

In-Depth Science Review

February 14, 2022

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COVID-19 severity and vaccine effectiveness in the era of the Omicron variant.

This science review is a snapshot of the new and emerging scientific evidence related to COVID-19 during the period specified. It is a review of important topics and articles, not a

guide for policy or program implementation.

The findings captured are subject to change as new information is made available. We welcome comments and feedback at covid19-eiu@vitalstrategies.org.

COVID-19 severity and vaccine effectiveness in the era of the Omicron variant.

Main message:

Since the emergence of the Omicron variant of SARS-CoV-2 in November 2021, COVID-19 cases have surged globally to levels beyond those seen at any other point during the pandemic. Although Omicron causes less severe disease than Delta, health care systems have been overwhelmed, and deaths from COVID-19 have continued to climb globally.

We have learned an enormous amount about Omicron over the past 11 weeks. Studies from around the world show a clear and consistent picture: Omicron is much less likely to cause severe disease than previous variants.

However, Omicron's extremely high transmissibility has led to massive increases in cases, followed by surges in hospitalizations.

A critical question when Omicron first emerged was how effective our COVID-19 vaccines would be against it: early studies showed that Omicron can escape immunity – whether from vaccination or prior infection – better than previous variants. We now have evidence from around the world that vaccines continue to provide excellent protection against severe disease caused by all variants that have emerged so far, including Omicron. Although the effectiveness offered by a primary series

wanes over time, protection against severe disease is relatively preserved and fully restored by a booster dose.

What follows is an overview of what we know about Omicron severity and the protection offered by vaccines against it, as well as how to approach vaccination globally when Omicron predominates.

For further details on the studies that informed this review, please see the accompanying Annex.

The severity of COVID-19 caused by Omicron

How is COVID-19 severity defined?

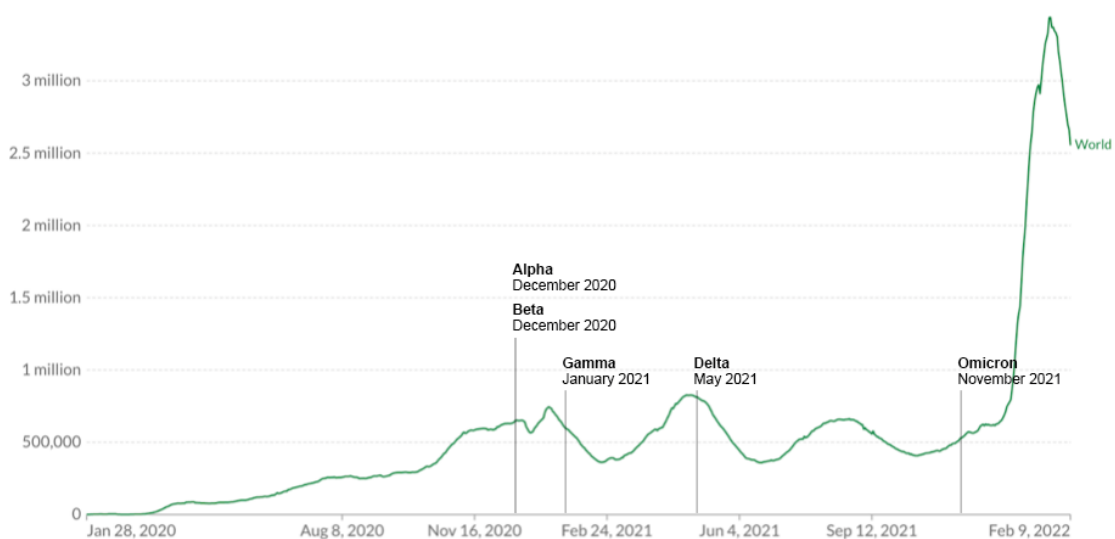
COVID-19 severity can be defined several ways. In clinical studies, severe COVID-19 is often defined by a set of clinical manifestations such as symptoms and the degree to which lung function is impaired. Some studies provide their own criteria; others use definitions developed by the [National Institutes of Health](#) or the [World Health Organization](#).

Epidemiologic studies may assess severity through clinical resource utilization (e.g., supplemental oxygen or mechanical ventilation) and/or outcomes (e.g., admission

to intensive care or death). How a study defines severity is critical to the interpretation of results and to the application of findings outside clinical trials.

