COUNCIL on FOREIGN RELATIONS

Backgrounder

A Guide to Global COVID-19 Vaccine Efforts

The swift development of effective vaccines against COVID-19 was an unprecedented scientific achievement. But production challenges, vaccine nationalism, and new variants have all presented hurdles.

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Summary

Governments, multilateral organizations, and private firms have spent billions of dollars to develop effective vaccines for COVID-19.

More than thirty vaccines are being distributed, though highly effective mRNA vaccines have become the most sought after worldwide.

Vaccines go through rigorous testing for safety and effectiveness before they are approved for public use.

Introduction

The global effort to develop and distribute effective vaccines against the COVID-19 coronavirus disease has produced various safe and effective options. The development of multiple vaccines within one year of the virus's emergence is unprecedented; the process typically taken eight to fifteen years.

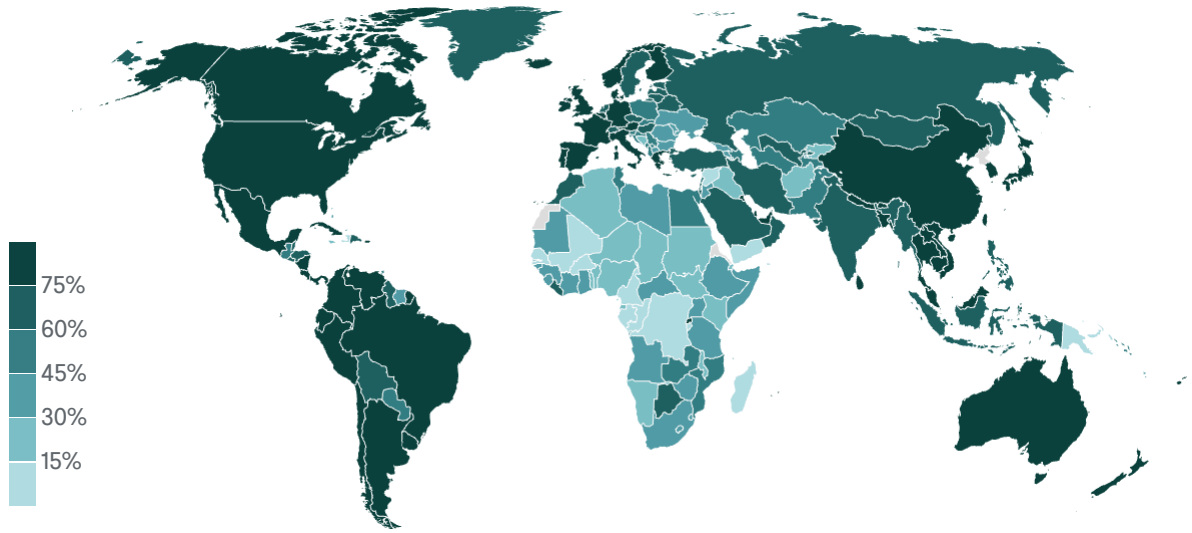
However, the immunization of a critical mass of the world's population—which is crucial ending the pandemic—continues to confront challenges, including new strains of the viru global competition over a limited supply of doses, and public hesitation about the vaccine

What is the status of COVID-19 vaccinations globally?

More than thirty vaccines have been approved for general or emergency use in countries around the world. By the end of 2022, over thirteen billion doses had been administered worldwide. In dozens of countries, at least three-quarters of the population has been fully vaccinated; Qatar, Singapore, and the United Arab Emirates are among those with the highest immunization rates. However, many others—mostly in Africa—have vaccinated o small fractions of their populations. Close to three years after COVID-19 emerged, nearly one-third of the global population is yet to receive a vaccine dose.

The Global COVID-19 Vaccination Divide

Share of people who have received at least one dose as of December 4 or most recent date available



Source: Our World in Data.

Many countries implemented vaccination mandates. For example, Italy and Saudi Arabia mandated COVID-19 vaccinations for both government and private-sector workers. The United States did the same for its public sector and large private employers, but courts

blocked both mandates, and legal challenges are ongoing. Other countries have enacted mandates for health-care workers only. China has stopped short of a nationwide mandate despite challenges with vaccine uptake, particularly among elderly people.

At the same time, children's access to COVID-19 vaccines is gradually expanding: in China children aged three and above can be vaccinated, and in the United States, children as young as six months old are eligible.

How does a vaccine work?

Traditionally, vaccines are dead or weakened virus molecules—known as antigens—that trigger defensive white blood cells in the immune system to create antibodies that bind to the virus and neutralize it. Sinopharm's COVID-19 vaccine, which contains inactivated coronaviruses, is one example. Another well-established method uses isolated proteins from a virus, or fragments of them, to stimulate an immune response; U.S.-based Novavax's COVID-19 vaccine is protein-based.

There are also several types of vaccines that use the virus's genetic material—DNA or RNA—to prompt the body to create antibodies. The vaccines by U.S. pharmaceutical giant Pfizer and partnering German firm BioNTech and by U.S.-based Moderna use mRNA, or messenger RNA. No vaccine of this kind had ever been approved for commercial use in humans before the COVID-19 pandemic.

