

COVID-19: YOUR QUESTIONS ANSWERED

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The American Association of Immunologists (AAI) is pleased to present this short primer on coronavirus disease 2019 (COVID-19). Here, we focus on four key areas:

Vaccines

Symptoms

Therapies

Prevention

Because scientific research regarding coronavirus disease 2019 (COVID-19) and severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the virus that causes the disease, is ongoing, our understanding of the disease is rapidly growing. In response, public health advice is naturally and appropriately evolving. We urge readers to regularly consult the websites of the [National Institutes of Health \(NIH\)](#), the [Centers for Disease Control and Prevention \(CDC\)](#), and the [Food and Drug Administration \(FDA\)](#) for new developments.

Vaccines

Vaccine Development

COVID-19, the disease caused by SARS-CoV-2, has spread around the world with more than 430 million laboratory-confirmed cases and almost six million deaths as of February 2022.¹ High global vaccination rates are urgently needed to control this pandemic and to help people safely resume the usual activities of daily life. Vaccination slows the spread of disease, reduces the severity of illness to minimize hospitalizations and deaths, and eases the pressure on our strained health care system.

Historically, developing vaccines requires many years of research and involves complex interactions between public and private institutions. However, with the national and global mobilization efforts in response to COVID-19, we have seen the rapid development, testing, approval, manufacture, and distribution of highly effective vaccines against SARS-CoV-2.²

As of February 2022, ten COVID-19 vaccines, generated across multiple platforms (methods of generating vaccines), have been authorized by the World Health Organization (WHO) and are being used in countries around the world.³ In the U.S., two messenger RNA (mRNA) vaccines have been fully approved, and one viral vector vaccine has been authorized under an Emergency Use Authorization (EUA), by FDA. These vaccines induce protective immune responses against the SARS-CoV-2 spike protein, a protein needed for the virus to infect cells. Clinical trials and real-world evidence have demonstrated that all three vaccines are safe and highly effective at preventing severe disease, hospitalization, and death. These vaccines are:

1. [Pfizer-BioNTech mRNA COVID-19 vaccine](#) (Comirnaty®)
2. [Moderna mRNA COVID-19 vaccine](#) (Spikevax™)
3. [Johnson & Johnson \(Janssen\)](#) viral vector COVID-19 vaccine

The Pfizer-BioNTech and Moderna vaccines rely on mRNA technology. Because mRNA technology has been studied for decades, this platform was able to be rapidly adapted to generate a vaccine against SARS-CoV-2.⁴

¹ World Health Organization (WHO) (<https://covid19.who.int/>)

² Mallapaty, Callaway, Kozlov, Ledford, Pickrell and Van Noorden. [How COVID vaccines shaped 2021 in eight powerful charts](#). Nature. 2020; 600, 580-583.

³ <https://covid19.trackvaccines.org/agency/who/>

⁴ Dolgin, E. [The tangled history of mRNA vaccines](#). Nature. 2021; 597, 318-324.

The mRNA vaccines enable human cells to produce a harmless version of the SARS-CoV-2 spike protein, which prompts the immune system to mount a response against the virus that helps limit symptoms and protect against severe disease from future infection. No live virus is involved, and recipients cannot get COVID-19 from the vaccine.

Johnson & Johnson's vaccine uses viral vector technology, which has been studied in the context of vaccines, gene therapy, and cancer, since the 1970s.^{5,6} This platform uses a harmless, non-replicating version of a virus that enters a cell, which then produces a single protein (in the case of COVID-19, the SARS-CoV-2 spike protein) instead of the whole virus and promotes the development of protective antibodies. Recipients cannot get COVID-19 from this vaccine.

The mRNA vaccines require long term storage at very low temperatures, though Moderna reports that its vaccine can be stored at normal refrigerator temperatures for up to 30 days.⁷ The Johnson & Johnson vaccine can be stored for up to six months at normal refrigerator temperatures. Storage requirements are an important consideration in ensuring global accessibility to vaccines.

Rigorous testing and evaluation of a vaccine candidate are required before it is authorized or approved by FDA and recommended for use by CDC. AAI has described these steps in a short primer accessible [here](#).

Vaccine Administration

Safe and effective vaccines against COVID-19 are available and recommended by CDC for individuals five years of age and older. Federal guidelines regarding vaccine administration are being continually updated based on the latest scientific data. For information after February 2022, please consult the [CDC website](#).