Determining severity is often somewhat subjective. Decisions to hospitalize a patient or admit them to intensive care may be influenced by a range of clinical and health systems factors, and outcomes depend on individual risk factors as well as on the availability and quality of care. Furthermore, comparison of Omicron with prior variants is complicated by the much higher rate of immunity (from vaccination, prior infection, or both) among those infected with Omicron than those infected with prior variants earlier in the pandemic. This makes it challenging to compare severity, as data on different variants may come from different populations, settings and periods of time.

Despite abundant data and many analyses, there is no scientific consensus on the relative severity of the Alpha, Beta, Gamma and Delta variants, although available evidence suggests that all four variants cause more severe disease than earlier strains of SARS-CoV-2. There is greater consensus on the relative severity of Omicron compared with previous variants.



Global daily new confirmed COVID-19 cases from January 2020 to February 2022, with the month of designation of each Variant of Concern by the World Health Organization.

Sources: [Our World in Data](#) and [WHO](#)

What do we know about Omicron severity?

Available evidence from around the world consistently shows that Omicron is associated with less severe disease than Delta. These are some of the major conclusions that can be drawn from available data, with summaries of supporting evidence below.

- 1. The strain on health care systems during the Omicron surge was likely driven by the rapid spread of the variant, leading to much higher rates of infection at any given time, rather than by the severity of disease caused by Omicron.**
- 2. Omicron is associated with a much lower risk of hospitalization than Delta.**
- 3. Compared with Delta, Omicron is associated with a lower risk of severe COVID-19 outcomes, but robust estimates of the risk of death are lacking.**

A. Severity assessed through patterns in health care resource utilization

The way a new variant affects the health care system provides clues about the variant's severity. A [preprint study on the first four weeks of each variant wave in Gauteng Province, South Africa](#), showed that there were far more COVID-19 cases diagnosed during Omicron than other variant waves (over 100,000 cases during Omicron and under 50,000 cases during Beta and Delta each) but hospital resources were relatively spared during Omicron: the proportion of hospitalized patients admitted to intensive care was 7% during Omicron, 20% during Beta and 26% during Delta. A [study on the early period of each variant wave in South Africa](#) showed that the proportion of hospitalized COVID-19 cases

requiring supplemental oxygen was 18% during Omicron, 74% during Delta and 82% during Beta. A [study on COVID-19 severity trends during high transmission periods in the U.S.](#) showed that the maximum 7-day average of cases during Omicron (799,000) was 4.8 times higher than the maximum during Delta (164,000), whereas the maximum 7-day average of hospitalizations during Omicron (22,000) was 1.8 times higher than the maximum during Delta (12,000). This suggests that Omicron causes less severe disease than Delta even though there was a higher absolute number of hospitalizations during Omicron.

B. Risk of hospitalization

Numerous analyses have shown that those with Omicron are much less likely to be hospitalized than those with Delta. An [early study from South Africa](#) showed that among COVID-19 cases diagnosed from October 1 to December 6, 2021, those with Omicron were 80% less likely to be hospitalized than those with Delta. National COVID-19 data from England have consistently shown that Omicron is associated with a lower risk of hospitalization than Delta; an [analysis of data collected through the end of December 2021](#) showed that those with Omicron were 67% less likely to be hospitalized than those with Delta. A [preprint study on COVID-19 outcomes among patients in California](#) showed that those with Omicron were 52% less likely to be hospitalized than those with Delta.

