COVID-19 vaccines are probably less effective at preventing transmission than symptoms – here's why

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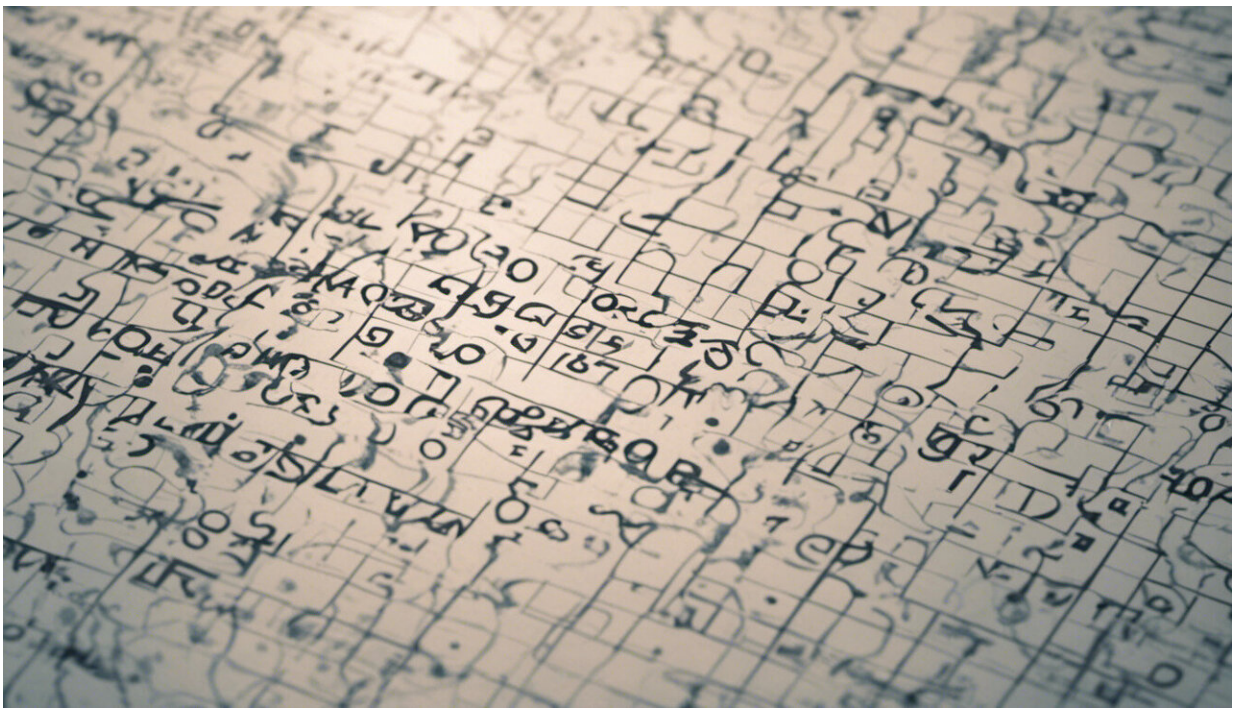

Credit: AI-generated image (disclaimer)

Countries where COVID-19 vaccines have rolled out quickly, such as Israel and the UK, are starting to give an indication of how well they work. Their early results suggest the vaccines are highly effective at preventing people from being hospitalized or dying from the disease.

Israeli data shows that the Pfizer/BioNTech vaccine has reduced severe disease by 92% and hospitalisations by 87%. And a Public Health England preprint – a paper yet to be reviewed by other scientists—suggests that one dose of either the Pfizer or Oxford/AstraZeneca vaccine cuts the risk of hospitalization by 80%.

However, it's less clear how good the vaccines are at stopping people from spreading the virus. But given what we know about how they work, we shouldn't be surprised if they are less effective at stopping people transmit the virus than preventing them becoming ill. This is because the type of immunity they generate is likely to be better at fighting off severe rather than mild infections.

