

# Answering Your Questions About the Safety and Effectiveness of COVID-19 Vaccines

## Do clinical trial results show whether vaccines are effective?

Yes, clinical trials provide data and information about how well a vaccine prevents a disease and how safe it is. The Food and Drug Administration (FDA) evaluates these data, along with information from the manufacturer, to assess the safety and effectiveness of the vaccine. FDA then decides whether to approve the vaccine or authorize it for emergency use in the United States.

## Why would the effectiveness of vaccines be different after the clinical trials?

Many factors can affect how well a vaccine works in real-world conditions. These factors can include how a vaccine is transported and stored and how the vaccine is given. Vaccine effectiveness can also be affected by differences in the underlying medical conditions of people vaccinated as compared to those vaccinated in the clinical trials.

CDC is assessing how well COVID-19 vaccines work in real-world conditions. Some real-world assessments observe both people who get vaccinated and those who don't to see how many people in each group become ill with COVID-19. Some assessments look at how COVID-19 vaccine effectiveness differs for people who are partially vaccinated compared to those who are fully vaccinated.

Assessments of vaccine effectiveness can also provide important information about how well a vaccine is working in groups of people who were either not included or were not well represented in clinical trials, and how well vaccines protect against COVID-19 variants.

## How are experts evaluating the COVID-19 vaccine effectiveness in real-world conditions?

Experts are working on many types of assessments to determine vaccine effectiveness in real-world conditions. Each study type uses a different method:

- **Case-control assessments** include cases (people who have COVID-19) and controls (people who do not have COVID-19). People who agree to participate in a case-control assessment provide information on whether they received a COVID-19 vaccine or not. Experts look to see if the cases were less likely to be vaccinated than controls, which would show the vaccine is working.
- **Test-negative design assessments** enroll people who are seeking medical care for symptoms that could be due to COVID-19. In this special type of case-control assessments, experts compare the COVID-19 vaccination status of those who test positive (meaning they have COVID-19) to those who test negative (meaning they do not have COVID-19).



[www.cdc.gov/coronavirus/vaccines](https://www.cdc.gov/coronavirus/vaccines)

- **Cohort assessments** observe groups of people who are and are not vaccinated against COVID-19, and then follow them for a period of time to see if they get COVID-19. Experts compare the vaccinated and unvaccinated groups to see how well COVID-19 vaccines protected against COVID-19. This can be done in real time (prospectively) or by looking back in time (retrospectively) using data already collected, such as information in participants' medical records.
- **Screening method assessments** look at vaccination status among a group of people infected with COVID-19 (for example, those detected through ongoing COVID-19 surveillance) and compare that with the vaccination coverage in the overall population where those cases arise (for example, people from the same state). By comparing vaccination coverage between these two groups, researchers can get an early estimate of whether a vaccine is working as expected.
- **Ecologic analysis assessments** look at groups of people—such as those in different geographic locations or at different times—to see if there is a correlation between how many were vaccinated and how many were diagnosed with COVID-19. These analyses may be hard to interpret broadly because a correlation may be detected at the group level, but that doesn't necessarily mean the correlation exists on an individual level.

CDC uses several study methods because they can all contribute different information and build a base of evidence about how COVID-19 vaccines are working.

### Can these assessments determine if the vaccines protect people from severe COVID-19 illness?

Yes. CDC defines severe illness from COVID-19 as needing care in a hospital or intensive care unit (ICU), needing to be on a ventilator, or dying from COVID-19.

- Experts assess how well COVID-19 vaccines protect people against severe illness using case-control studies among hospitalized patients.
- Experts also use cohort studies of electronic health records to see if people hospitalized with COVID-19 received a vaccine or not.

### Can these assessments determine if the vaccines protect people against mild COVID-19 illness?

Yes. CDC uses case-control studies to assess how well COVID-19 vaccines protect people against less severe forms of COVID-19—for example, people with COVID-19 who need to visit a doctor but don't need to be hospitalized.

### Can these assessments determine if the vaccines protect people who are infected but have no symptoms?

Yes. Some people can be infected with or “carry” the virus that causes COVID-19, but not feel sick or have any symptoms. Experts call this “asymptomatic infection.” It is important to know whether COVID-19 vaccines can prevent infection without symptoms (asymptomatic infection). People with an asymptomatic infection could unknowingly spread the virus to others.