C. Risk of severe outcomes other than hospitalization

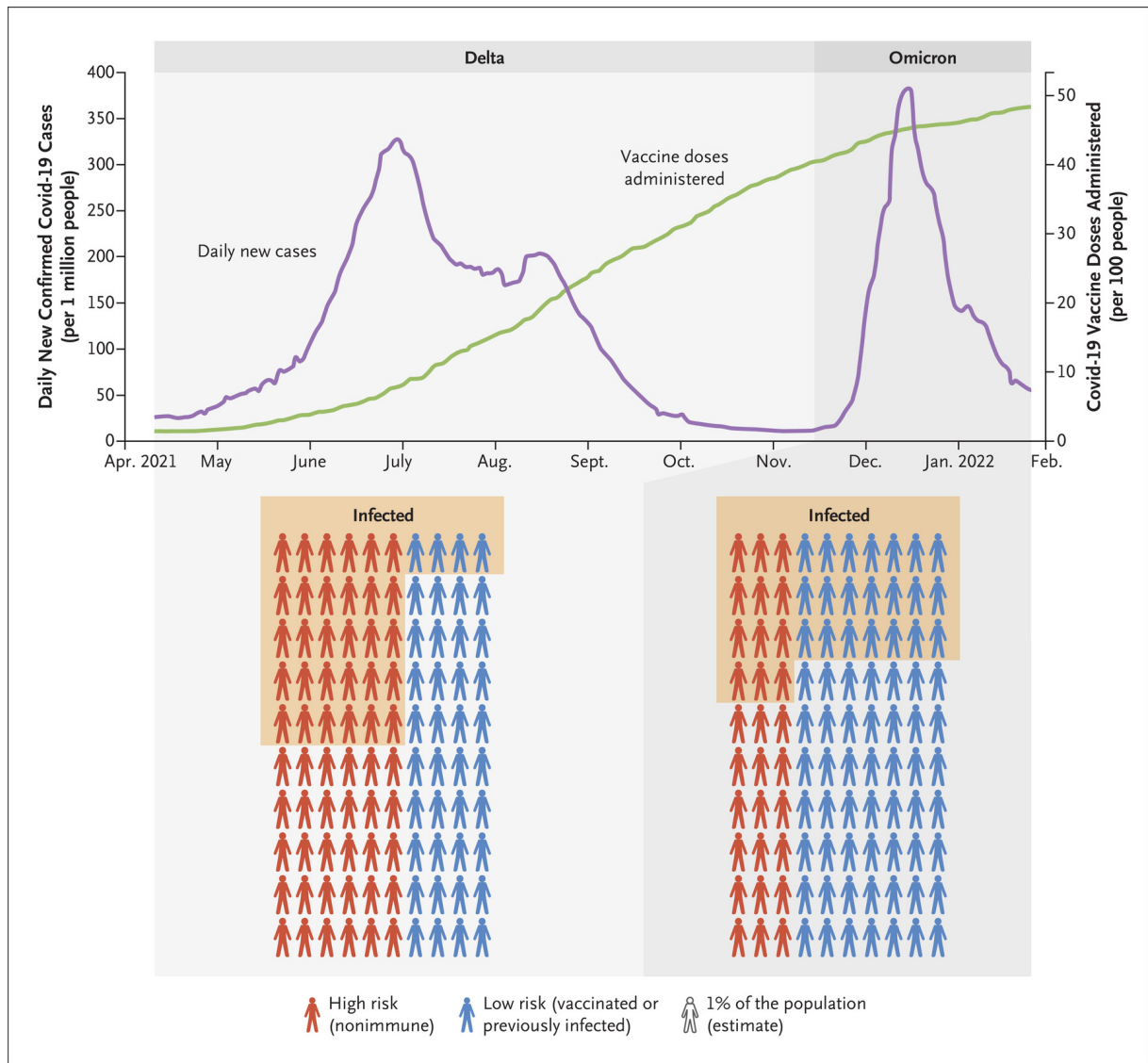
Several studies suggest that Omicron is associated with a lower risk of severe outcomes than Delta. However, there is some uncertainty about the magnitude of risk reduction, especially with respect to the risk of death. An early study from South Africa could not determine whether there was a difference in the risk of severe disease among those with Omicron versus Delta, potentially due to small sample size. A [preprint study that used data from 63 health care organizations across the U.S.](#) showed that those with Omicron had one-third the risk of ICU admission and one-tenth the risk of receiving mechanical ventilation than those with Delta. A [preprint study from a large health care network in California](#) showed that compared to those with Delta, those with Omicron had a 70% lower risk of ICU admission and a 90% lower risk of death. However, the analysis of mortality did not control for potential confounders because of the small number of deaths (1 Omicron, 14 Delta). A [preprint study on long-term care facility residents in England](#) showed that the rate of death was lower among those with Omicron (0.6%) than among those with Delta (10%), but the small number of deaths (8 Omicron, 14 Delta) precluded further analysis. Analyses that include more patients who are followed for longer periods of time will improve our understanding of the risk of severe outcomes associated with Omicron, including among specific high-risk populations.

Why is the severity of Omicron different from other variants?

