Comparing the COVID-19 Vaccines: How Are They Different?

BY **KATHY KATELLA** NOVEMBER 22, 2024

Information to help you make your best choice.

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Note: The Johnson & Johnson (Janssen) COVID-19 vaccine expired as of May 6, 2023, and is no longer available in the U.S. Those who did get the J&J shot are considered up-to-date when they get one

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updated (2023–2024 formula) COVID vaccine.

Information in this article was accurate at the time of original publication. Because information about COVID changes rapidly, we encourage you to visit the websites of the Centers for Disease Control & Prevention (CDC), World Health Organization (WHO), and your state and local government.

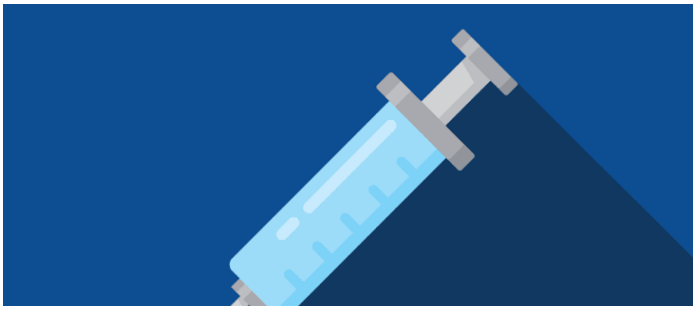
COVID-19 is now in its fifth year, and the subvariants of the Omicron strain continue to drive infections in the United States. The good news is that vaccines, which have been updated each year since 2022, are still expected to be effective at preventing severe disease, hospitalization, and death from COVID.

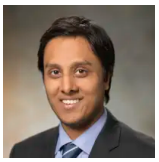
In the U.S., infants, children, and adults ages 6 months and older are eligible to be vaccinated, according to the Centers for Disease Control and Prevention (CDC).

As the SARS-CoV-2 virus mutates and new variants continue to emerge, it's important to keep up with how well the updated vaccines are performing.

We mapped out a comparison of the COVID vaccines in the United States.

The three vaccines in the U.S.





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Pfizer-BioNTech

The Pfizer-BioNTech vaccine (brand name: Comirnaty) was granted full Food and Drug Administration (FDA) approval in August 2021 for people ages 16 and older. Before that, it was the first COVID vaccine to receive FDA Emergency Use Authorization (EUA) back in December 2020, after the company reported that its vaccine was highly effective at preventing symptomatic disease. This is a messenger RNA (mRNA) vaccine, which uses a relatively new technology.

Status: Pfizer's vaccine has been updated over time to target new virus variants. First introduced in December 2020, the original COVID mRNA vaccines from both Pfizer and Moderna protected against the original SARS-CoV-2 virus. They have been replaced three times since then with shots targeting different iterations of the Omicron strain of the virus. In 2022, "bivalent" vaccines targeted both the original virus and Omicron variants BA.4 and BA.5; in 2023, a monovalent shot targeted the XBB lineage of the Omicron variant; and in 2024, a new updated shot aims to protect against KP.2, which circulated in the U.S. earlier in the year. The previous vaccines are no longer in use.

Who can get it: People 6 months and older. The CDC has specific recommendations for the following groups, noting that anyone who recently had COVID may need to consider delaying their vaccination by 3 months:

- **Children ages 6 months to 4 years** need multiple doses (check the CDC website for more specific recommendations), including at least one dose of the 2024-2025 updated vaccine.
- **Children ages 5 to 11 years** may get one dose

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of the 2024-2025 updated vaccine.

- **People ages 12 and older** may get one dose of the 2024-2025 updated vaccine

People 65 years and older, and those who are moderately or severely immunocompromised, may receive a second dose six months after their first dose. People who are moderately or severely immunocompromised may decide to receive additional doses in consultation with their healthcare provider.

Possible side effects: Pain, redness, or swelling at the site where the shot was administered, and/or tiredness, headache, muscle pain, chills, fever, or nausea throughout the rest of the body. If these side effects occur, they should go away in a few days. A few side effects are serious, but rare. These include anaphylaxis, a severe reaction that is treatable with epinephrine (the drug in EPIPENs®).

FDA warnings: The FDA added a warning label on the mRNA vaccines regarding serious (but rare) cases of inflammation of the heart muscle (myocarditis) and of the outer lining of the heart (pericarditis) in adolescents and young adults, more often occurring after the second dose of an mRNA vaccine. The inflammation, in most cases, gets better on its own without treatment.

