are They? A Look at New Anesthesia Professionals Billing Medicare

Thomas R. Miller, PhD, MBA

Workforce issues were a key concern in health care in 2021, and they continue to be a focus of attention among clinical specialties in 2022. Relevant to anesthesiology were headlines about potential shortages of anesthesiologists, certified registered nurse anesthetists (CRNAs), and certified anesthesiologist assistants (CAAs). The concern for potential workforce shortages exists despite a record-setting number of physicians entering anesthesiology residency programs in each of the last five years (ASA Monitor 2021;85:40-1). In addition, the growth rate in the number of CRNAs and CAAs continues to outpace the growth rate in the number of anesthesiologists. Given the elevated competition for anesthesia professionals

among academic medical centers, large national group practices, and smaller regional and local practices, I was curious about where new anesthesia professionals initially practice.

Data sources

I identified a sample of "new" anesthesia professionals in 2021 based on new National Provider Identifiers (NPIs) present in the 11 Centers for Medicare & Medicaid Services (CMS) National Downloadable Files (NDFs) between July 16, 2021, and December 4, 2021 (asamonitor.pub/3tDFACx). These files include NPIs and related information for anesthesiologists, CRNAs, and CAAs who submitted Medicare fee-for-service claims in the previous six months. I designated

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Guest Editor: Thomas E. Grissom, MD, MSIS, FASA, FCCM

In the Know: How Virulent is Omicron?

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the medical professionals and public health specialists in South Africa. These are the same professionals whose thorough genomic surveillance and scientific transparency allowed rapid identification of what would become known as the Omicron variant of SARS-CoV-2 in the Gauteng Province in November 2021 (asamonitor.pub/333NABm). The world owes them a debt of gratitude.

Figure 1 shows the time course of cases, hospitalizations, and deaths since November 1 in South Africa. As seen in Figure 1, cases rose initially, but deaths did not. This provides evidence that Omicron is less virulent than previous variants.

However, the story is more complex. Figure 2 shows the multiple waves of cases and deaths that have swept over South Africa since the beginning of the pandemic. As expected, there is a lag between the rise and fall in cases and the corresponding rise and fall in deaths. Figure 2 shows the time lag (estimated with correlation analysis) for each wave. For the first three waves, the time lag was 20 days, 10 days, and 14 days, respectively. However, for Omicron, the lag between cases and deaths is longer – about 26 days. This can also be seen in Figure 1, where careful inspection of the rise and fall in cases (dotted green line) shows that hospitalizations lagged about three weeks, and deaths about four weeks.

It is possible to calculate an approximate case fatality rate (the percentage of cases that eventually succumb to COVID-19) from the daily case and death numbers, and from estimates of the delay between diagnosis and death. This is shown in Figure 3, using the delays estimated in Figure 2. Throughout the pandemic, about 2.5% to more than 7.5% of reported cases have died. Only at the tail end do we see a difference. Highlighted in red is the Omicron surge now trailing off in South Africa. The case mortality rate has been running at 0.7%. That is a reduction of at least 75% from the virulence of prior strains. Omicron is different.

However, everything is relative. The 2019-2020 influenza season in the U.S. resulted in 34,949,979 infections and 20,342

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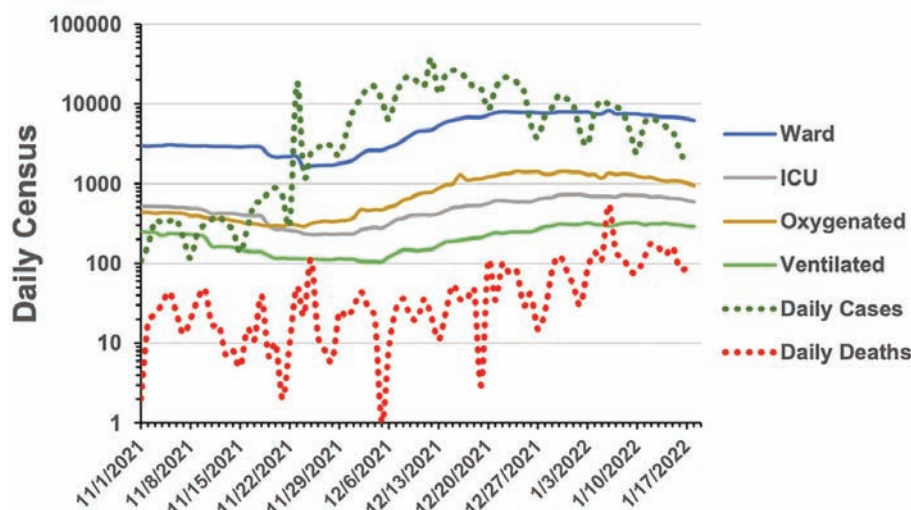