The severity of any infectious disease is determined by the intrinsic characteristics of the infecting pathogen as well as by the human immune response to that pathogen. It can be difficult to discern the relative contribution of each to disease severity.

SARS-CoV-2 variants of concern are [intrinsically biologically distinct from one another](#). One reason Omicron may cause less severe disease is because of how it affects cells and tissues. Animal models have demonstrated that, compared with other variants, [Omicron may be found at lower concentrations and cause less damage in the lungs of animals infected in the lab](#).

Omicron's mutations allow it to [evade existing immunity better than previous variants](#). Those who have been vaccinated or previously exposed to SARS-CoV-2 are [less protected against Omicron infection than against Delta infection](#). In addition, a higher proportion of the population had been vaccinated or previously exposed to SARS-CoV-2 at the beginning of the Omicron wave than when Delta emerged. Because immunity can blunt the severity of infection, the low apparent severity of Omicron could be largely due to the increased prevalence of immunity over time, as illustrated in the figure below. Because the severity of Omicron may vary between populations with different levels of immunity, caution should be exercised when interpreting study results.



The changing prevalence of immunity among those infected with SARS-CoV-2 during the Delta and Omicron periods.

Source: [NEJM](#)

COVID-19 vaccine effectiveness against Omicron

Multiple analyses have produced estimates of vaccine effectiveness (VE) against COVID-19 caused by Omicron. Most of these estimates come from Europe, South Africa and the U.S., where the most commonly used vaccines are AstraZeneca, Moderna and Pfizer. J&J is also used though to a lesser extent. Effectiveness estimates for other vaccines are lacking; laboratory data may provide some insight but cannot substitute for real-world data. What follows is a summary of what we know about VE against Omicron.

1. Vaccines provide strong protection against severe disease caused by all variants of concern, although effectiveness against Omicron is lower than against previous variants.
2. The effectiveness offered by a primary series wanes over time, more so against Omicron than against Delta, and protection against severe disease is more durable than against infection for all variants.
3. A booster dose restores vaccine effectiveness against COVID-19 of any severity caused by either variant and

protection appears more durable, although long-term data are lacking.

These conclusions are supported by a recent [COVID-19 vaccine surveillance report from the United Kingdom](#). This report summarized VE

estimates from multiple studies that used robust national data from the U.K.; summary estimates are shown in the table below.

		Two doses			Three doses	
		0-3 months	4-6 months	6+ months	0-3 months	4-6 months
Symptomatic disease	Omicron	25-70%	5-30%	0-10%	50-75%	40-50%
	Delta	65-90%	45-65%	40-60%	90-99%	90-95%
Hospitalization	Omicron	65-85%	55-65%	30-35%	80-95%	75-85%
	Delta	95-99%	80-90%	70-85%	95-99%	Insufficient data
Death	Omicron	Insufficient data	Insufficient data	40-70%	85-99%	Insufficient data
	Delta	95-99%	90-95%	80-99%	95-99%	Insufficient data

