

# News in focus



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The Omicron coronavirus variant is spreading rapidly in several countries.

## OMICRON LIKELY TO WEAKEN COVID VACCINE PROTECTION

Existing vaccines could be less effective against the fast-spreading coronavirus variant, but boosters should improve immunity.

By Ewen Callaway

**T**he fast-spreading Omicron SARS-CoV-2 variant is highly likely to compromise some of the protection from vaccines, suggest the first laboratory studies of Omicron's ability to evade immunity.

But the preliminary results – released by teams in South Africa, Germany and Sweden, as well as by the Pfizer–BioNTech collaboration – hint that protection from existing vaccines won't be totally wiped out, and that boosters should improve immunity to Omicron.

“We're likely to see reduced effectiveness of vaccines against preventing infection,” says Penny Moore, a virologist at the University of Witwatersrand in Johannesburg, South Africa, who co-authored one of the studies. “I think it's a strong argument to get boosters out there.”

The studies, which measure the capacity of antibodies in people's blood to block the infection of cells in a dish, have not yet been peer reviewed, and do not tell researchers the extent to which vaccines' ability to protect against COVID-19 – in particular, its most severe forms – could be compromised.

“We still need to wait for more effectiveness data and clear signals from the places where this is blowing up first,” says Ben Murrell, an interdisciplinary virologist and immunologist at the Karolinska Institute in Stockholm, who co-led one of the studies.

### Many mutations

Researchers in Botswana and South Africa identified Omicron in late November, and teams worldwide have since been racing to understand the variant's properties and the risks that it poses. Preliminary data from South

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Africa and elsewhere suggest that the variant is highly transmissible – spreading several times faster than Delta – and might be able to infect people who are immune to other variants.

Omicron carries a large number of mutations in its spike protein – the prime target of immune responses – and some of these changes, when present in other variants, affect the ability of antibodies to recognize the virus and block infection.

Scientists used two types of laboratory assay to test how well Omicron can evade neutralizing, or virus-blocking, antibodies. One approach uses infectious SARS-CoV-2 particles, typically isolated from individuals infected with Omicron. The other relies on pseudovirus particles – genetically modified versions of another virus (often HIV) that use the SARS-CoV-2 spike protein to infect cells.

The results from the four teams all suggest that Omicron blunts the potency of neutralizing antibodies more extensively than any other circulating SARS-CoV-2 variant. But the magnitude of Omicron's impact varied between the studies, which examined blood from people with different vaccination and infection histories.

A study led by virologist Alex Sigal, at the Africa Health Research Institute in Durban, South Africa, found that serum – the antibody-containing portion of blood – from 12 people who received the Pfizer–BioNTech vaccine was around 40 times less potent against Omicron, on average, than against an earlier strain of SARS-CoV-2. That finding was similar to the results from two other studies: one reported by Pfizer and BioNTech in an 8 December press release, and the other released on Twitter and later posted on medRxiv by virologist Sandra Ciesek at the Goethe University Frankfurt, Germany (A. Wilhelm *et al.* Preprint at medRxiv <https://doi.org/g8sz>; 2021).

A fourth study, led by Murrell and virologist Daniel Sheward, also at the Karolinska Institute, reported a smaller reduction in levels of Omicron-neutralizing antibodies in two groups of participants: 17 health-care workers, who had all been previously infected, and 17 Swedish blood donors. The researchers cannot determine the vaccine status of the anonymous blood donors, but say they will soon update their paper with vaccination information from the health-care workers.

Despite differences in results – which are common in such virus-neutralization assays – the labs' conclusions are similar, and show that Omicron's effects on neutralizing antibodies are “not complete knockouts”, says Murrell. “The magnitude is still a little up for question.”

### Booster protection

The results suggest that vaccines' effectiveness is likely to be significantly modified by Omicron – but precisely how much is hard to

say. Sigal's team found that people who had already been infected before vaccination tended to have higher levels of neutralizing antibodies against Omicron than vaccinated people with no known history of infection. “I think retaining some neutralization against Omicron can only be helpful,” says Moore, a co-author on the study, whose lab is also working on neutralization experiments.

**“Omicron is scarier than anything we've known before, because it's a little bit worse still than Delta.”**

A previous case of COVID-19 isn't the only way to improve antibody levels against Omicron. The Pfizer–BioNTech study found that people who had received a third dose of its vaccine had neutralizing antibody levels against Omicron comparable to those, triggered by two vaccine doses, against other SARS-CoV-2 variants. On the basis of those results, “we expect significant protection against any type of COVID-19 mediated by Omicron in individuals who have received

the third vaccine”, said BioNTech's chief executive, Uğur Şahin, at a press conference on 8 December.

Danny Altmann, an immunologist at Imperial College London, agrees that jacking up antibody levels with booster shots should help protect against Omicron, just as boosters have improved protection against the Delta variant. “Omicron is scarier than anything we've known before, because it's a little bit worse still than Delta. But we were in quite a bad situation with Delta in unboosted populations,” Altmann says.

Jesse Bloom, an evolutionary biologist at the Fred Hutchinson Cancer Research Center in Seattle, Washington, says that it will be important to determine the extent to which immune mechanisms other than neutralizing antibodies, such as T cells, ameliorate severe disease caused by infection.

It will also be important to see further studies confirming the latest results, because variables such as the type of cell used can affect conclusions, says Pei-Yong Shi, a virologist at the University of Texas Medical Branch at Galveston. “In the next week or ten days, there will be a lot of confirmatory results coming out,” he says.

## HALF OF CANCER STUDIES FAIL HIGH-PROFILE REPLICATION TEST

Barriers to reproducing preclinical results included unhelpful author communication.

By Asher Mullard

**A** US\$2-million, 8-year attempt to replicate influential preclinical cancer research papers has released its final – and disquieting – results. Fewer than half of the experiments assessed stood up to scrutiny, reports the Reproducibility Project: Cancer Biology (RPCB) team in *eLife*<sup>1,2</sup>. The project – one of the most robust reproducibility studies performed so far – documented how hurdles including vague research protocols and uncooperative authors delayed the initiative by five years and halved its scope.

“These results aren't surprising. And, simultaneously, they're shocking,” says Brian Nosek, an RPCB investigator and executive director of the Center for Open Science in Charlottesville, Virginia. Although initially planning to repeat 193 experiments from 53 papers, the team ran just 50 experiments from 23 papers.

The low replication rate is “frankly, outrageous”, says Glenn Begley, an oncologist and co-founder of Parthenon Therapeutics in Cambridge, Massachusetts, who was not involved in the study. But it isn't unexpected, he agrees. In 2012, while at the biotech firm Amgen in Thousand Oaks, California, Begley's team helped to draw attention to growing evidence of a ‘reproducibility crisis’, the concern that many research findings cannot be replicated. Over the previous decade, his haematology and oncology team had been able to confirm the results of only 6 of the 53 (11%) landmark papers it assessed, despite working alongside the papers' original authors. Other analyses have reported low replication rates in drug discovery, neuroscience and psychology.

### Double take

The RPCB – a partnership between the Center for Open Science and Science Exchange, a marketplace for research services in Palo