Figure 1: Cases, hospitalizations, and deaths in South Africa since November 1, 2021. Hospitalizations peaked about 3 weeks after the peak in cases. Deaths appear to have peaked in early January. Correlation analysis suggests that deaths follow cases with a delay of 26 days. Hospitalization data from the South Africa National Institute for Communicable Diseases (asamonitor.pub/3AgVP9D). Case and death data from COVID-19 Data Repository by the Center for Systems Science and Engineering at Johns Hopkins University (asamonitor.pub/3KqHZa).

deaths, for a case fatality rate of 0.06%. Omicron may be less virulent than prior strains of SARS-CoV-2, but this simple analysis suggests Omicron in South Africa remains 10-fold more deadly than influenza in the U.S.

This analysis really doesn't answer Danny's question, though, because it does not match the patients who are infected with the patients who die, nor does it stratify by vaccination status, age, immunocompetency, or frailty. In a paper from Harvard University and Massachusetts General Hospital, Bhattacharyya and Hanage note that "Without accounting for vaccination rates and prior infections, among other

factors, the true risk of severe infection will be systematically underestimated" (asamonitor.pub/3FMemvI). The authors caution that it is "premature to consider Omicron infections to be intrinsically milder than those caused by preceding variants."

The fact that so many of the infected individuals in South Africa had immunity from prior infection and/or vaccination when the Omicron variant began circulating makes it difficult to compare population-level infection fatality rate with earlier waves of COVID-19. However, the conclusions above are supported by two other available studies of Omicron virulence in South Africa

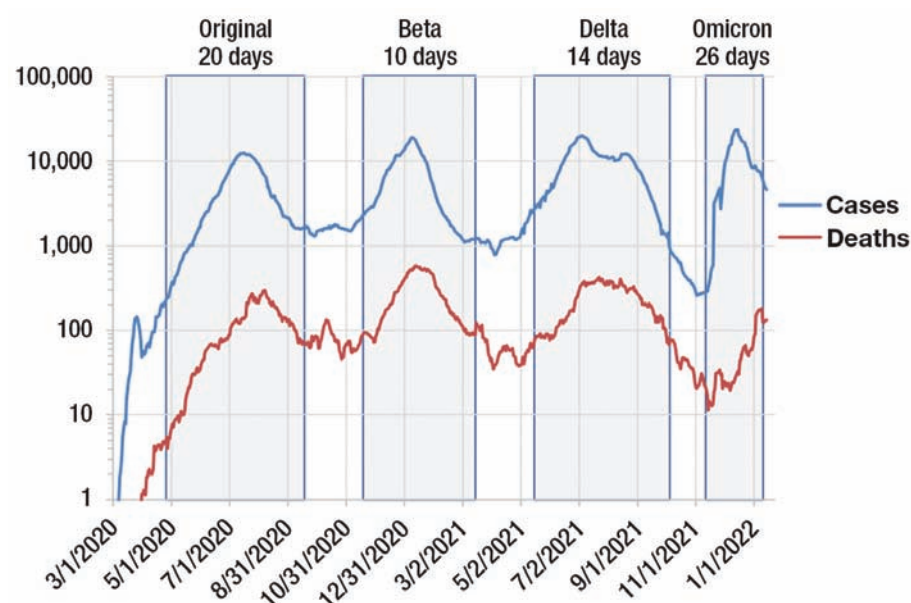


Figure 2: There have been four SARS-CoV-2 surges in South Africa. By looking at the correlation between cases and deaths, it is possible to determine the typical time interval between cases and deaths. Patients typically died about 20 days after diagnosis over the summer of 2020. The Beta and Delta strains were associated with death after 10 and 14 days, respectively. The delay with Omicron is longer: 26 days. As a result, even after the wave of new cases has crested in the U.S., we may still see rising deaths for another month after the crest.

(medRxiv December 2021; medRxiv December 2021).

Infection fatality rate vs. case fatality rate

Two important quantities used to assess the virulence of a virus are infection fatality rate (IFR) and case fatality rate (CFR). The IFR for a virus is the number of fatalities divided by the number of infections. Unfortunately, the number of infections isn't known. All that is known is the number of positive tests for SARS-CoV-2.

