Centers for Disease Control and Prevention

Ensuring COVID-19 Vaccines Work

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Before the U.S. Food and Drug Administration (FDA) determines whether to approve a vaccine or authorize a vaccine for emergency use, clinical trials are conducted to determine **how well it works.** This is known as **effectiveness**.

After FDA approves a vaccine or authorizes a vaccine for emergency use, it continues to be studied to determine **how well it works under real-world conditions**. CDC and other federal partners will be assessing **COVID-19 vaccine effectiveness under real-world conditions**.

CDC will further assess vaccine effectiveness now that a COVID-19 vaccine has been authorized for emergency use by FDA. Many of these assessments will build on existing CDC programs, such as the Emerging Infections Program, Coronavirus Disease 2019-Associated Hospitalization Surveillance Network (COVID-NET), and systems used to estimate the effectiveness of influenza vaccines.

Learn about how the U.S. vaccine safety system is ensuring the safety 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 an infectious disease and about how safe it is. The FDA evaluates these data, as well as manufacturing information, to assess the safety and effectiveness of vaccines. FDA then decides whether to approve a vaccine or authorize it for emergency use in the United States.

However, more assessments take place after a vaccine is either approved or authorized for emergency use by FDA and then 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.

CDC will further assess the effectiveness of COVID-19 vaccines after they are approved or authorized for emergency use by FDA and recommended for public use. 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 assess how well COVID-19 vaccines are working to protect people.

Why do experts continue to assess vaccine effectiveness in real-world conditions?

The major reason for conducting additional vaccine effectiveness assessments is to make sure a vaccine protects people from getting a disease under real-world conditions, outside of the strict setting of clinical trials. There are many factors that 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 in the real-world compared to those in the clinical trials. Vaccine effectiveness assessments can also provide important information about how well a vaccine is working in groups of people not included or not well represented in clinical trials.

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

Experts are working on many different types of real-world vaccine effectiveness assessments, and each uses a different method. These methods are described below.

- **Case-control studies:** These assessments 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). The people who agree to participate in a case-control assessment 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.
  - **Test-negative design**: This is a special type of case-control study. These assessments will enroll people who are seeking medical care for symptoms that could be due to COVID-19. Experts will then 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).
- **Cohort studies:** These assessments 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' electronic health records (medical records).
- **Screening method**: These assessments look at vaccination coverage among a group of cases (for example, cases detected through ongoing COVID-19 surveillance) and compares it with vaccination coverage among the overall population where those cases come from (for example people from the same state). By comparing coverage among these two groups, researchers can get an early estimate of whether a vaccine is working as expected.
- **Ecologic analyses**: These assessments look at groups of people – such as those in different geographic locations or at different times – and find out how many people were vaccinated and how many people were diagnosed with COVID-19. These analyses may be hard to interpret since the number of COVID-19 illnesses has changed rapidly over time and in different places.

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

How is CDC coordinating with other U.S. government agencies to ensure COVID-19 vaccines work as expected?

CDC is coordinating with several other federal agencies to assess how well COVID-19 vaccines work under real-world conditions after FDA approval or authorization for emergency use. These agencies include:

- Centers for Medicare and Medicaid Services (CMS)
- Department of Defense (DoD)
- Food and Drug Administration (FDA)
- Indian Health Service (IHS)
- Veteran's Health Administration (VHA)

Some examples of how these agencies are working together include:

- CDC, FDA, and VHA are holding working group discussions to understand how each will use electronic health records (medical records) to see if people who received a COVID-19 vaccine are protected against developing COVID-19.
- FDA and CMS are planning to further assess how well COVID-19 vaccines protect against developing COVID-19 among older adults, including those living in nursing homes and long-term care facilities.

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. Learn more about people at increased risk of severe illness from COVID-19. Experts

hospitalized patients. Experts will also use electronic health record cohort studies to see if people hospitalized with COVID-19 received the vaccine or not.

Will assessments provide information about how well vaccines protect against less severe COVID-19 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 the assessments try to find out if the vaccines protect people from all kinds of infections with the virus that causes COVID-19, including those with 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 help reduce the number of people that have asymptomatic infection as these people can unknowingly spread the virus to others.

A special type of cohort study will try to answer this question. 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.

What groups of people will be included in the real-world vaccine assessments?

CDC is working to make sure real-world vaccine assessments include diverse groups of people, such as healthcare personnel, essential workers, older adults and those living in nursing homes, people with underlying medical conditions, racial and ethnic minority groups, and tribal nations. It is important to measure how well COVID-19 vaccines work in groups of people who are at increased risk of getting COVID-19, as well as in those who are at increased risk of severe COVID-19.

CDC may recommend that some groups of people get COVID-19 vaccination first. If so, it will be important to see how COVID-19 vaccines work in these initial groups to be vaccinated to ensure the vaccines work as expected. Learn more about how CDC is making COVID-19 vaccination recommendations.

Healthcare personnel and essential workers

Experts will rapidly assess vaccine effectiveness among healthcare personnel working in hospitals or nursing homes in selected sites across the United States. This assessment will inform how well COVID-19 vaccines protect healthcare personnel from getting sick or severe illness. Additionally, assessments among healthcare personnel and essential workers will inform how well COVID-19 vaccines protect against getting infected, regardless of whether they have symptoms.

Older adults and those living in nursing homes

Making sure COVID-19 vaccines protect older adults is critical since the risk for severe illness from COVID-19 increases with age. People living in nursing homes and long-term care facilities are at especially high risk of getting COVID-19 and severe disease. FDA and CMS will assess COVID-19 vaccine effectiveness among older adults, including those living in nursing homes and long-term care facilities, using CMS Medicare billing data. These data will include information about whether people got a COVID-19 vaccine, whether they got sick with COVID-19, and if they needed to receive care in a hospital. This information will help inform how well the vaccine works in preventing COVID-19 and severe illness among older adults.

Experts will also conduct 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. They will then compare how many cases and controls received a COVID-19 vaccine to estimate vaccine effectiveness.

Underlying medical conditions

Adults of any age with **certain underlying medical conditions** are at increased risk for severe illness from the virus that causes COVID-19.

Making sure COVID-19 vaccines protect people with certain underlying medical conditions is important. Experts are working to make sure various real-world vaccine assessments will include enough adults with heart conditions, obesity, and diabetes to provide information about how well vaccines protect them.

The real-world vaccine effectiveness assessments will also collect information about many other underlying medical conditions. This information will be used to better understand how well COVID-19 vaccines protect people with underlying medical conditions.

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 vaccine effectiveness assessments include diverse populations, including people from racial and ethnic minority groups that are disproportionately affected by COVID-19. CDC also is working with the Indian Health Service (IHS), tribal nations, and other partners to ensure that real-world COVID-19 vaccine effectiveness 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 that everyone has a fair opportunity to be as healthy as possible. Learn more about COVID-19 and health equity considerations.

Related pages

- Vaccine Effectiveness Presentation at the Oct. 22, 2020, FDA Vaccines and Related Biological Products Advisory Committee Meeting
- FDA's Center for Biologics Evaluation and Research Plans for Monitoring COVID-19 Vaccine Safety and Effectiveness
- Ensuring the Safety of COVID-19 Vaccines in the United States
- COVID-19 8 Things to Know about Vaccine Planning
- Food and Drug Administration COVID-19 Vaccines
- Combat COVID: Information about Clinical Trials

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