A special type of cohort study looks at how effectively the vaccine prevents asymptomatic infection. People who agree to participate in such a study are tested for COVID-19 every week, whether they have symptoms or not. Experts then compare the proportion of people who develop COVID-19 who were vaccinated to the proportion of people with infection who were not vaccinated.



### Who is included in the real-world vaccine effectiveness assessments?

CDC is working to make sure real-world vaccine assessments include diverse groups of people, including:

#### Healthcare personnel

- CDC is rapidly assessing vaccine effectiveness among healthcare personnel working in all healthcare settings. Healthcare personnel are more likely to get COVID-19 while taking care of patients. Healthcare personnel are among the groups that will provide a first look at how COVID-19 vaccines work in real-world conditions.

#### Essential workers

- Essential non-healthcare workers are people who are needed to maintain critical infrastructure, services, and functions. Essential workers may be more likely to get COVID-19 because they are unable to physically distance or are exposed to people with COVID-19 at their jobs. Many essential workers are part of racial and ethnic minority groups, who are disproportionately affected by COVID-19.

### Older adults and those living in nursing homes

- Making sure COVID-19 vaccines protect older adults is critical because the risk for severe illness from COVID-19 increases with age. People living in nursing homes and other long-term care facilities are much more likely to get COVID-19 and have a severe illness. FDA and the Centers for Medicare and Medicaid Services (CMS) are using CMS Medicare billing data to assess COVID-19 vaccine effectiveness among older adults, including those living in nursing homes and other long-term care facilities. These data include information about whether people are vaccinated against COVID-19, whether they got sick with COVID-19, and if they needed to receive care in a hospital for COVID-19. Experts are also conducting a case-control assessment using data from CDC and CMS. Experts will identify older adults hospitalized for COVID-19 and older adults hospitalized for other reasons. To estimate vaccine effectiveness, they will then compare how many in each of these groups received a COVID-19 vaccine.

### Underlying medical conditions

- Adults of any age with certain underlying medical conditions are at increased risk for severe illness from COVID-19. CDC is looking at how COVID-19 vaccines protect people who have heart conditions, obesity, diabetes, and other underlying medical conditions that place them at increased risk for severe illness from COVID-19.

### Racial and ethnic minority groups

- The proportion of people who become ill, are hospitalized, or die from COVID-19 is higher among Hispanic or Latino, non-Hispanic Black, and non-Hispanic American Indian or Alaska Native people than among non-Hispanic White people. Vaccine uptake among racial and ethnic minority groups is also lower than among non-Hispanic White people. Experts are working to make sure real-world vaccine assessments include groups of adults who are racially and ethnically diverse. CDC also is working with the Indian Health Service (IHS), tribal nations, and other partners to ensure real-world COVID-19 vaccine effectiveness assessments include American Indian and Alaska Native populations. It is important real-world vaccine effectiveness studies include diverse populations to ensure COVID-19 vaccines help achieve health equity.

### These vaccines were produced so quickly. How do we know they are safe?

COVID-19 vaccines are safe and effective. Millions of people in the United States have received COVID-19 vaccines under the most intense vaccine safety monitoring in U.S. history.

In addition, COVID-19 vaccines were evaluated in tens of thousands of participants in clinical trials. The vaccines met FDA's rigorous scientific standards for safety, effectiveness, and manufacturing quality needed to support an Emergency Use Authorization (EUA).

### Is CDC continuing to watch for problems with these vaccines?

Yes. As of May 11, 2021, more than 245 million people in the United States have received at least one dose of a COVID-19 vaccine under the most intense safety monitoring in U.S. history. This monitoring is ongoing and includes using both established and new safety monitoring systems to make sure that COVID-19 vaccines are safe.

Results from these monitoring efforts are reassuring. People may have some side effects, which are normal signs that the body is building protection. These side effects may affect ability to do daily activities, but they should go away in a few days. Some people have no side effects.



Common side effects include pain, redness, and swelling on the arm where you got the shot. Other common side effects include tiredness, headache, muscle pain, chills, fever, and nausea.