The CFR is the number of fatalities divided by the number of cases. The number of cases is typically the number reported by health authorities, based on positive test results. CFR estimates may be much higher than IFR estimates because true infections may vastly outnumber documented infections. If Omicron is causing less severe disease, then many individuals with Omicron may not be getting tested. Thus, the IFR for Omicron may be much less than the 0.75% estimated below.

The other problem is that reported fatality rates likely underestimate total number of deaths. The IHME estimates that cumulative deaths in the U.S. exceed the reported total by 16% (asamonitor.pub/3fEZQeK). However, the IHME estimates that the true death toll in Africa is 580% greater than the reported death toll (asamonitor.pub/33qbDex).

Thus, the reduced case mortality rate for South Africa shown in the figures is complicated not only by changing population immunity over time, but also by changing certainty in both the number of cases and the number of deaths. However, since the data are from one country, it is likely that the abrupt decrease in case fatality rate in South Africa with the onset of the Omicron surge is real.

Animal studies

The problems with interpreting IFR and CFR do not apply to animal studies, where investigators can exactly determine the number of cases and deaths. Animal studies demonstrate a considerable reduction in COVID-19 virulence. Prior strains of COVID-19 caused about 15% weight loss in hamsters, but infection with Omicron did not cause any detectable weight loss (bioRxiv January 2022). Similar results have been reported in mice (Res Sq December 2021; bioRxiv December 2021).

Kaiser Permanente Southern California Omicron study

In an effort to assess the risk for severe clinical outcomes associated with the Omicron variant, researchers within Kaiser Permanente Southern California Health Care undertook a study among

COVID-19 patients within their system (medRxiv January 2022). The investigators used data from 69,279 confirmed and genotyped cases of COVID-19 from November 30, 2021, through January 1, 2022.

In outpatient COVID-19 cases, the rate for hospitalization in patients with the Omicron variant was half that of the rate for patients with the Delta variant. Seven patients with Omicron were admitted to the ICU and one died. For patients with the Delta variant, 23 were admitted to the ICU and 14 died. Patients with Omicron were only one quarter as likely to be admitted to the ICU and were only one tenth as likely to die as patients with Delta.

These researchers concluded that “infections with presumed Omicron variant infection were associated with substantially reduced risk of severe clinical endpoints and shorter durations of hospital stay.” However, since Omicron demonstrates considerable immune escape (Nature December 2021), it is likely that a greater fraction of the patients with Omicron had some level of immunity to SARS-CoV-2. This highlights additional challenges even in well-controlled environments, like the Kaiser Permanente system, because the populations infected with Delta and Omicron will be different at baseline.

Vaccination status

Danny was surprised to be so sick despite being vaccinated. He did not go to the hospital, which I attributed to his treating himself with anti-inflammatory/antipyretic drugs at home. However, vaccination probably helped keep him out of the hospital as well, as shown in Figure 4.

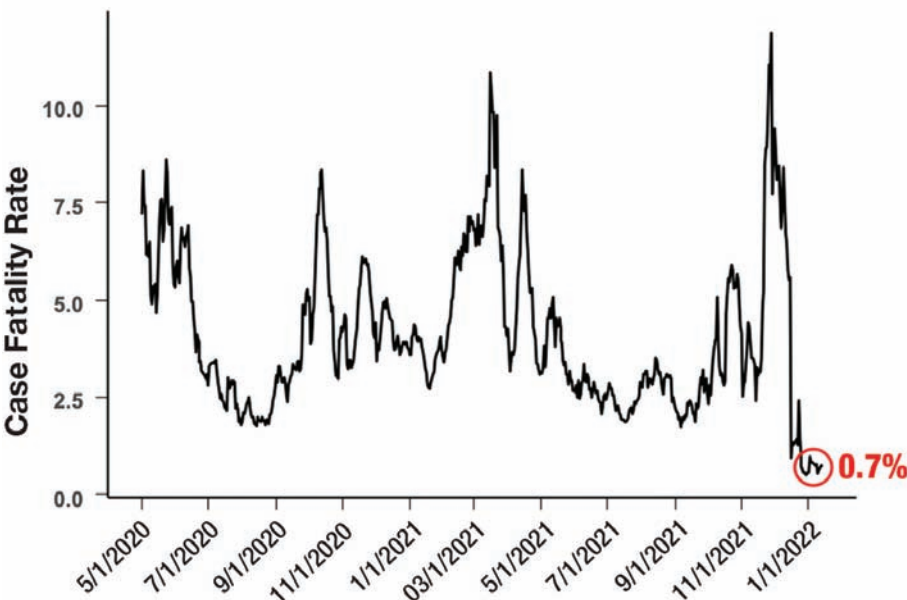


Figure 3: The case mortality rate in South Africa has fluctuated from 2.5 to >7.5 throughout the pandemic, except since Omicron. During and after the Omicron surge, the case fatality rate fell to about 0.7%, a fraction of what it had been previously as highlighted in the red circle. The dates along the x-axis are death dates, not case dates.