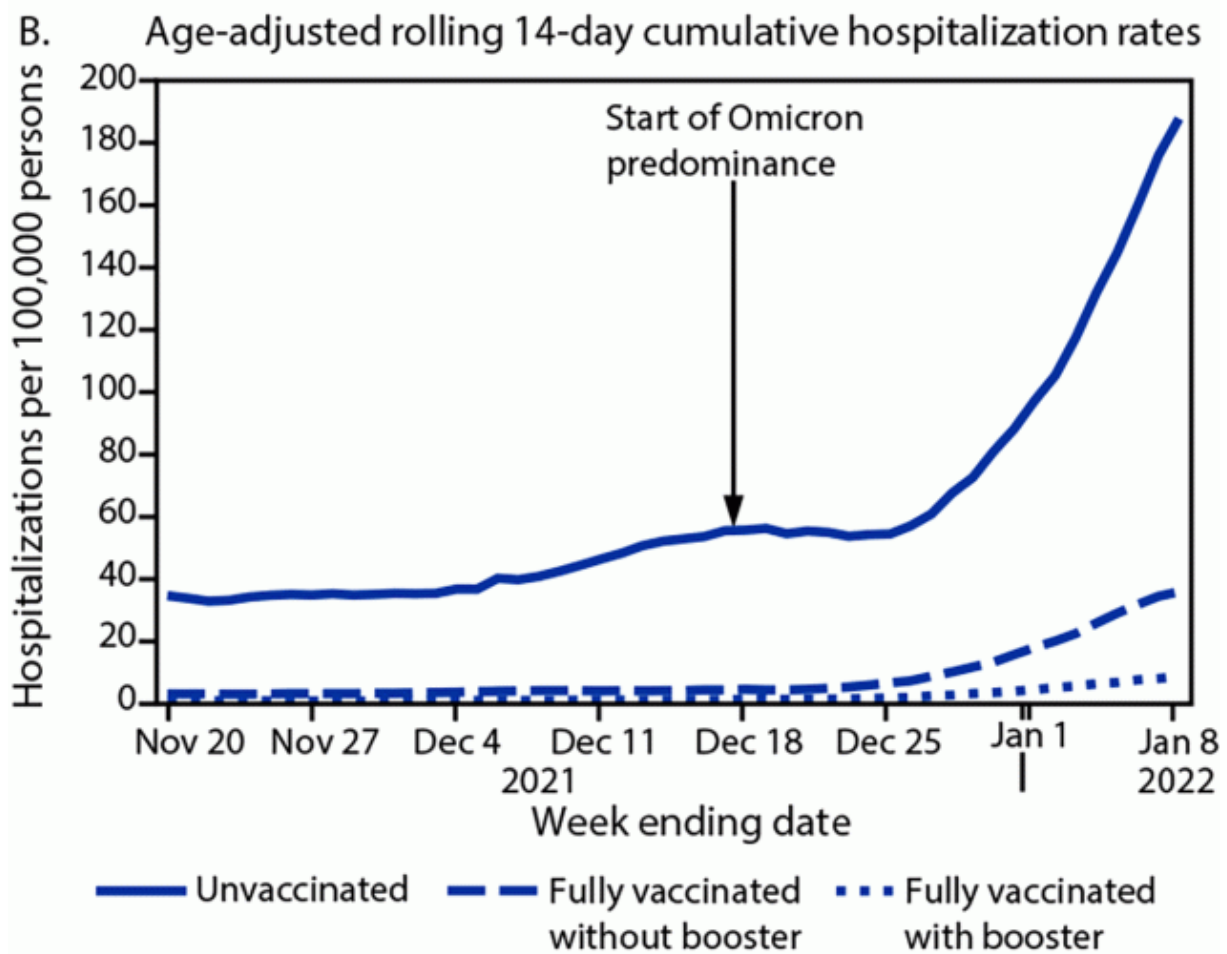
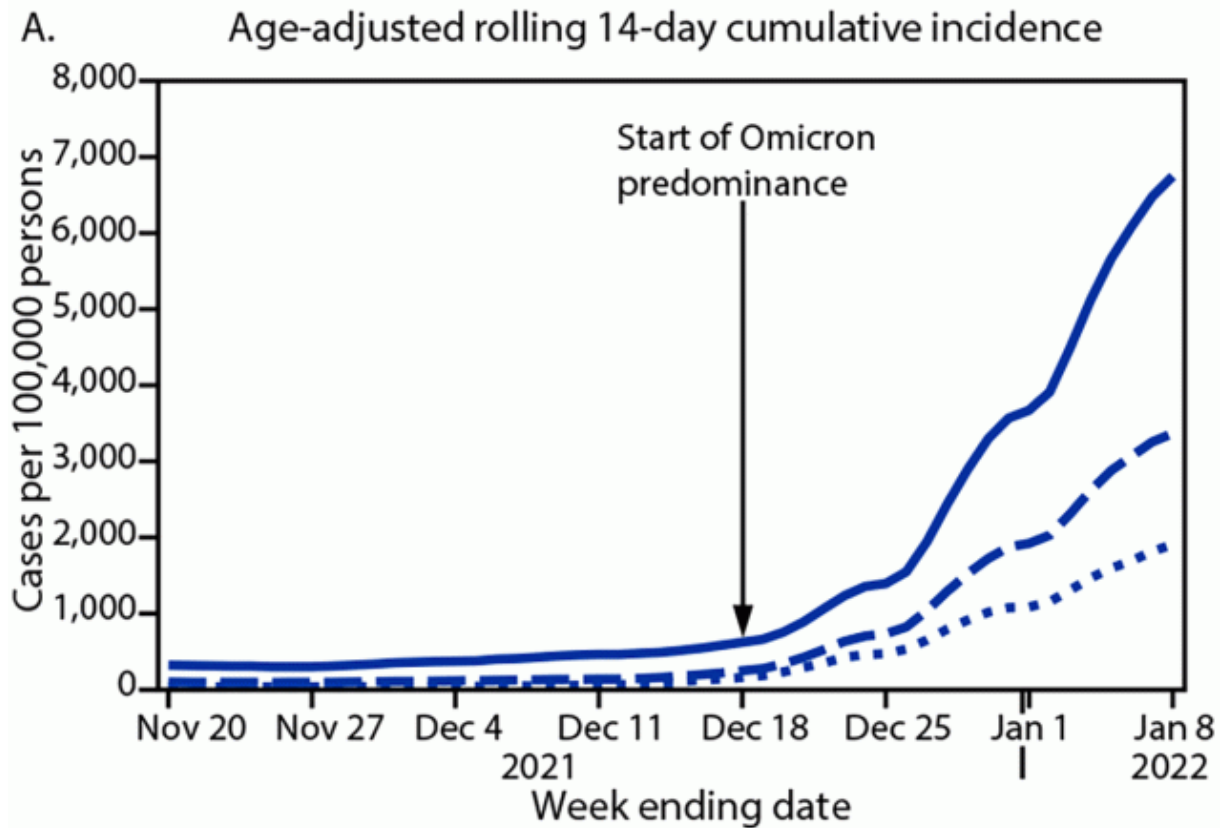
Summary of select vaccine effectiveness estimates from the United Kingdom, stratified by variant, outcome, number of vaccine doses, and time since last dose.

