# Answering Your Questions About the New 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 an infectious disease and about 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 a vaccine. FDA then decides whether to approve a vaccine or authorize it for emergency use in the United States.

After a vaccine is either approved or authorized for emergency use by FDA, more assessments are done before a vaccine is recommended for public use. The goal of these assessments is to understand more about the protection a vaccine provides under real-world conditions, outside of clinical trials.

After COVID-19 vaccines are approved or authorized for emergency use by FDA and recommended for public use, CDC will further assess their effectiveness. These real-world assessments will compare groups of people who do and don't get vaccinated and people who do and don't get COVID-19 to find out how well COVID-19 vaccines are working to protect people.

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

Many factors can affect a vaccine's effectiveness in real-world situations. These factors can include things such as how a vaccine is transported and stored or even how patients are vaccinated. 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.

Assessments of vaccine effectiveness can also provide important information about how well a vaccine is working in groups of people who were not included or were not well represented in clinical trials.

## How will experts evaluate the COVID-19 vaccines in real-world conditions?

Experts are working on many types of real-world studies to determine vaccine effectiveness, and each uses a different method:

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

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- **Cohort studies** will follow people who have and haven't had a COVID-19 vaccine for several months to see if getting vaccinated protects them from getting the disease. This can be done in real time (prospectively) or by looking back in time (retrospectively) using data that were already collected, such as information in participants' medical records.
- **Screening method assessments** look at vaccination status among a group of cases (for example, cases detected through ongoing COVID-19 surveillance) and compares those cases with vaccination coverage among the overall population where those cases come from (for example people from the same state). By comparing 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 find out how many were vaccinated and how many were diagnosed with COVID-19. These analyses may be hard to interpret because the number of COVID-19 illnesses has changed rapidly over time and in different places.

CDC will use several methods because they can all contribute different information about how the vaccine is working.

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

Yes. Severe illness from COVID-19 is defined as needing care in a hospital or intensive care unit (ICU), needing to be on a ventilator, or dying due to COVID-19.

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

## Will assessments determine if the vaccines protect people against mild illness?

Yes. CDC will use 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.

## Will assessments determine if the vaccines protect people who are ill with no symptoms at all?

Yes. Some people can be infected with or "carry" the virus that causes COVID-19, but they don't feel sick or have any symptoms. Experts call this asymptomatic infection. It is important to know whether COVID-19 vaccines can help lower the number of people who have asymptomatic infection. People with asymptomatic infection can unknowingly spread the virus to others.

A special type of cohort study will find out how effective the vaccine is when people are asymptomatic. People who agree to participate will be tested for COVID-19 every week whether they have symptoms or not. Experts will then compare the proportion of people with infection who were vaccinated to the proportion of people with infection who were not vaccinated.

## Who will be included in the real-world vaccine assessments?

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

**Healthcare personnel and essential workers**

Experts will rapidly assess vaccine effectiveness among healthcare personnel working in hospitals, long term care/skilled nursing facilities, or nursing homes in selected sites across the United States. These assessments will show how well COVID-19 vaccines protect healthcare personnel from getting sick or having severe illness. Assessments among healthcare personnel and essential workers will also inform how well COVID-19 vaccines protect them against getting infected, regardless of whether they have symptoms or not.

**Older adults and those living in nursing homes**

The risk for severe illness from COVID-19 increases with age, so making sure these vaccines protect older adults is critical. People living in nursing homes and long-term care facilities are at especially high risk of getting COVID-19 and severe disease. The Food and Drug Administration (FDA) and the Centers for Medicare and Medicaid Services (CMS) will

use CMS Medicare billing data to assess COVID-19 vaccine effectiveness among older adults, including those living in nursing homes and long-term care facilities. These data will include information about whether people received a COVID-19 vaccine, whether they got sick with COVID-19, and if they needed hospital care. This information will help inform how well the vaccine works in preventing COVID-19 and severe illness among older adults.

Experts will also use data from CDC and CMS to conduct a case-control assessment. Experts will identify older adults hospitalized for COVID-19 and older adults hospitalized for other reasons. They will then compare how many cases and controls received a COVID-19 vaccine to estimate vaccine effectiveness.

**People with underlying medical conditions**

To better understand how well COVID-19 vaccines protect people with underlying medical conditions who may be at increased risk for severe illness. Experts are working to make sure various real-world vaccine assessments will include adults with heart conditions, obesity, and diabetes. The real-world vaccine effectiveness assessments will also collect information about other underlying medical conditions. This information will be used to better understand how well COVID-19 vaccines protect people with underlying medical conditions.

**People in racial and ethnic minority groups**

Long-standing systemic health and social inequities have put many people from racial and ethnic minority groups at increased risk of getting sick and dying from COVID-19. CDC is working to ensure that real-world assessments of vaccine effectiveness include diverse populations, such as people from racial and ethnic minority groups disproportionately affected by COVID-19.

CDC also is working with the Indian Health Service (IHS), tribal nations, and other partners to ensure that these real-world assessments include American Indian and Alaska Native populations who have been disproportionately affected by COVID-19. This is important to ensure that COVID-19 vaccines can help achieve health equity, so everyone has a fair opportunity to be as healthy as possible.

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

It is the U.S. vaccine safety system's job to make sure that all vaccines are as safe as possible. Safety has been a top priority while federal partners have worked to make COVID-19 vaccines available for use in the United States.

The new COVID-19 vaccines have been evaluated in tens of thousands of individuals, who volunteered to be vaccinated and to participate in clinical trials. The information from these clinical trials allowed the U.S. Food and Drug Administration (FDA) to determine the safety and effectiveness of the vaccines. These clinical trials were conducted according to rigorous standards set forth by FDA.

FDA has determined that the newly authorized COVID-19 vaccines meet its safety and effectiveness standards. Therefore, FDA has made these vaccines available for use in the United States under what is known as an Emergency Use Authorization.

## Will CDC continue to watch for problems with these new vaccines?

Yes. Even though no safety issues arose during the clinical trials, CDC and other federal partners will continue to monitor the new vaccines for serious side effects (known as adverse events) using many vaccine safety monitoring systems.

This continued monitoring can pick up on side effects that may not have been seen in clinical trials. If an unexpected side effect with the new COVID-19 vaccines is seen, experts can quickly study it further to determine if it is a true safety concern. Monitoring vaccine safety is critical to help ensure that the benefits of the COVID-19 vaccines continue to outweigh the risks for people who are vaccinated.

The current vaccine safety system is strong and robust, with the capacity to monitor COVID-19 vaccine safety effectively. Existing data systems can rapidly detect if a vaccine has any possible safety problems. These systems are being scaled up to fully meet the needs of the nation. Additional systems and data sources are also being developed to further enhance safety monitoring capabilities.

## New vaccine safety monitoring systems and information sources

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 as safe as possible:

- **CDC: V-SAFE** — A new smartphone-based, after-vaccination health checker for people who receive COVID-19 vaccines. V-SAFE will use text messaging and web surveys from CDC to check in with vaccine recipients for health problems following COVID-19 vaccination. The system also will provide telephone follow up to anyone who reports medically significant (important) adverse events.
- **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 or VAERS
- **FDA: Other large insurer/payer databases** — A system of administrative and claims-based data for surveillance and research

## Existing Safety Monitoring Systems

The safety of vaccines is monitored all the time 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 followed up with specific studies
- **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
- **FDA: Sentinel Initiative** — 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 the 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 immunizations
- **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): IHS VAERS data** — Spontaneous adverse event reporting to VAERS for populations served by IHS and Tribal facilities