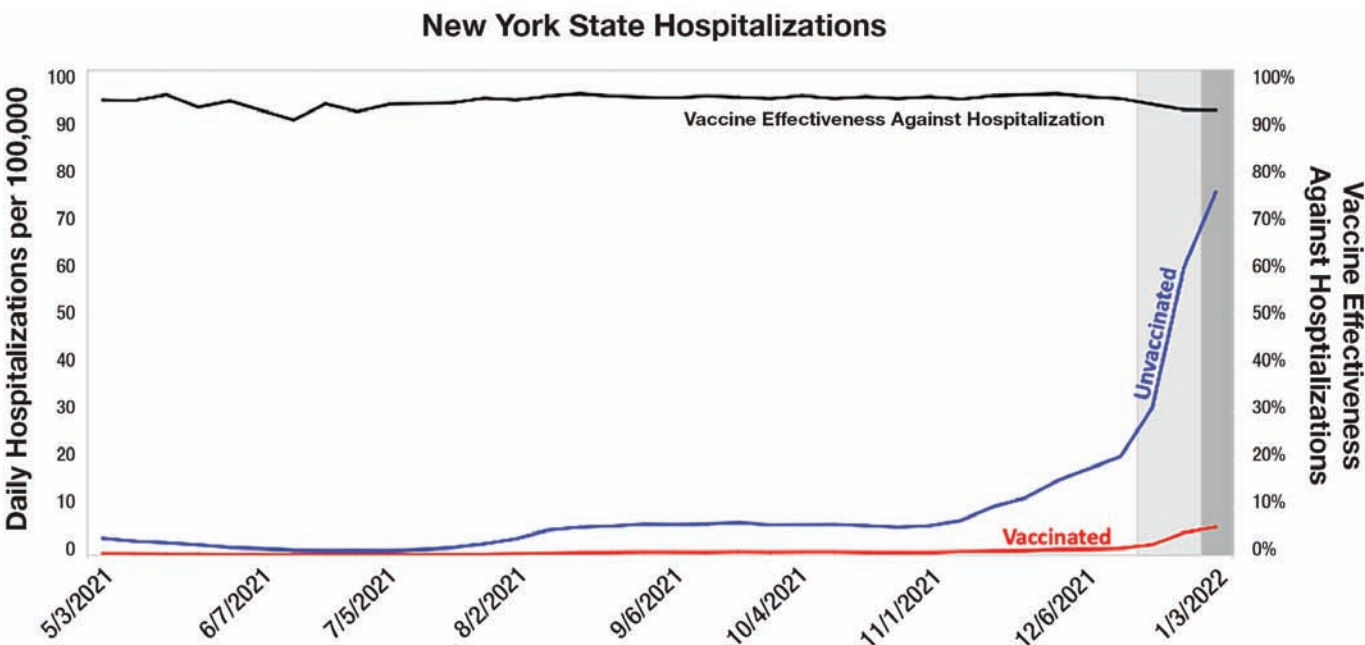


Figure 4: For the first time since the pandemic, vaccinated patients are being hospitalized in sizeable numbers, as shown in red. However, the per capita rate is far higher for unvaccinated individuals, as seen in blue. Despite immune escape, vaccines remain >90% effective against hospitalizations. Data are from the New York State Department of Health (asamonitor.pub/3AhUYWj).

According to figures compiled by the New York State Department of Health, vaccination reduces the likelihood of hospitalization by more than 90% with Omicron. These data are comparable to the 85%-90% vaccine efficacy documented by the U.K. Health Security Agency against hospitalization from Omicron (asamonitor.pub/3fChjob).

Surprised by the severity of Danny’s illness, the authors of this report, older and less fit than Danny, decided to increase non-pharmaceutical interventions (mask-wearing, social distancing) until the Omicron wave has passed. The good news (relatively speaking) is that Omicron will complete the task of providing worldwide immunity. This will come at a terrible cost. COVID-19 is

again the leading cause of death in the U.S. and is likely to cause at least 50,000 additional deaths through April 2022 (asamonitor.pub/3fEZQeK). SARS-

CoV-2 will not be gone, but the pandemic of deaths from a virulent pathogen unleashed on a population without natural immunity will be over. ■

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