Gray shading - Little evidence is available; analyses are inconclusive. Adapted from: [UK Health Security Agency](#)

Estimates on the performance of specific vaccines are also available. This [technical briefing on SARS-CoV-2 variants of concern and variants under investigation in England](#) includes estimates of VE against symptomatic COVID-19 caused by Omicron or Delta, stratified by vaccine type, number of doses and time since vaccination. The trends in VE over time suggest that both time since vaccination and variant affect VE. Data on the durability over time of the protection offered by boosters are limited. A [preprint study from the U.S.](#) showed that VE of a Moderna booster to prevent Omicron infection was 50% among those boosted 3-4 months prior – from 68% among those boosted 1-2 months prior – while effectiveness against Delta was >85% throughout the study.

Of note, there are several sub-lineages of Omicron characterized by unique genetic mutations. The BA.1 sub-lineage, which was the

globally predominant sub-lineage at the beginning of the Omicron wave, was overtaken by the BA.2 sub-lineage in several countries in January 2022. Early data suggest that [BA.2 may be even more transmissible and more immune-evasive than BA.1](#). However, preliminary evidence suggests that [VE against symptomatic disease caused by BA.2 and BA.1 are similar](#). There is no evidence of a difference in disease severity between BA.1 and BA.2. The most critical function of vaccines is to prevent severe disease and death. A [study from South Africa](#) showed that the effectiveness of a Pfizer primary series to prevent symptomatic COVID-19 hospitalization during the Omicron wave was 50%. An [analysis of data from one U.S. county](#) showed that after Omicron emerged, compared to those who were vaccinated, those who were unvaccinated had four times the risk of infection and 23 times the risk of hospitalization, and those who were boosted had even better protection.



Age-adjusted rolling 14-day SARS-CoV-2 cumulative incidence (A) and hospitalization rates (B), by vaccination status – Los Angeles County, California, November 7, 2021-January 8, 2022.

Another [study from the U.S.](#) showed that the effectiveness of a Moderna or Pfizer primary series against hospitalization waned over time but a booster gave a higher and more durable level of protection. Two-dose VE against hospitalization with Omicron was 71% among those vaccinated less than two months prior and 54% among those vaccinated at least five months prior; three-dose VE against hospitalization was 91% among those boosted less than two months prior and 78% among those boosted at least four months prior.