Primary Series

[According to CDC](#), both mRNA vaccines should be administered as a primary series of two shots spaced three weeks (Pfizer-BioNTech) or four weeks (Moderna) apart for people who are moderately to severely immunocompromised, are 5-11 years old (eligible for Pfizer-BioNTech only), are 65 years or older, or need rapid protection due to increased community transmission or risk of severe disease.⁸ People between 12 and 64 years old, especially males aged 12-39, should consider getting their primary series doses spaced eight weeks apart due to potentially increased vaccine effectiveness and decreased risk of a rare side effect known as myocarditis.⁹ The Pfizer-BioNTech vaccine has been FDA-approved for use by individuals 16 years of age and older (August 2021) and has received an EUA for the two dose primary series for individuals 5-15 years old (October 2021). In January 2022, FDA granted full approval of the Moderna vaccine for use by individuals 18 years of age and older.

A third dose to complete the primary series of the mRNA vaccines is recommended for people who are moderately to severely immunocompromised (who may not have had a sufficient immune response to two doses).⁹

The Johnson & Johnson vaccine requires a primary series of one shot and has received an EUA for use in individuals 18 years of age and older. Due to higher vaccine effectiveness of the mRNA vaccines and the real but rare risk of “serious adverse events” from the Johnson & Johnson vaccine, [CDC recommends](#) vaccination with the Pfizer-BioNTech or Moderna mRNA vaccines for most people.¹⁰

⁵ <https://www.cdc.gov/coronavirus/2019-ncov/vaccines/different-vaccines/janssen.html>

⁶ <https://www.cdc.gov/coronavirus/2019-ncov/vaccines/different-vaccines/viralvector.html>

⁷ <https://www.modernatx.com/covid19vaccine-eua/providers/storage-handling>

⁸ <https://www.cdc.gov/coronavirus/2019-ncov/vaccines/different-vaccines.html>

⁹ <https://www.cdc.gov/vaccines/covid-19/clinical-considerations/covid-19-vaccines-us.html>

¹⁰ <https://www.cdc.gov/mmwr/volumes/71/wr/mm7103a4.htm#:~:text=On%20December%2016%2C%202021%2C%20after,years%20in%20the%20United%20States.>

Pediatric clinical trials are ongoing to determine the appropriate dosage, safety, and efficacy of COVID-19 vaccines in children aged 6 months to 4 years.

Booster Shots

All three vaccines are authorized for use as a booster shot (an extra dose in addition to the recommended primary series) and can be given in a “mix and match” fashion. As with the primary series, [CDC also recommends](#) that most individuals receive the Pfizer-BioNTech or Moderna mRNA vaccine as a booster shot rather than the Johnson & Johnson vaccine, unless the person had an adverse reaction to an mRNA vaccine or would not otherwise choose to get boosted. [CDC recommends](#) a booster shot for maximal protection against the omicron strain of SARS-CoV-2, currently the dominant strain circulating in the United States,¹¹ for all eligible individuals. Booster shots are particularly important for the elderly and immunocompromised, who may not induce or retain robust immunity.

Side Effects

The most common side effects for all three vaccines are similar. Some recipients have experienced transient injection site pain and/or flu-like symptoms, including fever, chills, fatigue, headaches, and/or muscle pain.¹² These mild to moderate side effects are a normal response to the immune system being primed to defend against an actual infection, and do not mean that a recipient has been infected with SARS-CoV-2. Vaccines cannot cause COVID-19.

All three vaccines authorized or approved by FDA are safe and effective for the recommended populations. [AAI urges](#) all eligible individuals to get fully vaccinated against COVID-19 and to receive a booster shot.



¹¹ <https://www.cdc.gov/coronavirus/2019-ncov/variants/omicron-variant.html>

¹² <https://www.cdc.gov/coronavirus/2019-ncov/vaccines/expect/after.html>

How Vaccines Work

As pictured to the right, a vaccine prepares the immune system to recognize and combat the virus if the immune system encounters it. After vaccination, when a person gets exposed to SARS-CoV-2, their immune system can more easily and quickly block or control the infection, limiting symptoms and transmission. This is why a vaccinated person usually has less severe symptoms and may not even get infected as compared to an unvaccinated person.

Understanding Vaccine Induced Immunity: Antibodies and T cells

There are two types of immune cells that are particularly important in the response to a vaccine: B cells and T cells. B cells produce antibodies that can block the virus from spreading from cell to cell. This is known as “humoral immunity.” T cells can seek out and kill infected cells, also preventing viral spread. This is known as “cellular immunity.” Although much remains to be understood regarding immune protection for SARS-CoV-2 infection, emerging data have demonstrated the importance of both humoral and cellular immunity in protection. Research is ongoing to better understand the relative contribution of vaccine-induced antibodies and T cells to controlling SARS-CoV-2 infection.