Additionally, some COVID-19 vaccines rely on viral vectors, or modified versions of a different virus, to prompt an immune response. Several approved COVID-19 vaccines use viral vectors, such as that by the University of Oxford and British-Swedish company AstraZeneca.

When most of a population has been vaccinated and is immune to a particular disease, even those who are not immune are considered protected because the likelihood of an outbreak is small. This is known as herd immunity. Chicken pox, measles, mumps, and polio are all examples of diseases for which the United States has achieved herd immunity due to vaccines. However, many experts believe that herd immunity for this coronavirus is unreachable due to uneven vaccination rates, vaccine hesitancy, and the proliferation of new strains.

Who is involved in vaccine development?

Vaccines are frequently collaborative efforts across sectors of society, with private pharmaceutical firms teaming up with public health agencies or university labs. Here are snapshots of some of the major players in the COVID-19 vaccine field.

Governments. Public health agencies have played critical roles in supplying funds to devel COVID-19 vaccines. In the United States, President Donald Trump's administration launcl Operation Warp Speed, a project aimed at developing an effective vaccine and manufacturing enough doses for all three hundred million Americans. The effort, which pledged billions of dollars to companies with promising candidates, brought together seve agencies within the Department of Health and Human Services—including the Centers f Disease Control and Prevention, the National Institutes of Health (NIH), and the Food ar Drug Administration (FDA)—and the Department of Defense. Across the Atlantic, the European Commission dedicated several hundred million euros to COVID-19 vaccine development. In China, the government closely oversaw efforts, with developers includin Sinopharm being state-run.

International institutions. The WHO and other multilateral institutions such as the World Bank are focused on financing and manufacturing COVID-19 vaccines for global use, in particular to ensure fair allocation among all countries. Also at the forefront of multilate efforts is the Coalition for Epidemic Preparedness Innovations (CEPI), a global alliance th was founded by Norway, India, the Bill & Melinda Gates Foundation, the UK-based Wellc Trust, and the World Economic Forum. Gavi, the Vaccine Alliance—also founded by the Gates Foundation—is a public-private partnership focused on improving vaccine access fc lower-income countries. In June 2020, the WHO, CEPI, and Gavi launched COVAX, a globa initiative that initially aimed to have two billion vaccine doses available by the end of 202

P (As of November 2022, it had delivered around 1.8 billion doses.)

Private sector. The pharmaceutical industry has driven much of the push. Companies rang from biotech start-ups to giants such as U.S.-based Johnson & Johnson shifted their resear and development efforts to focus on COVID-19. Early research into a vaccine candidate typically receives government funding, such as NIH grants in the case of the United State

but the bulk of financing for clinical development generally comes from private sources. With COVID-19, however, massive government funding for promising vaccines removed much of the risk for pharmaceutical companies.

Research institutions and nonprofits. Many of the COVID-19 vaccine candidates have involv a university or college assisting in preclinical research or clinical trials. In the case of the University of Oxford's vaccine, the research team was already working on vaccines for an unknown disease that could cause a pandemic; then, in January 2020, the group zeroed in COVID-19. The Gates Foundation has been the leading nonprofit funding COVID-19 vacc efforts.

What are the leading COVID-19 vaccines?

Most of the vaccines approved for use have been developed by firms and research groups China, Russia, and the United States. As scientists have continued to collect data on the different vaccines, the Western-made mRNA vaccines have become the most sought after their consistent effectiveness against preventing serious illness. Concerns have grown, meanwhile, about the waning durability of other COVID-19 vaccines, including China's, billions of doses of which have been distributed around the globe. Russia's Sputnik vaccin faced relatively low acceptance globally before the Ukraine war threw another wrench in distribution.

Leading COVID-19 Vaccines

Prominent COVID-19 vaccines with approval in at least one country as of August 2022

Country	Developer	Clinical phase
China	**CanSino**	3
China	**Sinopharm**	3
China	**Sinovac**	3
India	**Bharat Biotech**	3
Russia	**Gamaleya**	3
United Kingdom, Sweden	**Oxford-AstraZeneca**	2 and 3
United States, Germany	**Pfizer-BioNTech**	3
United States, India	**Baylor, Biological E**	3
United States	**Johnson & Johnson**	3
United States	**Moderna**	3
United States	**Novavax**	3

Note: Efficacy can depend on dosage, severity of infection, and COVID-19 variant.

Source: New York Times.

Scores of other COVID-19 vaccine candidates are undergoing large-scale clinical trials and around two hundred others are in preclinical development by pharmaceutical companies, academic institutions, and government agencies. "The COVID vaccine 2.0, 3.0, and 4.0 rea

are possibilities," the University of Minnesota's Michael Osterholm tells CFR. "Can we find vaccines that have more durability, that are more likely to be able to withstand a number different variants that might emerge?"

How is a vaccine developed?

There are many stages involved in the development and production of a vaccine, from ini academic research to distribution to hospitals and doctor's offices.