COVID-19 vaccines other than AstraZeneca, Moderna and Pfizer against Omicron

The above studies on vaccine effectiveness were performed in countries where AstraZeneca, Moderna and Pfizer are used most commonly as primary series, and Moderna and Pfizer are used as boosters. There are limited data on the J&J vaccine from a [study in South Africa](#): among health care workers who received a J&J booster six to nine months after their first J&J dose, VE against hospitalization with Omicron was 85% up to two months after receipt of the second dose. Unfortunately, real-world data on the protection against Omicron offered by [other COVID-19 vaccines approved by the World Health Organization](#) are lacking. This puts public health decision-makers in a difficult position, particularly in countries where some of the widely-used and available vaccines are those with little evidence about their performance against Omicron.

There are some laboratory data on other vaccine products against Omicron. In [this study](#), antibodies from most individuals who received a primary series of J&J, Sputnik or Sinopharm could not neutralize Omicron. Antibodies from those who received AstraZeneca, Moderna or Pfizer could – though

to a lesser extent than an earlier strain of SARS-CoV-2. In [another study](#), antibodies from individuals who received two doses of Sinovac could not neutralize Omicron, but antibodies from those who also received a Pfizer booster could. These data suggest that without a booster – and potentially without an mRNA booster – some vaccines may not provide much protection against Omicron infection. It is impossible to draw conclusions about the effectiveness of these vaccines against severe disease caused by Omicron.

Conclusion:

We are becoming oriented to a new reality of living with COVID-19 – with Omicron as the predominant variant. Omicron means less fear of severe disease for most. Its immune escape potential means that boosters, which restore waning protection, are more important than ever. Living with Omicron means managing an extremely transmissible variant. In order to protect individuals and health care systems from future Omicron surges, being up-to-date on COVID-19 vaccination – which provides excellent protection against hospitalization and severe COVID-19 – is critical.

But if Omicron is much less severe than Delta, how important is COVID-19 vaccination? Is vaccination during Omicron a priority when there are numerous other health threats that cause a much greater burden of morbidity and mortality? If vaccines don't provide good protection unless a booster is given, what should be done in places where even primary vaccine series coverage is low?

These are good questions.

Although Omicron is less severe than Delta, it has caused hundreds of thousands of hospitalizations and tens of thousands of

deaths, and health care systems have been overwhelmed. Vaccination is the best way to protect against these outcomes. Vaccination of everyone at high risk of severe COVID-19 could save many lives. And it is essential to vaccinate all health care workers – for their health, the health of their families and patients, and to protect the health care system by preventing absenteeism due to COVID-19.

Primary vaccines series – and boosters – offer strong protection against severe disease, including hospitalization, for months after vaccination. Several months after a primary series, effectiveness against hospitalization with Omicron wanes. Informed by emerging evidence on vaccine effectiveness against Omicron, the World Health Organization recently revised its [roadmap for prioritizing uses of COVID-19 vaccines](#). The roadmap recommends increasing the use of boosters and balances this against the priority of expanding primary series coverage.

Vaccines for which there are reliable real-world performance data, including against the Omicron variant, should be prioritized for use. Studies on the effectiveness of all authorized vaccines against the Omicron variant are needed. Especially for those who received vaccines without supporting data on real-world effectiveness against Omicron, emerging evidence supports heterologous boosting

strategies (the booster and the primary series are different vaccine products) against COVID-19 more generally. Several studies have demonstrated that [heterologous boosters are safe and can increase immune responses to SARS-CoV-2 more than homologous boosters](#). Recipients of a J&J primary series (single dose) [who received an mRNA booster](#) had half the risk of SARS-CoV-2 infection as J&J recipients with a homologous booster; recipients of a [Sinovac primary series who received an AstraZeneca, Pfizer or Sinovac booster](#) all had excellent protection against severe COVID-19, but vaccine effectiveness was highest among those with heterologous boosters.

Ultimately, the goal of vaccination is to protect against COVID-19, not just against Omicron. We do not know how long Omicron will continue to predominate, when the next variant may emerge, or what its characteristics will be. Our vaccines have provided strong protection against severe disease caused by all variants that have emerged thus far, and the most protective and reasonable approach is to anticipate that vaccines will continue to be our best tool against the future risks of COVID-19.

For further details on the studies that informed this review, please see the accompanying Annex.

Suggested citation: Cash-Goldwasser S. and Frieden TR. In-Depth COVID-19 Science Review February 14, 2022. Resolve to Save Lives. 2022

February 14. Available from <https://preventepidemics.org/covid19/science/review/>