How it works: It uses mRNA technology, which is a way of sending instructions to host cells in the body for making copies of a spike protein (like the spikes you see sticking out of the coronavirus in pictures). Our cells recognize that this protein doesn't belong, and the immune system reacts by activating immune cells and producing antibodies. This will prompt the body to recognize and attack the real SARS CoV-2 spike protein if you become exposed to the actual virus.

How well it works: The 2024-2025 updated vaccines were approved based on preclinical studies of their efficacy against circulating strains. People may still become infected even though they have been

vaccinated, but the goal of the vaccines now is to prevent severe disease, hospitalization and death. Understanding the effectiveness of the latest updated vaccines in the real world beyond the clinical trials can be difficult, since companies manufacture updated vaccines based on preclinical information and educated predictions of which variants will be circulating when the shots become available (a similar process is used for the annual flu shot). But, according to a CDC summary issued in November, the 2024-2025 vaccines are expected to work well against predominant strains, such as KP.3.1.1, and variants that could become more common, including XEC and MC.1.

Research has suggested that people who are infected after vaccination also are less likely to report Long COVID (defined as signs, symptoms, and conditions that continue or develop after acute COVID infection), compared to those who were not vaccinated.

In December 2020, Pfizer-BioNTech's Phase 3 clinical data for its original vaccine (which is no longer in circulation) showed 95% efficacy for preventing symptomatic COVID. Later data on real-world effectiveness for adults showed that the protection from the mRNA two-dose primary series waned over time, suggesting that updated vaccines would be needed to bring the immune system back to robust levels.

Additional information is available on the FDA's Pfizer-BioNTech 2024-2025 vaccine fact sheet.

Moderna

The FDA granted the Moderna vaccine (brand name: Spikevax) full approval for people 18 and older in January 2022, upgrading the vaccine's EUA, which was granted in December 2020 (a week after Pfizer-BioNTech). Moderna uses the same mRNA technology as Pfizer-BioNTech and had a similarly high efficacy at preventing symptomatic disease when the companies applied for authorization.

Status: Moderna's vaccine has been updated over time to target new virus variants. First introduced in December 2020, the original COVID mRNA vaccines from both Pfizer and Moderna protected against the original SARS-CoV-2 virus. They have been replaced three times since then with shots targeting different iterations of the Omicron strain. In 2022, "bivalent" vaccines targeted both the original virus and Omicron variants BA.4 and BA.5; in 2023, a monovalent shot targeted the XBB lineage of the Omicron variant; and in 2024, a new updated shot aims to protect against KP.2, which circulated in the U.S. earlier in the year. The previous vaccines are no longer in use.

Who can get it: People ages 6 months and older. The CDC has specific recommendations for the following groups, noting that anyone who recently had COVID may need to consider delaying their vaccination by 3 months:

- **Children ages 6 months to 4 years** need multiple doses (check the CDC website for more specific recommendations), including at least one dose of the 2024-2025 updated vaccine.
- **Children ages 5 to 11 years** may get one dose of the 2024-2025 updated vaccine.
- **People ages 12 and older** may get one dose of the 2024-2025 updated vaccine.

People 65 years and older, and those who are moderately or severely immunocompromised, may receive a second dose six months after their first dose. People who are moderately or severely immunocompromised may decide to receive additional doses in consultation with their healthcare provider.

Possible side effects: The side effects are similar to Pfizer-BioNTech's vaccine: Pain, redness, or swelling at the site where the shot was administered—and/or tiredness, headache, muscle pain, chills, fever, or nausea throughout the rest of the body. If any of these side effects occur, they should go away in a few days. A few side effects are serious, but rare. These

include anaphylaxis, a severe reaction that is treatable with epinephrine (the drug in EPIPENs®).

FDA warnings: The FDA placed a warning label on the Moderna vaccine regarding a "likely association" with reported cases of heart inflammation in young adults. This inflammation may occur in the heart muscle (myocarditis) or in the outer lining of the heart (pericarditis)—it more often occurs after the second dose of an mRNA vaccine. The inflammation, in most cases, gets better on its own without treatment.

How it works: Similar to the Pfizer vaccine, this is an mRNA vaccine that sends host cells in the body instructions for making a spike protein that will train the immune system to recognize it. The immune system will then attack the spike protein the next time it sees one (attached to the actual SARS CoV-2 virus).

