Should you get a COVID-19 booster shot now or wait until fall? Two immunologists help weigh the options

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While COVID-19 vaccines continue to be highly effective at preventing

hospitalization and death, it has become clear that the protection offered by the current vaccines wanes over time. This necessitates the use of booster shots that are safe and effective in enhancing the immune response against the virus and extending protection.

But when to get a first or second booster, and which shot to choose, are open questions. Many people find themselves unsure whether to wait on new, updated formulations of the COVID-19 vaccines or to mix and match combinations of the original vaccine strains.

SARS-CoV-2, the virus that causes COVID-19, uses its knob-shaped spike protein to gain entry into cells and to cause infection. Each of the existing and upcoming vaccines relies on emulating the spike protein to trigger the immune response. However, each vaccine type presents the spike protein to the immune system in different ways.

As immunologists studying inflammatory and infectious diseases, including COVID-19, we are interested in understanding how the COVID-19 vaccine designs differ in the type of immunity they trigger and the protection that results.

New bivalent vaccines

Moderna and Pfizer-BioNTech, the two companies whose mRNA vaccines have been the primary options for COVID-19 vaccination across all age groups, both have new vaccine formulations on the way. An advisory committee of the Food and Drug Administration is set to meet on June 28, 2022, to evaluate the newest versions and to decide on which are likely to be recommended for use in this fall's booster shots.

Moderna's new bivalent vaccine mixes mRNA that encodes for the spike proteins of the original SARS-CoV-2 virus as well as the slightly different spike protein of the more infectious omicron variant.

In early June 2022, Moderna said that in clinical trials, its bivalent vaccine outcompetes the original vaccine strain, inducing a stronger immune response and longer protection against the original SARS-CoV-2 and its variants, including omicron.

Moderna later announced that its newest formulation also performs well against the newest omicron subvariants, BA.4 and BA.5, which are quickly becoming the dominant strains in the U.S. Because of the significantly stronger immune response that the new shot induces, Moderna predicts that such protection may last a year and plans to introduce its new vaccine in August.

And most recently, on June 25, Pfizer-BioNTech also announced results for its two new COVID-19 vaccine formulations: a bivalent formulation consisting of mRNA that encodes for the spike proteins of the original SARS-CoV-2 strain and the original BA.1 omicron subvariant, and a "monovalent" version that is only directed at the spike protein of BA.1.

The company's preliminary studies demonstrated that both the monovalent and the bivalent vaccines triggered antibodies that neutralized the newer omicron BA.4 and BA.5 subvariants, although to a lesser degree than the BA.1 subvariant. However, Pfizer's monovalent vaccine triggered better virus-neutralizing antibodies against the omicron BA.1 subvariant than did the bivalent vaccine.

However, whether the differences in the levels of such antibodies seen with the monovalent versus bivalent vaccines translate into different levels of protection against newer omicron variants remains to be established in clinical trials.

Progress on the Novavax vaccine

Another vaccine formulation that is working its way toward

authorization is Novavax, a vaccine built using the spike protein of the original SARS-CoV-2 virus. The Novavax vaccine has the advantage of being similar to traditional vaccines, such as the DTaP vaccines against diphtheria, tetanus and pertussis, or the vaccines against other viral infections such as hepatitis and shingles. The Novavax vaccine has been clinically tested in South Africa, the United Kingdom and the U.S. and found to be safe and highly effective with 90% efficacy against mild, moderate and severe forms of COVID-19.

An advisory committee to the Food and Drug Administration endorsed the Novavax vaccine in early June 2022. Now, the FDA is reviewing changes that Novavax made during its manufacturing process before making its decision to authorize the shot.

In Australia, the Novavax vaccine was recently registered provisionally as a booster for individuals aged 18 years and over. The company is performing phase 3 clinical trials to determine if its vaccine can be used safely and effectively as a booster in people who have previously taken mRNA vaccines.

When these new vaccines become available in the coming months, people will have significantly more options for mixing and matching vaccines in order to enhance the duration and quality of their immune protection against COVID-19.

Mixing and matching

Until then, clinical studies have shown that even mixing and matching the existing vaccine types is an effective strategy for boosting. For example, recent studies suggest that when adults who were fully vaccinated with any of the original three COVID-19 vaccines—Pfizer-BioNTech, Moderna or Johnson & Johnson—received a booster dose with a different vaccine brand from the one they received in their initial

series, they had a similar or more robust immune response compared to boosting with the same brand of vaccine.

Vaccine mixing has been found to be safe and effective in various studies. The reason why mixing vaccines might produce a more robust immune response goes back to how each one presents the spike protein of the virus to the immune system.

When the SARS-CoV-2 virus mutates in regions of the spike protein, as has been the case with each of the variants and subvariants, and tries to evade the immune cells, antibodies that recognize different parts of the spike protein can stop it in its tracks and prevent the virus from infecting the body's cells.

So whether you decide to get a booster shot now or wait until the fall, for many it's heartening to know that more options are on the way.

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