

STAT

Covid-19 vaccines flirted with perfection at first. Reality is more complicated



By [Helen Branswell](#) Aug. 25, 2021



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When Covid-19 vaccines were reported last fall to be roughly [95% effective](#) at preventing symptomatic Covid-19 infections, the world rejoiced — and even veteran scientists were blown away. Very few vaccines are that protective. Those made to fend off viruses like SARS-CoV-2 — viruses that invade the nose and throat, like flu — typically aren't at the high end of the efficacy scale.

That was the good news. Now, however, our soaring expectations for Covid-19 vaccines are in the process of sinking back to earth.

With the more transmissible [Delta variant of SARS-2](#) circulating, it is increasingly apparent that, even if mRNA vaccines like Pfizer's and Moderna's offer impressive protection against severe Covid infections, they aren't going to prevent infections in the upper respiratory tract of some proportion of vaccinated people.

The vaccines are wondrous weapons, but they aren't impenetrable armor.

“We all wish that that this would be gone. That we would get a vaccine and ... we would control it,” Kathryn Edwards, a vaccine expert at Vanderbilt University, told STAT. “But I think that looking back, probably that wasn't always realistic.”

There are still open questions about exactly how much less protection mRNA vaccines may be providing. Evidence of the downward creep of their efficacy is based in part on as-yet-unpublished data from Israel, one of the first countries to vaccinate a high percentage of its elderly.

Ran Balicer, director of Israel's Clalit Research Institute and one of the scientists involved in this research, said the group has seen a decline in vaccine effectiveness since the Delta variant started to take off in the country. But figuring out what is behind that — waning immunity? Delta's increased transmissibility? The advanced age of the Israelis who

were first vaccinated? A combination of those factors? — is very challenging, he said.

Balicer said he and his team were “acutely aware of various types of confounding [factors]” and the difficulty of finding a good way to compare data on the vaccinated and unvaccinated in a way that allows for a methodologically sound study to be run. It is, he said, “why it is taking us more time than usual to release our assessments and publications.”

There’s another factor that complicates researchers’ ability to figure out what’s behind the data in Israel and how much it can tell other countries about the mRNA vaccines as a class. Israel used Pfizer vaccine exclusively; its findings may not apply to the [Moderna jab](#).

“Israeli data can only give hints regarding Pfizer vaccines. Everything else needs to be inferences from other countries,” Balicer said.

For Michael Osterholm, the jury is still out on what is behind the increase in cases among vaccinated people, and how big a threat it poses.

“It all comes down to: Is it waning immunity against severe illness, hospitalization, and deaths, or is it waning against mild illness? And I don’t think we’ve answered that yet,” said Osterholm, who is director of the University of Minnesota’s Center for Infectious Disease Research and Policy. “Now I think it’s the right question to pose.... The challenge is we just don’t have an answer to that yet.”

Though the Israeli data haven’t yet been published, top-line findings have been made available. Based on them and on some preliminary U.S. data, the Biden administration’s public health leaders announced last week that Americans [would be offered a third dose](#) of the mRNA vaccines starting the week of Sept. 20, because the breakthrough infections may presage a decline in efficacy against severe disease. A

third shot of mRNA vaccine should follow eight months after the second, they said.

“We are concerned that the current strong protection against severe infection, hospitalization, and death could decrease in the months ahead, especially among those who are at higher risk, or who were vaccinated earlier during the phases of our vaccination rollout,” Rochelle Walensky, director of the Centers for Disease Control and Prevention, said in explaining the decision.

A critic of the booster decision, Anna Durbin, believes the high bar set by the results of the Phase 3 clinical trials of the Pfizer and Moderna vaccines is now negatively impacting U.S. vaccination policy.

“I think these vaccines are a victim of their own success,” said Durbin, a vaccine researcher in Johns Hopkins Bloomberg School of Public Health. “Now we expect perfection. And if it’s less than perfect, we want a booster.”

Some scientists have noted that a year ago when the Phase 3 trials for these vaccines were first underway, the world would have been ecstatic at the prospect of vaccines that prevented severe Covid infections in most vaccinated people. But vaccine efficacy estimates in the 90% range against even mild infections reset what we thought these vaccines would be able to do for us.

Vincent Munster, chief of the virus ecology section at the National Institute of Allergy and Infectious Diseases’ Rocky Mountain Laboratories in Montana, also thinks our expectations may be unrealistic.

He and his team tested some Covid vaccines in the early stages of development, before human trials were conducted. In animals, the vaccines did not block infection in the upper airways, but did protect the lungs. If the animal work is predictive of what happens in humans, it

would mean vaccinated people could catch colds or experience flu-like symptoms if they contract SARS-2, but would not — in most cases — develop severe or life-threatening illness.

“We were making a vaccine against the severe Covid and, all of a sudden, all these expectations of transmission-blocking were piled up on these vaccines,” he said.

Case in point: In announcing the decision to offer third shots, Walensky cited a study from New York state that showed the mRNA vaccines’ efficacy against any infection had declined to 79.8%. But that same study showed protection against serious illness was still above 90%. For many experts, it was evidence not of a problem, but of a success.

There were also questions about drawing too many conclusions based on the study. Even the authors cautioned that waning protection might not be the whole story. People were more afraid of Covid in the summer and fall of 2020, and many were more rigid about following social distancing measures.

“Variations from clinical trial findings could be because the trials were conducted during a period before the emergence of new variants and when non-pharmaceutical intervention strategies (e.g., wearing masks and physically distancing) were more stringently implemented, potentially lessening the amount of virus to which persons were exposed,” they wrote.

Munster, Durbin, and many other experts insist that the vaccines are still standing up as well as they can in the face of a daunting challenge. With vaccination rates in a number of states still far too low, the amount of SARS-2 circulating is dismayingly high at this point, more than a year-and-a-half into the pandemic in the United States. The way to make progress in the fight is to get more people vaccinated — both here and

abroad — to cut transmission and the risk of new variants emerging, they insist.

“Giving a booster to vaccinated people is not going to control Delta. What’s going to control Delta is vaccinating unvaccinated people,” Durbin said. “That is the bottom line.”

Edwards, from Vanderbilt, thinks we’re going to have to curb our expectations, warning that as time goes on, there will likely be vaccinated people who aren’t immunocompromised who will get severely ill — and some will die.

“I don’t think it’s going to be a lot, but I think it will be there and I think that will make us all *very* uncomfortable,” she said. “I think that we have to be realistic about what we can expect.”

About the Author



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