

NEWS | 25 May 2022

# Long COVID risk falls only slightly after vaccination, huge study shows

Results suggest that vaccines offer less protection against lingering symptoms than expected.

Sara Reardon



A health worker administers a booster dose of COVID-19 vaccine. Credit: Algi Febri Sugita/SOPA Images/LightRocket/Getty

Vaccination against SARS-CoV-2 lowers the risk of long COVID after infection by only about 15%, according to a study of more than 13 million people<sup>1</sup>. That's the largest

cohort that has yet been used to examine how much vaccines protect against the condition, but it is unlikely to end the uncertainty.

Long COVID – illness that persists for weeks or months after infection with SARS-CoV-2 – has proved difficult to study, not least because the array of symptoms makes it hard to define. Even finding out how common it is has been challenging. Some studies<sup>2,3</sup> have suggested that it occurs in as many as 30% of people infected with the virus. But a November study<sup>4</sup> of about 4.5 million people treated at US Department of Veterans Affairs (VA) hospitals suggests that the number is 7% overall and lower than that for those who were not hospitalized.

Another mystery has been whether long COVID is less likely to occur after a breakthrough infection – one in a person who has been vaccinated. In a 25 May study<sup>1</sup> in *Nature Medicine*, nephrologist Ziyad Al-Aly at VA Saint Louis Health Care System in St Louis, Missouri, and his colleagues – the same team that authored the November study – looked at VA health records from January to December 2021, including those of about 34,000 vaccinated people who had breakthrough SARS-CoV-2 infections, 113,000 people who had been infected but not vaccinated and more than 13 million people who had not been infected.

## Chinks in the armour

The researchers found that vaccination seemed to reduce the likelihood of long COVID in people who had been infected by only about 15%. That's in contrast to previous, smaller studies, which have found much higher protection rates. It's also a departure from another large study<sup>5</sup>, which analysed self-reported data from 1.2 million UK smartphone users and found that two doses of a COVID-19 vaccine halved the risk of long COVID.

The authors of the latest study also compared symptoms such as brain fog and fatigue in vaccinated and unvaccinated people for up to six months after they tested positive for SARS-CoV-2. The team found no difference in type or severity of symptoms between those who had been vaccinated and those who had not. "Those same fingerprints we see in people who have breakthrough infections," Al-Aly says.

There have been more than 83 million COVID-19 infections in the United States alone, he notes. If even a small percentage of those turn into long COVID, “that’s a staggeringly high number of people affected by a disease that remains mysterious”.

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The limited protection provided by vaccines means that withdrawing measures such as mask mandates and social-distancing restrictions might be putting more people at risk – particularly those with compromised immune systems. “We’re literally solely reliant, now almost exclusively, on the vaccine to protect us and to protect the public,” says Al-Aly. “Now we’re saying it’s only going to protect you 15%. You remain vulnerable, and extraordinarily so.”

“Generally speaking, this is horrifying,” says David Putrino, a physical therapist at Mount Sinai Health System in New York City who studies long COVID. He praises the study, which was difficult to perform because of the amount and quality of data, but adds that it is limited because it does not break the data down by key factors, such as the participants’ medical history. “These are very important questions we need answers to,” Putrino says. “We don’t have any really well constructed studies just yet.”

## Another Omicron unknown

Steven Deeks, an HIV researcher at the University of California, San Francisco, points out that the study includes no data from people infected during the period when the Omicron variant was causing the majority of infections. “We have no data on whether Omicron causes long COVID,” he says. The findings, he adds, “apply to a pandemic that has changed dramatically”.

However, Deeks adds, the results do point to the need for more research on long COVID, and for accelerated development of therapies. “We don’t have a definition, we don’t have a biomarker, we don’t have an imaging test, a mechanism or a treatment,” he says. “We just have questions.”

doi: <https://doi.org/10.1038/d41586-022-01453-0>

## References

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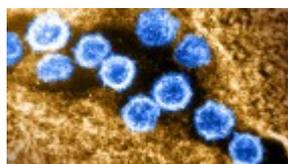
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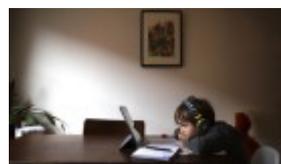
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