



Belfast, UK

chrisbaraniuk@gmail.com

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Covid-19: How effective are vaccines against the delta variant?

The delta variant is now the dominant form of SARS-CoV-2 in the UK and many other countries. **Chris Baraniuk** asks how effective the leading vaccines are against this new threat

Chris Baraniuk *freelance journalist*

"Two days after my first symptoms, I began to feel seriously ill," wrote BBC TV presenter Andrew Marr.¹ He described how he had previously felt invulnerable having received both of his covid vaccine doses. Nonetheless, he became infected with the virus, which he suspects he caught at the G7 summit in Cornwall.

Marr recovered but some have not. Data from Public Health England (PHE) reveal that of all the people who died within 28 days of testing positive for the delta variant between 1 February and 19 July, 49% (224) had had two vaccine doses. Almost all of these people, 220, were aged 50 or older.²

As the statistician David Spiegelhalter notes, in a population where less-than-perfect vaccines have been distributed widely, one would expect to see deaths occurring among vaccinated people as the virus spreads. And so far, in contrast to the winter when far fewer people had received vaccines, the rate of hospital admissions and deaths in the UK is not rising as sharply as cases.

Although uncertainty remains, there is reason to be confident about the protection offered by current covid vaccines, says Eleanor Riley, professor of immunology and infectious disease at the University of Edinburgh. Referring to Marr, who had a major stroke in 2013, she says: "A man over 60 with significant prior health problems got a mild, flu-like illness and was back at work in a week."

Warning signs

Data up to 4 August from Imperial College London's React study found that people who said they had received two vaccine doses were half as likely to test positive for covid-19, adjusting for other factors such as age and whether or not they had symptoms.³ The researchers estimated a 50-60% lower risk of infection from the delta variant if a person was double vaccinated.

The picture emerging from various countries does, however, suggest that vaccinated people are more likely to experience symptoms after catching the delta variant compared with earlier forms of the virus.

Data published by the Israeli government suggest that the Pfizer BioNTech jab's efficacy against symptomatic infection fell from 94% to 64% after the delta variant began spreading in the country.⁴

Figures from Public Health Scotland published in the *Lancet* also show a drop in protection against symptomatic illness,⁵ from 92% against the alpha variant, which was first detected in the UK, to 75% against delta among people with two doses of the Pfizer BioNTech vaccine. For the Oxford AstraZeneca

vaccine, the reduction was from 81% to 61%. Data from Canada, yet to be peer reviewed, also show a drop in efficacy.⁶

It's difficult to compare data from multiple countries because they all have different protocols determining when people become eligible for a covid-19 test, for example. And symptomatic infection can take many forms, from very mild to severe illness.

But Riley points out that the PHE data to date are consistent with estimates that suggest—despite these drops in efficacy—vaccines in use in the UK (Pfizer BioNTech, AstraZeneca, and Moderna) all reduce the risk of death by more than 85%, regardless of variant.

What about transmission?

A lingering question is to what extent the vaccines may be losing effectiveness at preventing onward transmission from people who become infected. After all, each of the new variants is characterised by increased transmissibility compared with the original (wild type) SARS-CoV-2.

Akiko Iwasaki of Yale University says we won't know unless we can get more observational studies following household contacts.

One yet to be peer reviewed study looked at a single outdoor wedding near Houston, Texas, in April where all 92 guests were required to be fully vaccinated.⁷ A couple who had travelled from India later tested positive for delta, with one dying a month later. Of the people they interacted with at the wedding, four became ill with delta. One required monoclonal antibody treatment, but all four survived.

A recently released report from the US Centers for Disease Control and Prevention suggests that the viral load of vaccinated people infected with the delta variant is similar to that of unvaccinated people.⁸ People remain less likely to become infected in the first place when they have been vaccinated, however.⁹

Neutralising antibodies

It's not yet clear how the body's immune system fights SARS-CoV-2. Without knowing for sure what the correlates of protection are, it's hard to say why a vaccine may be less effective against variants. Evidence is accumulating, however, that the ability of antibodies to neutralise the delta variant is reduced compared with, say, the alpha variant.

A study published in *Nature* found that antibodies in blood samples (sera) from convalescent patients up to 12 months post-infection were four times less effective at neutralising the delta variant than the alpha variant.¹⁰ Sera from people who had only a single dose of the Pfizer BioNTech or Oxford AstraZeneca vaccines "barely" inhibited delta, wrote the authors.

They did, however, see a neutralising response in sera from almost all people who had received two doses of a vaccine.

Another study on neutralising antibodies, published in the *Lancet*, found that, following two doses of the Oxford AstraZeneca vaccine, the number of people who had quantifiable antibodies against delta was significantly lower, at 62% (39 of 63), than against the original wild type SARS-CoV-2 (100% of participants).

That may sound worrying, but Akiko Iwasaki, professor of immunobiology and molecular, cellular, and developmental biology at Yale University, says there is reason to be hopeful that people who have had two vaccine doses can still fend off severe disease when infected by delta. This is likely to be in part because of other aspects of the immune system, such as T cells that stimulate B cells to produce antibodies or killer T cells that destroy infected cells in the body.¹¹

She also points out that a reduction in neutralising antibodies does not necessarily mean that antibodies will fail to have an impact. “I assume that the reason we can still prevent severe disease from the delta variant is that we are generating enough antibody response against the spike protein,” she says.

Laboratory based analysis of antibody and T cell responses to the original SARS-CoV-2 virus and multiple variants coauthored by Iwasaki and yet to be peer reviewed found that, against delta, vaccination still prompted neutralising antibodies.¹² There were, however, more antibodies in people who had caught covid-19 before vaccination.

The bottom line is that delta—a variant with distinct mutations making it much more transmissible, blunting immune protection as much as 10-fold—poses a challenge to the vaccines currently used. But in most people the vaccine induced levels of neutralising antibodies are large enough that even a 10-fold drop keeps them well protected.

So, while it's sobering to see cases occurring in fully vaccinated people, their protection is holding up well, as judged by numbers of hospital admissions and fatalities relative to what might have been. As Iwasaki puts it: the message should still be to get vaccinated as soon as possible.

Manufacturers confident

“We haven't seen any evidence that the circulating variants result in a loss of protection provided by the Pfizer BioNTech covid-19 vaccine (BNT162b2) in our laboratory studies,” a spokeswoman for Pfizer told *The BMJ*.

AstraZeneca said in a statement: “Real world data from Public Health Scotland published in the *Lancet*, reaffirmed the AstraZeneca covid-19 vaccine was effective in reducing the risk of SARS-CoV-2 infection and hospital admissions because of the delta variant but at a slightly lower level compared with the alpha variant.”

Moderna has said tests show that its vaccine continued to produce neutralising activity against multiple variants of concern, including delta,¹³ while a Janssen spokesperson told *The BMJ*, “Against the emerging variants of concern, neutralising antibodies were higher against the delta variant than what was observed for the beta variant in South Africa.”

Despite this universal confidence, however, Pfizer, for one, is at work on an updated version of its vaccine, targeting the delta variant specifically. The company hopes this will enter clinical studies in August.

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