Q&A: CDC greenlights two updated COVID-19 vaccines, but how will they fare against the latest variants?

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On Sept. 12, 2023, the Centers for Disease Control and Prevention recommended the newly formulated COVID-19 vaccines for all Americans ages 6 months and up, hours after its expert advisory committee voted 13 to 1 in favor of recommending the vaccines.

The CDC's broad recommendation comes one day after the Food and Drug Administration approved Moderna's and Pfizer's updated mRNA vaccines that target a previously dominant variant of the omicron family called XBB.1.5. The updated shots will be available to the public within days.

The Conversation asked Prakash Nagarkatti and Mitzi Nagarkatti, a husband and wife team of immunologists from the University of South Carolina, to weigh in on how the new vaccines might stand up against the latest COVID-19 variants that are swirling across the globe.

1. How are the new vaccines different from the previous?

When the first vaccine against COVID-19 was rolled out in December 2020, it was designed as a monovalent vaccine, meaning that it was formulated against only the original SARS-CoV-2 virus. That vaccine, as well as the updated ones, target the spike protein, which the virus uses to infect our cells and cause the disease.

That design made sense before the virus began mutating into a complex family tree of variants and sublineages. But as the virus structure shifted over time, the antibodies produced in response to the original vaccine

became less effective against the new variants.

This necessitated the development in 2022 of new "bivalent" vaccines that targeted both the original strain of SARS-CoV-2 and new viral variants such as the omicron BA.4 and BA.5 lineages that were dominant in mid-2022.

But, not surprisingly, new variants of the virus continued to emerge.

In June 2023, the FDA asked vaccine developers to formulate new fall shots to target the then-dominant XBB.1.5 subvariant.

The FDA approved that monovalent mRNA-based vaccine based on the overall efficacy data presented by the vaccine manufacturers.

Unfortunately, XBB.1.5 is no longer the dominant strain in the U.S.; it has been displaced by other variants from the XBB lineage, thereby raising concerns about the potential efficacy of the new shot. As of mid-September, the dominant variants nationwide are EG.5, also known as Eris, followed by FL.1.5.1—called Fornax—and XBB.1.16.6.

Meanwhile, a new highly mutated omicron offshoot, BA.2.86, nicknamed Pirola, is making its way across the globe—albeit so far in small numbers.

2. Who should get a new shot?

The CDC recommended that everyone ages 6 months old and up should get an updated COVID-19 vaccine so that they can be better protected against developing serious outcomes from COVID-19, including hospitalization. The agency noted that people who received the 2022–2023 bivalent COVID-19 shot "saw greater protection against illness and hospitalization than those who did not."

Most Americans will be able to get the newly formulated vaccine at no cost, according to the CDC.

The FDA approved a single shot of the updated vaccine for anyone ages 5 and older—regardless of whether they were previously vaccinated or not. The agency also approved unvaccinated individuals 6 months to 4 years of age to receive three doses of the updated Pfizer vaccine or two doses of the updated Moderna vaccine.

3. How effective could the updated shot be against the latest variants?

Based on its current assessment, the CDC indicates that the BA.2.86 variant may be able to cause infection even in people who have been previously vaccinated or those who have had COVID-19 infection in the past. But the CDC says it still expects the updated fall 2023 booster shot to be effective at reducing severe disease and hospitalization.

Moderna reported in August 2023 that the new monovalent mRNA COVID-19 vaccine gave a "significant boost" in antibodies that are protective against two of the currently circulating variants: EG.5—which is responsible for most cases in the U.S. as of mid-September—and FL.1.5.1. Then, in early September, Moderna announced that its most recent data from human trials showed an 8.7-fold increase in neutralizing antibodies against the newest variant, BA.2.86, following vaccination with the updated shot.

Similarly, new pre-clinical data from Pfizer shows that its version of the new mRNA vaccine produced antibodies that were effective at neutralizing the XBB.1.5, BA.2.86 and EG.5.1 variants.

This early research suggests that the new mRNA vaccines—although

developed specifically against XBB.1.5—are still effective against some of the most prevalent variants.

Novavax, which specializes in traditional protein-based vaccines, also announced in August that its updated COVID-19 vaccine directed against the XBB variant produced a broad neutralizing antibody response against key variants in animal studies. However, the company does not yet have data on its vaccine's performance against two other key variants, FL.1.5.1 and BA.2.86. The Novavax vaccine has not yet gone up for FDA review, but its approval is also expected within months.

It is important to keep in mind that while all three vaccines have been shown to trigger antibodies that can neutralize most of the currently circulating variants, it is unclear whether the vaccines will be able to effectively prevent COVID-19 infection in humans. Such clinical studies are time-consuming, so given the urgency and speed needed to develop vaccines against the ever-changing COVID-19 variants, vaccine manufacturers rely on antibody levels as an indicator of protection.

4. Is there a 'right' time to get the new vaccine?

Antibodies produced after a COVID-19 infection or vaccination last for about six months, and then their levels start declining. This is called "waning immunity."

About a year after getting a COVID-19 infection or vaccination, only a small fraction of antibodies can be detected. This is why health care providers recommend getting another shot if a year has passed since you were vaccinated or had an active infection.

It has become very clear that vaccines against COVID-19 do not provide 100% protection against catching a new COVID-19 infection, but they can make illness from the infection milder, shorter or both.

In addition, vaccines provide significant protection from hospitalization and death and may help protect against developing long COVID.

Viral infections normally peak in the winter, which is why experts advise getting both COVID-19 and flu vaccine shots in the months of September and October. For convenience, the two shots can be safely taken at the same time. This is because the immune cells that produce antibodies against one vaccine agent are distinct from those that produce antibodies against the other vaccine agent.

However, taking two different vaccines at the same time could cause more side effects, such as fever, aches and pain. This is especially the case for people who have experienced such side effects in the past after taking the COVID-19 and flu vaccines separately.

In addition, a newly approved vaccine against the respiratory syncytial virus, or RSV, is now recommended for people ages 60 and up.

5. Should some people wait for the updated Novavax vaccine?

The Moderna and Pfizer vaccines use the more recent vaccine technology based on mRNA, which instructs the body to produce a protein from a small portion of the SARS-CoV-2 virus. The immune system responds by producing antibodies.

In contrast, the Novavax vaccine relies on a more traditional approach to vaccine production, injecting the viral protein directly into the body to stimulate antibody production. So while the two vaccine types use different pathways to trigger antibodies against the virus, the end result is the same.

The CDC has reported rare cases of myocarditis, which is inflammation of the heart muscle, following vaccination with the Moderna and Pfizer mRNA vaccines. However, the same is true of the Novavax vaccine. So all three vaccines carry this very rare risk.

It is noteworthy that myocarditis is most frequently seen in adolescent and young adult males.

Although some people may have a preference for the traditional protein-based vaccine by Novavax, those who are at higher risk of catching COVID-19 should not wait for the approval of the Novavax vaccine to get their shot.

Provided by The Conversation

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