A small number of people have had a severe allergic reaction (called "anaphylaxis") after vaccination, but this is rare, and when it does happen, vaccination providers have medicines available that they can use to effectively and immediately treat the reaction. You will be asked to stay for 15–30 minutes after you get your vaccine so you can be observed.

CDC has received a small number of reports of a rare and severe type of blood clot with low platelets happening in people who received Johnson & J&J/Janssen COVID-19 vaccine. However, after reviewing all available safety data, CDC and FDA recommend use of this vaccine resume in the United States given that the known and potential benefits outweigh the known and potential risks. [Learn more.](#)

## Expanded vaccine safety monitoring systems

The following systems and information sources add another layer of safety monitoring, giving CDC and FDA the ability to evaluate COVID-19 vaccine safety in real time and make sure COVID-19 vaccines are safe:



**CDC: v-safe** A smartphone-based tool that uses text messaging and web surveys to provide personalized health check-ins after you receive a COVID-19 vaccine. Through v-safe, you can quickly tell CDC if you have any side effects after getting a COVID-19 vaccine. Depending on your answers to the web surveys, someone from CDC may call to check on you and get more information. V-safe will also remind you to get your second COVID-19 vaccine dose if you need one.

### **v-safe COVID-19 Vaccine Pregnancy Registry**

The v-safe COVID-19 Vaccine Pregnancy Registry is for v-safe participants who self-identify as pregnant at the time of vaccination or shortly thereafter (within 30 days

of vaccination). The registry activities are in addition to the v-safe health check-ins that participants receive via text message. Pregnant participants in the registry will be contacted to answer questions about their pregnancy and medical history. Participants will also be asked for permission to contact their healthcare provider(s).

### **CDC: National Healthcare Safety Network (NHSN)**

An acute care and long-term care facility monitoring system with reporting to the Vaccine Adverse Event Reporting System (VAERS) that allows determination of COVID-19 vaccine adverse event (health problem) reporting rates.

## Existing Safety Monitoring Systems

The safety of vaccines is monitored continuously with multiple approaches. As people get vaccinated, CDC, FDA, and other federal partners will use the following existing, robust systems and data sources to conduct ongoing safety monitoring in the following groups:

### **General public**

- **CDC and FDA: Vaccine Adverse Event Reporting System (VAERS)** — The national system that collects reports from healthcare professionals, vaccine manufacturers, and the public of adverse events that happen after vaccination; reports of adverse events that are unexpected, appear to happen more often than expected, or have unusual patterns are further assessed
- **CDC: Vaccine Safety Datalink (VSD)** — A network of 9 integrated healthcare organizations across the United States that conducts active surveillance and research; the system is also used to help determine whether possible side effects identified using VAERS are actually related to vaccination
- **CDC: Clinical Immunization Safety Assessment (CISA) Project** — A collaboration between CDC and 7 medical research centers to provide expert consultation on individual cases and conduct clinical research studies about vaccine safety
- **FDA and the Centers for Medicare and Medicaid Services: Medicare data** — A claims-based system for active surveillance and research
- **FDA: Biologics Effectiveness and Safety System (BEST)** — A system of electronic health record, administrative, and claims-based data for active surveillance and research

### **Members of the military**

- **Department of Defense (DOD): DOD VAERS data** — Adverse event reporting to VAERS for DOD populations
- **DOD: Vaccine Adverse Event Clinical System (VAECS)** — A system for case tracking and evaluation of adverse events following immunization in DOD and DOD-affiliated populations
- **DOD: DOD Electronic Health Record and Defense Medical Surveillance System** — A system of electronic health record and administrative data for active surveillance and research

### **Veterans**

- **Department of Veterans Affairs (VA): VA Adverse Drug Event Reporting System (VA ADERS)** — A national reporting system for adverse events following receipt of drugs and vaccinations
- **VA Electronic Health Record and Active Surveillance System** — A system of electronic health record and administrative data for active surveillance and research

### **Tribal nations**

- **Indian Health Service (IHS)** — Spontaneous adverse event reporting to VAERS for populations served by IHS and tribal facilities and other IHS safety monitoring programs