Variant-Specific Booster Shots

Viruses such as SARS-CoV-2 mutate over time, leading to the presence of new viral “variants,” or “strains,” which can evade vaccine induced immunity. While T cells induced by primary series vaccination are able to recognize and combat currently existing variants of concern, booster shots have been effective in increasing antibody production by B cells, providing enhanced protection. To prepare for potential variants that may evade current vaccines, scientists are working to develop booster shots that could enable better immune protection against viral variants and are testing the ability of current vaccines to protect against emerging variants. The rapid deployment of effective vaccines worldwide could help to reduce the spread of existing variant strains and reduce the chance that new strains will prolong the pandemic. Continued basic research is needed to improve pre-clinical models to rapidly test the infectivity of new variants, determine protection by current vaccines, and identify new vaccine targets.

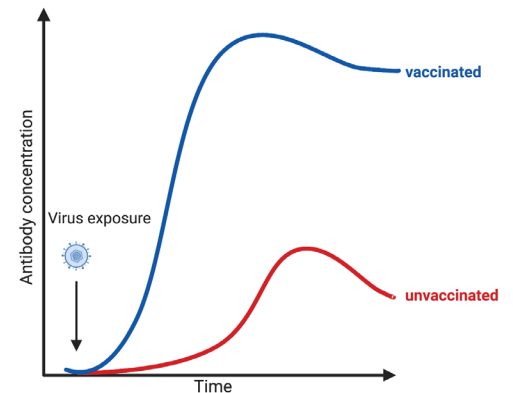
Symptoms

Symptoms of COVID-19

COVID-19 can present differently across individuals, from asymptomatic infection to severe disease.

- Commonly reported symptoms of COVID-19, which may or may not require seeking medical care, include¹³.
 - Cold-like symptoms (cough, sore throat, congestion, runny nose, headache)
 - Loss of taste and/or smell
 - Fever and/or chills
 - Shortness of breath or difficulty breathing

Induction of immune responses after virus exposure or vaccination:



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¹³ <https://www.cdc.gov/coronavirus/2019-ncov/symptoms-testing/symptoms.html>

- Fatigue
- Muscle or body aches
- Gastrointestinal symptoms (nausea, vomiting, diarrhea)
- Severe symptoms of COVID-19 that require seeking emergency medical care¹³:
 - Trouble breathing
 - Skin, lip, or nail bed discoloration (pale, blue, gray)
 - Constant chest pain or pressure
 - Confusion
 - Extreme fatigue/inability to wake up or stay awake

Severe disease most commonly occurs in the elderly, immunocompromised, and those with underlying conditions including hypertension, diabetes, and obesity.¹⁴ It is important to note, however, that severe disease can occur in all age groups. In rare cases, people can develop multisystem inflammatory syndrome (MIS-C in children and MIS-A in adults), a serious disease associated with COVID-19 in which patients develop inflammation of the heart, lungs, kidneys, brain, skin, eyes, or gastrointestinal organs.¹⁵

COVID-19 Long-Term Effects¹⁶

COVID-19 can have long-term adverse effects on the neurological, cardiovascular, gastrointestinal, musculoskeletal, and pulmonary systems, as well as on mental health. These post-COVID conditions are also called long COVID, long-haul COVID, or post-acute sequelae of COVID-19 (PASC) and can linger for weeks or months after first being infected by SARS-CoV-2. Long-term effects are more likely in vulnerable populations, such as the elderly and those with certain comorbidities (having two or more diseases or medical conditions simultaneously) but can occur in anyone who has been infected with SARS-CoV-2.

- Commonly reported [adverse effects](#) include:
 - Change in smell or taste
 - Difficulty breathing or shortness of breath
 - Tiredness or fatigue
 - Worsening symptoms after physical or mental activities
 - Brain fog
 - Cough, chest pain, heart palpitations
 - Fever, headache, dizziness, lightheadedness
 - Joint or muscle pain, pins and needles feeling
 - Stomach pain, diarrhea
 - Sleep problems



¹⁴ <https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-with-medical-conditions.html>

¹⁵ <https://www.cdc.gov/mis/index.html>

¹⁶ <https://www.cdc.gov/coronavirus/2019-ncov/long-term-effects/index.html>

- Rash
- Mood changes
- Changes in menstrual period cycles
- Rare but serious adverse effects¹⁷⁻¹⁹
 - Brain: Inflammation of the brain tissue (encephalitis) and lack of oxygen can result in cognitive impairment (changes in memory and attention), mood swings, mental health disorders (anxiety, depression, post-traumatic stress disorder), sleep problems, seizures, and increased risk of Alzheimer’s disease and Parkinson’s disease. Further, COVID-19 increases the risk of blood clots and the weakening of blood vessels, making it a risk factor for stroke.
 - Heart: Inflammation of the heart muscle (myocarditis) and/or the covering of the heart (pericarditis) can result in damage to heart tissue and an increased risk of heart attack and heart failure.
 - Lung: Inflammation of the lungs can result in lung tissue damage, impaired pulmonary function, and an increased risk of pulmonary embolism (blood clots).

