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COVID-19 vaccine FAQs: Efficacy, immunity to illness vs. infection, new variants and the likelihood of eradication

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As of March 8, four COVID-19 vaccines have been approved for emergency use in Canada. Two of them, the mRNA vaccines from

Pfizer/BioNTech and Moderna vaccines, were approved for use in Canada in December 2020. The Oxford/AstraZeneca vaccine was approved on Feb. 26, followed by the Johnson & Johnson vaccine on March 5.

A fifth vaccine was submitted on Jan. 29 by Novavax for approval in Canada. If approved, the vaccine would be produced in Canada.

How effective these vaccines may be in ending the COVID-19 pandemic has been equated to their "efficacy rates." It's important to know what these numbers mean to understand what can be expected from these vaccines and the ones that follow.

What is a vaccine's efficacy rate?

The high efficacy rates of the first approved vaccines made headlines, but what do these numbers actually mean? Efficacy rates indicate how well a vaccine met specified primary and secondary "end point(s)," which, in lay terms, are the goals determined at the outset of a clinical trial: what the study is measuring. In the case of COVID-19 pandemic, these goals had to do with the ability of the vaccines to lower the risk of a symptomatic disease—especially a severe one—hospitalization and death.

The term efficacy, as opposed to effectiveness, specifically refers to a drug or vaccine's performance under clinical trial conditions, by meeting the primary and secondary end points.

For example, in the case of the Pfizer/BioNTech Phase 3 clinical trial, the primary end point was the efficacy rate of the vaccine in preventing *symptomatic* COVID-19 (including mild, moderate and severe disease) with the onset at least seven days after the second dose. The secondary end point on this trial was the efficacy rate against severe COVID-19.

In the case of the Johnson & Johnson vaccine, which requires only one shot, the primary end point was defined as protection against moderate and severe COVID-19, assessed at day 14 and day 28 after the vaccination.

So the efficacy rates of these vaccines, as determined from their Phase 3 clinical trials, indicate protection against different forms of *symptomatic* COVID-19 (mild, moderate and/or severe disease), and outcomes of the disease (hospitalization and death).

What do the vaccines protect against?

In general, a vaccine teaches the body to recognize a specific pathogen (virus or bacterium) without having to experience a disease. As a result, future exposure to the pathogen leads to a fast immune response whereby the body recognizes the pathogen by its antibodies (humoral response) and can destroy the pathogen and the infected cells through the means of specialized immune cells (cellular response).

Moreover, the vaccines can also induce long-term immune memory of the pathogen whereby dormant specialized immune cells reactivate and produce a humoral response.

In the case of the approved COVID-19 vaccines, or those currently awaiting approval, the efficacy rate indicates how well these vaccines protect against symptomatic COVID-19 disease.

Indeed, a study in Israel—where 42 percent of the population had received at least one dose of the Pfizer/BioNTech vaccine at the time of the study—found that this vaccine is 87-96 percent effective in preventing severe cases (the study has not yet been peer reviewed).

Does vaccination prevent infection?

Although the reported efficacy rates are a reflection of the vaccine's ability to protect against symptomatic COVID-19 illness, it is not currently known whether these vaccines protect against infection: whether a vaccinated person's immune response can eliminate the virus before it replicates in the body.

If the novel coronavirus can infect a vaccinated host (replicate within that host), it can also use that host to "jump" to another host, and lead to further transmission of the virus, and possibly illness if other hosts are not vaccinated.

By the same token, if you are not vaccinated and are surrounded by people who are vaccinated, they may not catch the disease (they will not get sick). However, they can catch the virus from you and pass it on to others who are not vaccinated and who may get sick as a result.

However, all these vaccines, through their interaction with the immune system, are expected to reduce infection (virus replication) and hence virus transmission at some level. Oxford/AstraZeneca, Novavax and Moderna have all reported that their vaccines reduce virus transmission.

These preliminary data appear to be supported by countries that have vaccinated a large portion of their population, such as Israel and the United Kingdom. Israel, which has vaccinated 75 percent of its older population, reported a 33 percent decrease in the transmission rate in this age group.

In a nutshell, while the current COVID-19 vaccines provide immunity to the disease, their impact on transmission of the virus has yet to be fully determined. We must understand their impact on the pandemic to protect those who have underlying health conditions and may not respond to vaccination or cannot be vaccinated.

How do COVID-19 vaccines compare to other vaccines?

Many existing vaccines work in the same way as the approved COVID-19 vaccines: they protect us from diseases, but they do not eliminate the virus during the replication process (or prevent infection).

The smallpox vaccine is the poster child among the vaccines that do prevent infection, also referred to as vaccines that induce sterilizing immunity. That is how smallpox was eradicated after 200 years of vaccination efforts. A few other vaccines that induce sterilizing immunity are the measles vaccine and the human papillomavirus vaccine .

However, vaccines against many diseases such as hepatitis B, rotavirus and polio (all caused by viruses), or whooping cough or chlamydia (both caused by bacteria) do not prevent infection (replication of the virus in the body), but they prevent their respective diseases.

The World Health Organization explains that, "Many vaccines are primarily intended to prevent disease and do not necessarily protect against infection." However, all these vaccines rely on high vaccination coverage and vaccine efficacy rates to protect the population from the disease through herd immunity. Where the vaccination rate is low, we get outbreaks, as is the case of mumps in recent years.

Will immunity lead to eradication of COVID-19?

There is still more to learn about the immune response against SARS-CoV-2, the virus that causes COVID-19. One thing for certain is that the current vaccines provide immunity at various efficacy rates against symptomatic COVID-19.

Eradication often is reached when there is sterilizing immunity, induced

by the virus or by a vaccine. While the coronavirus and the COVID-19 vaccines are not believed to elicit sterilizing immunity, they are likely to reduce infection and hence transmission. So high vaccination coverage with a vaccine with a high efficacy rate, and compliance with existing prevention measures, are key to protecting the general population from COVID-19, but not necessarily eradicating the virus.

Do the vaccines protect against SARS-CoV-2 variants?

Considering the potential impact of the emergence of SARS-CoV-2 variants, WHO recently provided the definitions for variants of concern and variants of interest in order to assess their public health relevance.

Variants of concern are those that show an increase in transmissibility or severity of the disease, or a reduction in vaccine effectiveness. Variants of interest are those that call for research and closer monitoring based on community transmission (a number of outbreaks) or detection in a number of countries.

Because the Phase 3 clinical trials were carried out at different times coinciding with the emergence of different dominant virus variants in different participating countries, efficacy rates of different vaccines cannot translate directly to their ability to protect against different variants of concern.

However, Johnson & Johnson Phase 3 clinical trial shows that its vaccine has an efficacy rate of 60 percent against moderate to severe COVID-19 caused by the B.1.351 variant (dominant in South Africa) and 66 percent against moderate to severe COVID-19 caused by the P1 variant (dominant in Brazil). The vaccine has an overall efficacy rate of 85 percent against severe COVID-19 across these variants.

The Novavax vaccine fared very well against B.1.1.7, which is dominant

in the U.K., with an efficacy rate of 85.6 percent against symptomatic COVID-19, but only 60 percent against B.1.351 (after removing the HIV positive volunteers).

The mRNA vaccines' Phase 3 clinical trials were done in the United States only, at a time when there was no circulation of any of those virus variants. Both Moderna and Pfizer/BioNTech have shown their vaccines have a reduced efficacy rate against the B.1.1.7 and B.1.351 variants, compared to the non-variant strain, but their efficacy is still considerable.

Recently, Oxford/AstraZeneca reported that its vaccine is efficacious against B.1.1.7 but not against B.1.351.

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