How well it works: The 2024-2025 updated vaccines were approved based on preclinical studies of their efficacy against the latest circulating strains. People may still become infected even though they have been vaccinated, but the goal of the vaccines now is to prevent severe disease, hospitalization, and death. Understanding the effectiveness of the latest updated vaccines in the real world beyond the clinical trials can be difficult, since companies manufacture updated vaccines based on preclinical information and educated predictions of which variants will be circulating when the shots become available (a similar process is used for the annual flu shot). But, according to a CDC summary issued in November, the 2024-2025 vaccines are expected to work well against predominant strains, such as KP.3.1.1, and variants that could become more common, including XEC and MC.1.

Research has suggested that people who are infected after vaccination also are less likely to report Long COVID (defined as signs, symptoms, and conditions that continue or develop after acute COVID infection), compared to those who were not vaccinated.

Moderna's initial Phase 3 clinical data in December 2020 was similar to Pfizer-BioNTech's—it showed about 95% efficacy for prevention of COVID. Later data on real-world effectiveness for adults showed that the protection from the mRNA two-dose primary series wanes over time, but booster doses brought the immune system back to robust levels.

Additional information is available on the FDA's Moderna 2024-2025 vaccine fact sheet.

Novavax

The Novavax vaccine (brand names: Nuvaxovid and Covovax) was the fourth COVID vaccine to be administered in the U.S (after Johnson & Johnson, which is no longer available). The Novavax vaccine is the only non-mRNA updated COVID vaccine that has been available in the U.S. This vaccine is a protein adjuvant that had a 90% efficacy in its clinical trial, performing almost as well as the mRNA vaccines in their early trials. It is simpler to make than some of the other vaccines and can be stored in a refrigerator, making it easier to distribute.

Status: The FDA authorized an updated COVID vaccine from Novavax at the end of August 2024 for everyone ages 12 and older. Novavax designed its updated shot to target JN.1, a predecessor of KP.2. Novavax's 2023–2024 vaccine is no longer available in the U.S., since all doses have expired.

Who can get it: People 12 and older. People 65 years and older, and those who are moderately or severely immunocompromised may receive a second dose six months after their first dose. People who are moderately or severely immunocompromised may decide to receive additional doses in consultation with their healthcare provider.

Possible side effects: Injection site tenderness, fatigue, headache, muscle pain. There were rare cases of myocarditis and pericarditis (six cases in 40,000 participants) in the clinical trial, and rare severe

allergic reactions.

How it works: Unlike the mRNA and vector vaccines, this is a protein adjuvant (an adjuvant is an ingredient used to strengthen the immune response). While other vaccines trick the body's cells into creating parts of the virus that can trigger the immune system, the Novavax vaccine takes a different approach. It contains the spike protein of the coronavirus itself but formulated as a nanoparticle, which cannot cause disease. When the vaccine is injected, this stimulates the immune system to produce antibodies and T-cell immune responses.

How well it works: While its 2024-2025 updated vaccine targets the JN.1 variant and not KP.2 like Pfizer and Moderna, Novavax reported that non-clinical data demonstrated broad cross-neutralizing antibodies against multiple variant strains, including JN.1, KP.2 and KP.3. Understanding how effective the latest updated vaccines are in the real world beyond the clinical trials can be difficult, since companies manufacture updated vaccines based on preclinical information and educated predictions of which variants will be circulating when the shots become available (a similar process is used for the annual flu shot). But, according to a CDC summary issued in November, the 2024-2025 vaccines are expected to work well against strains such as KP.3.1.1 that are predominant, and variants that could become more common, including XEC and MC.1.

Earlier studies of its original vaccine showed it to be 90% effective overall against lab-confirmed, symptomatic infection and 100% effective against moderate and severe disease in Phase 3 trial results published in *The New England Journal of Medicine* in December 2021.

Additional information is available on the FDA's Novavax 2024-2025 vaccine fact sheet.

Where to get a COVID vaccine

As with previous COVID vaccines, the 2024-2025 updated COVID vaccines are available at participating pharmacies and provider offices. To find a location near you that carries the vaccine and to schedule an appointment, go to Vaccines.gov. You can also call 1-800-232-0233 (TTY 1-888-720-7489).

This story was reviewed by Yale Medicine infectious diseases specialist Scott Roberts, MD.

Note: None of the COVID vaccines change—or interact with—a recipient's DNA.

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