

## Omicron threat may be countered with booster Covid vaccine dose, show studies

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The earliest studies on omicron are in and the glimpse they're providing is cautiously optimistic: while vaccines like the one made by Pfizer Inc. and BioNTech SE may be less powerful against the new variant, protection can be fortified with boosters.

Studies from South Africa and Sweden are showing that omicron does, as feared, cause a loss of immune protection -- but not a complete one. In a study of blood plasma from people given two doses of the Pfizer-BioNTech shot, there was a 41-fold drop in levels of virus-blocking antibodies compared with the strain circulating at the start of the pandemic.

A separate study from Stockholm's Karolinska Institute was more optimistic, finding the decline in antibodies against omicron was only slightly worse than for delta, the strain currently causing most Covid-19 cases worldwide.

The results offer early, as yet incomplete insight into how potentially damaging the spread of omicron could be. The studies are small, so their findings aren't conclusive. And the data aren't the full story, because antibody levels are only one piece of the immune system's response against the virus. So-called "killer" T cells also play an important role in protection against severe disease, and that's harder to measure in a lab.

Researchers saw reason for hope. The loss of immune protection is "robust, but not complete," said Alex Sigal, head of research at the Africa Health Research Institute in Durban, who presented the findings of the first study late Tuesday. "A good booster probably would decrease your chance of infection, especially infection leading to more severe disease," he said.

The World Health Organization has warned omicron could fuel surges with "severe consequences" amid signs that it makes the coronavirus more transmissible. Still, the jump in cases in South Africa following omicron's emergence hasn't overwhelmed hospitals so far, prompting some cautious optimism that the new strain may cause mostly mild illness.

Governments and financial markets are trying to gauge whether the new variant will have a significant impact on the world's attempt to move past the pandemic. Omicron's rapid spread has raised concern the strain would be sufficiently immune-evasive to require new vaccines, and hundreds of researchers have been working around the clock to answer the question.

"These Karolinska data are reason for optimism," said Shane Crotty, a professor in the Center for Infectious Disease and Vaccine Research at San Diego's La Jolla Institute for Immunology. "That is pretty close to the best-case scenario I was considering."

Levels of neutralizing antibodies are a key marker of immune protection. Although they naturally decline in the months after an infection or vaccination, the body's ability to spring into action to make

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more effective antibodies if needed has been shown to improve over time. What's more, studies have found that a third dose some six months after the second can bolster levels of these better-quality antibodies, making boosters an important weapon to fight omicron.

"There will be more breakthrough" of vaccine-induced immunity, Sigal said, adding that fully vaccinated people should get booster shots and those who've been previously infected should get vaccinated.

### **Preliminary Results**

The results are preliminary and exact levels of immune escape may change, said Sigal, whose lab was the first to isolate the beta variant identified in South Africa in late 2020. He noted that omicron escapes antibody neutralization more readily than beta, which had been considered the most immune evasive of the variants of concern detected previously.

A key question researchers are trying to address is whether existing Covid vaccines need to be altered to protect against omicron.

Any vaccine changes would require careful consideration, especially since delta is currently the main driver behind the Covid epidemics and existing shots provide a sufficient shield against it, Ana-Maria Henao-Restrepo, who co-leads the WHO's research and development blueprint for vaccines and innovations during outbreaks and pandemics, said last week.

### **More Data**

The magnitude of the drop in neutralizing antibodies against omicron could indicate a need for omicron-matched vaccines, though other considerations may play a role, said Stephen Goldstein, an evolutionary virologist at the University of Utah in Salt Lake City. Larger studies looking at neutralizing antibodies from people immunized with other vaccines are also needed, he said.

"More importantly though will be epidemiological studies looking at the frequency of reinfections and breakthrough infections, as well as disease severity in those patients," Goldstein said. "I am still optimistic that vaccination or prior infection will provide some measure of protection against severe disease."

The work in Sigal's lab involved testing 14 blood plasma samples collected from a dozen people who had been given a second Pfizer-BioNTech shot about a month earlier to gauge the concentration of antibodies needed to neutralize, or block, the live omicron virus. Levels of neutralizing antibodies against the variant were significantly higher in a subset of participants who had a bout of Covid about a year earlier, Sigal said.

### **Hybrid Immunity**

That indicates so-called hybrid immunity generated by natural infection followed by immunization may provide reasonable protection against omicron. In those who have never had Covid, this could be emulated by administering three doses of vaccine, the La Jolla Institute's Crotty said.

"What many of us want to see is head-to-head comparisons against other variants, because of the broader experience with them," he said. Scientists also want to better understand the significance of the reduction in levels of neutralizing antibodies against omicron, and to study the antibody responses

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against omicron in blood sera from people who have received three doses of either the Pfizer or Moderna vaccine, Crotty said.

In the weeks ahead, more clarity will also emerge from studies assessing the T cell response to omicron, like one being run by the La Jolla Institute's Alessandro Sette.

It's possible omicron will have a less extreme impact on T cells, the white blood cell the immune system uses to kill virus-infected cells, said Dan Barouch, the William Bosworth Castle professor of medicine at Harvard Medical School and head of Boston's Beth Israel Deaconess' Center for Virology and Vaccine Research.

The Swedish study tested 34 plasma samples, half of whom were from health workers infected by the coronavirus in the pandemic's first wave. The other 17 were from blood donors with detectable antibodies, possibly generated by vaccination.

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