Therapies

Several therapeutics have been identified for treatment of the different stages of COVID-19. Research is ongoing to develop additional treatments and therapies to stop viral replication and limit disease symptoms. Below, we describe FDA-authorized treatments that are being used and are most likely to provide clinical benefit (for updated information, see [covid19treatmentguidelines.nih.gov](https://www.covid19treatmentguidelines.nih.gov)).

For Prophylaxis After Exposure or Treatment of Presymptomatic or Mild-to-Moderate COVID-19

Most people without underlying medical conditions who are fully vaccinated and boosted will be asymptomatic or experience mild-to-moderate disease. To ease cold or flu-like symptoms, most people can safely take analgesics (e.g., over-the-counter and prescription acetaminophen) or nonsteroidal anti-inflammatory drugs (NSAIDs) (e.g., over-the-counter and prescription ibuprofen). Staying well hydrated and rested will also help recovery.

People who are at [high risk of severe disease](#) may benefit from the following treatments (should be taken only under a doctor’s supervision):

- Monoclonal antibodies²⁰ – Purified antibody preparations that bind to the spike protein of SARS-CoV-2 and prevent virus entry into host cells. Recommended for early treatment (before symptomatic infection) or prophylaxis after exposure and requires infusion on an outpatient basis. Not for use in hospitalized patients.
 - [Bamlanivimab plus etesevimab](#) (Eli Lilly) (Originally granted EUA by FDA on November 9, 2020) (not recommended by CDC for use against the omicron variant due to decreased efficacy²¹)
 - [Casirivimab and imdevimab](#) cocktail (REGEN-COV®, Regeneron) (Originally granted EUA by FDA on November 21, 2020) (not recommended by CDC for use against the omicron variant due to decreased efficacy²¹)

¹⁷ <https://www.hopkinsmedicine.org/health/conditions-and-diseases/coronavirus/covid-long-haulers-long-term-effects-of-covid19>

¹⁸ <https://www.nature.com/articles/s41590-021-01104-y>

¹⁹ Staff MC. COVID-19 (coronavirus): [Long-term effects: Mayo Foundation for Medical Education and Research](#); 2020 [updated 10/22/2021].

²⁰ <https://www.covid19treatmentguidelines.nih.gov/therapies/anti-sars-cov-2-antibody-products/anti-sars-cov-2-monoclonal-antibodies/>

²¹ <https://www.covid19treatmentguidelines.nih.gov/therapies/anti-sars-cov-2-antibody-products/summary-recommendations/>

- [Sotrovimab](#) – (GlaxoSmithKline) (Originally granted EUA by FDA on May 26, 2021)
- [Bebtelovimab](#) (Eli Lilly) (originally granted EUA by FDA on February 11, 2022)
- [Tixagevimab plus cilgavimab](#) (Evusheld™, AstraZeneca) (Originally granted EUA by FDA on December 8, 2021)
 - Administered to certain individuals with moderately to severely compromised immune systems or those with a history of severe adverse reactions to COVID-19 vaccines, who are not currently infected or exposed, for the prevention of COVID-19 disease.
- Oral Antiviral Therapy – Prescription tablets that prevent viral replication. They are recommended for the treatment of mild-to-moderate COVID-19 as soon as possible after COVID-19 diagnosis and within five days of symptom onset. Not for use in hospitalized patients.
 - [Paxlovid™](#) – (Pfizer) (Originally granted EUA by FDA on December 22, 2021)
 - [Molnupiravir](#) – (Merck) (Originally granted EUA by FDA on December 23, 2021)

For Symptomatic COVID-19 Requiring Medical Care²²

The following treatments are for therapeutic management of hospitalized adults and are administered based on disease severity.