How immunity is created

There are a number of distinct phases in the course of a coronavirus infection. Usually the virus starts with what's known as a "mucosal infection" because it infects the lining of the nose and throat, the nasopharyngeal mucosa.

This is the asymptomatic or pre-symptomatic phase. Mild symptoms such as cough or altered taste or smell may then develop. However, in a proportion of people, the infection then spreads down the respiratory tract to the lungs, causing more serious problems. Some may develop very severe illness, leading to respiratory and other organ failure. At this point, with the virus moving around the body and causing problems in multiple areas, the infection is "systemic."

People are most infectious during the early stages of infection, when the virus is largely restricted to the nasopharyngeal mucosa. Indeed, it's possible for people to be highly infectious without the virus spreading to other parts of the body or causing severe illness.

Importantly, the immune system responds differently to mucosal and systemic infections. A systemic immune response, which works across large swathes of the body, is associated with creating one type of antibody, IgG. Immunity generated in the mucosa (also called secretory immunity) is associated with creating another, IgA. As a result, immunisations that focus on generating systemic immunity—which is what injected vaccines do – rarely induce mucosal immunity. This likely applies to all the COVID-19 vaccines currently available.

And yet, the nasopharyngeal mucosa is ground zero for most coronavirus infections. So while COVID-19 vaccines may generate a response that's highly protective against systemic disease in the lungs and other organs, the vaccines are less likely to generate strong mucosal immunity that's effective against the mild but infectious early stage of infection in the nose and throat. We should therefore expect some difference in the vaccines' effects on preventing severe disease and blocking infection and transmission.

Indeed, it's because of this that there's interest in developing mucosal vaccines for COVID-19. These would focus on generating an immune response in the nasopharyngeal mucosa specifically, quickly fighting off the virus at the time and location where it is most infectious in the body. Such vaccines would be given by nasal spray. However, with mucosal vaccines against other diseases, the duration of immunity can be relatively short. If these are developed for COVID-19, they might need to be repeatedly delivered.

What are we seeing in practice?

We don't yet know if there's a difference in the development of systemic and mucosal immunity for COVID-19. Emerging evidence suggests there might be, but it isn't conclusive, and much of this research still needs to be fully reviewed.

A preprint from Public Health England suggests that around six weeks after a primary COVID-19 infection, reinfections start to occur in some people, but that these are more likely to be mild or asymptomatic (and so probably mucosal). This could indicate that these people developed differing levels of systemic and mucosal immunity—enough systemic protection to stop severe illness developing in the body subsequently, but not enough in the nasopharyngeal mucosa to prevent the virus getting a foothold again.

Early-stage analysis of the Oxford vaccine appears to support this possibility. A preprint analyzing data from the vaccine's phase 3 trial suggests that after two doses, the vaccine cuts infections by 67% but illness by 82% (if a 12-week or more gap is left between doses). Importantly, the trial involved periodically testing everyone for infection, regardless of their symptoms, so its method for assessing the vaccine's effect on infection is robust.

With the Pfizer vaccine, though, the picture is less clear. According to some research, it seems to be similarly protective against infection and disease. A study published in the *New England Journal of Medicine* (*NEJM*) that looked at the real-world effects of the vaccine in Israel found that it reduced all forms of infection by 92%. And a press release from Pfizer, also looking at Israeli data, claims the vaccine offers 94% protection against asymptomatic infection.

But we need to be careful with these numbers. The *NEJM* study seemingly only tested people who wanted or needed a test, rather than systematically testing everyone, so its findings could be overly optimistic . The Pfizer press release also gives no indication about how its estimates were derived.

Conversely, a US study that did use systematic testing found the vaccine reduced asymptomatic infections only by 80% after two doses. As other,

more robust studies like this come out, lower estimates like this might be more common.

Finally, it's worth remembering that even if these vaccines don't end up blocking infections to a high degree, that doesn't mean they won't make a major contribution to suppressing viral spread. Even if people still get infected, COVID-19 vaccines are likely to reduce the amount of virus generated during an infection, lowering what can be passed on.

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