- Remdesivir – This intravenously-delivered drug, originally developed to treat hepatitis and respiratory syncytial virus infection, reduces viral replication by binding to the viral machinery needed for replication. (Veklury®, Gilead Sciences, Inc., FDA granted full approval on October 22, 2020)
- Baricitinib – This orally-delivered arthritis drug inhibits a signaling pathway that leads to excessive inflammation and can result in tissue damage. (Originally granted EUA by FDA on November 19, 2020, in combination with remdesivir)
- Tofacitinib – An orally-delivered medication used to treat rheumatoid arthritis, psoriatic arthritis, and ulcerative colitis. It is administered as an alternative drug to baricitinib.
- Anticoagulants – This treatment minimizes the likelihood of blood clots and subsequent pulmonary embolism or deep vein thrombosis, which have been associated with severe COVID-19. (Originally granted EUA by FDA on August 13, 2020)
- Dexamethasone or steroid therapy – This orally-delivered drug limits the excessive inflammation that is associated with many of the symptoms of severe COVID-19.
- Tocilizumab – This antibody therapy, approved for arthritis, blocks an inflammation-inducing protein which amplifies immune responses that can lead to excessive inflammation and can cause tissue damage. (Originally granted EUA by FDA on June 24, 2021)

Post-COVID Conditions/Long COVID/Long-Haul COVID/Post-Acute Sequelae of COVID-19 (PASC)

Although most people will fully recover from COVID-19 within weeks, some people experience a range of new, returning, or ongoing symptoms four or more weeks after first being infected. The below treatments may help ease some of these symptoms.

²² <https://www.covid19treatmentguidelines.nih.gov/management/clinical-management/hospitalized-adults--therapeutic-management/>

- Analgesics and NSAIDs – reduce ongoing symptoms and inflammation
- Nasal steroids – reduce local inflammation, may help relieve loss of sense of smell

Prevention²³

1. **Vaccination:** Widespread immunization is the best way to achieve reliable, long-term control of COVID-19.

In January 2022, compared to fully vaccinated and boosted adults 18+, unvaccinated adults had a:

3.2x higher risk of testing positive
for COVID-19

9x higher rate of hospitalization
due to COVID-19

41x higher risk of dying
from COVID-19*

Source: CDC, COVID-19 Data Tracker²⁴ *data from December 2021

2. **Masks:** Because SARS-CoV-2 is transmitted within respiratory droplets/particles that are produced when a person breathes, sings, coughs, or sneezes, high quality, well-fitting masks can protect oneself and others from infection.^{25,26} The virus is spread primarily by two airborne routes:
 - droplet transmission: large respiratory droplets that contain virus are inhaled by someone close to the infectious person, generally within about six feet
 - aerosol transmission: small viral particles in the air (which can linger for minutes to hours) infect others by being inhaled through the nose or mouth, or (less likely) by deposition on the eyes
 AAI recommends that individuals consult current [CDC mask guidelines](#), and when appropriate, wear high quality masks with the best fit and protection possible.
3. **Social Distancing:** Social distancing will help reduce the risk of being exposed to SARS-CoV-2. Data show that being outdoors is far safer than being indoors, for the same activity and distance. The risk of transmission is much lower outside than inside because viruses that are released into the air can rapidly become diluted through the atmosphere.

Other ways to reduce risk include avoiding:

- places where people are not wearing masks, especially indoors;
- crowded spaces;
- close proximity (within six feet) to others, especially if they are vigorously exhaling as a result of loud talking/shouting/singing, or aerobic exercise;
- environments with poor ventilation; and
- contact with others whose vaccination and COVID-19 status are unknown.

4. **Testing:** Testing for SARS-CoV-2 is helpful in preventing the spread of disease. Two types of tests are

²³ <https://www.cdc.gov/coronavirus/2019-ncov/prevent-getting-sick/prevention.html>

²⁴ Centers for Disease Control and Prevention. [COVID Data Tracker](#). Atlanta, GA: US Department of Health and Human Services, CDC; 2022, March 02.

²⁵ <https://www.cdc.gov/coronavirus/2019-ncov/prevent-getting-sick/how-covid-spreads.html>

²⁶ <https://www.who.int/news-room/questions-and-answers/item/coronavirus-disease-covid-19-how-is-it-transmitted>

available to determine if an individual is infected with SARS-CoV-2:

- Polymerase chain reaction (PCR) tests, which are the most accurate for detecting the presence of any SARS-CoV-2 viral particles, infectious or not. These tests must be overseen by a professional and submitted to a laboratory for results, which usually yield results within a few days.
- Rapid antigen tests, which typically detect only infectious virus particles, can be taken anywhere, are easy to self-administer, and produce rapid results, usually within minutes.

5. Practice good hygiene:

- Thoroughly washing hands (with soap and water for 20 seconds) or using a hand sanitizer (that contains at least 60% alcohol) and disinfecting frequently touched objects and surfaces may protect an individual from contact droplet transmission, which, although rare with COVID-19, is infection spread through direct contact with an article or surface that is contaminated.
- Cover coughs and sneezes using an elbow or tissues and put on a new, clean mask after coughing or sneezing.