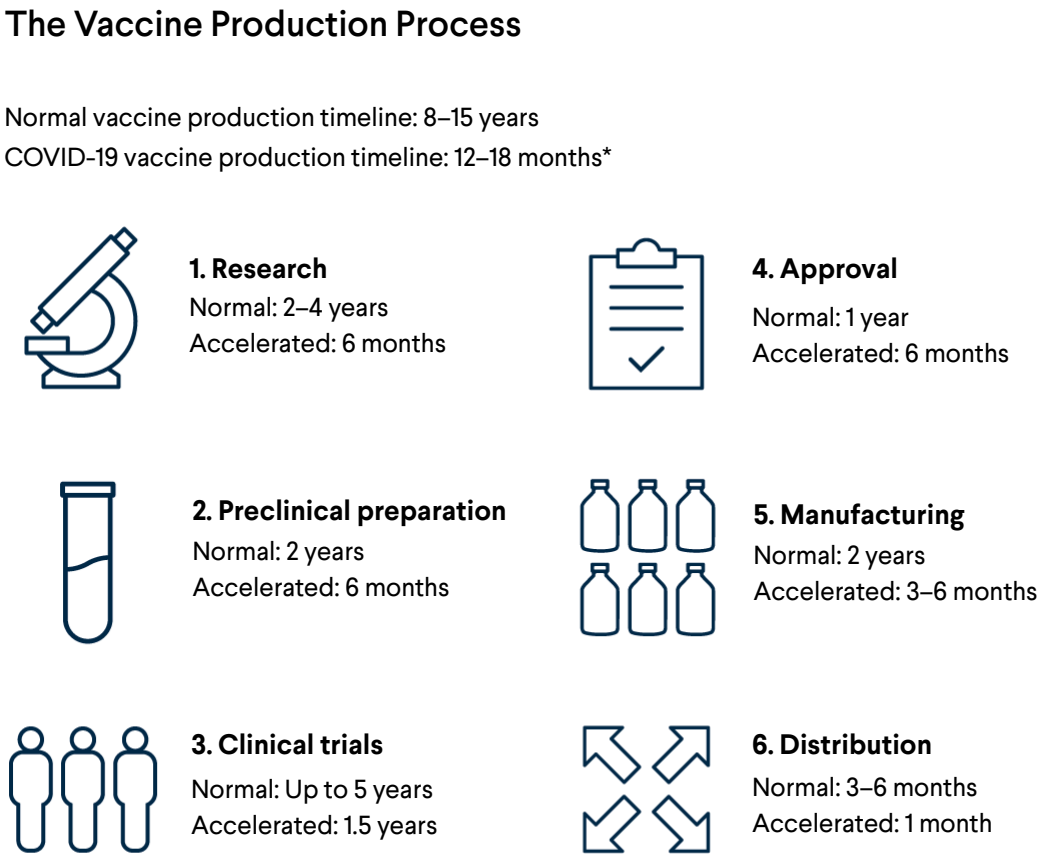
Clinical trials are crucial indicators of whether a vaccine is effective. Potential vaccines, as with other drugs, are commonly tested in animals first. Human trials are broken up into three phases, progressively increasing the number of volunteers. If a vaccine candidate appears to be ineffective, has harmful side effects, or is too similar to existing vaccines, it won't move on. Trials are often carried out "blind," by which some groups are administere the vaccine and some receive a placebo.

If a vaccine candidate is considered successful in human trials, the developers can seek approval by a national or regional regulatory agency, such as the FDA or the European Medicines Agency. In the United States, less than 10 percent of all drugs that go into clini trials make it past this part of the process. Prior to approval, a vaccine maker can ask the FDA for an emergency use authorization (EUA), which allows the sale of unapproved medical products. Finally, the vaccine must be approved by national regulators in other countries to be distributed abroad. Following approval, the vaccine can be manufactured broad use. In August 2021, the FDA granted approval to the Pfizer-BioNTech vaccine, the first to receive a license in the United States. Moderna's vaccine was approved the followi January.

Additionally, while the WHO does not approve drugs, the vaccine maker can request prequalification by the WHO—a process to determine quality assurance. Many low- and middle-income countries rely on WHO prequalification [PDF] when buying medicines. Th WHO similarly maintains an emergency use listing (EUL) for unlicensed vaccines and oth medical products during a health crisis; eleven COVID-19 vaccines have been issued an EU

How has development been sped up amid the pandemic?

Under normal circumstances, during which the stages of vaccine development occur sequentially, a vaccine takes eight to fifteen years on average to get from the lab into the hands of health-care providers. The fastest a vaccine had ever been developed before this pandemic was four years. Following the emergence of COVID-19, however, researchers around the globe accelerated the process by carrying out stages of development simultaneously and by looking to new vaccine technologies. "What we're seeing is remarkable," said Paul Offit, director of the Vaccine Education Center at the Children's Hospital of Philadelphia, in late 2020. "It is a scientific tour de force."



The U.S. Operation Warp Speed timeline hinged on overlapping stages of development; n production started for strong candidates even while clinical trials were ongoing. Before th vaccines were approved, Moderna received $2.5 billion in a deal under Warp Speed that included the purchase of one hundred million doses, while Pfizer and BioNTech signed a $1.95 billion contract to manufacture and distribute one hundred million doses of their vaccine. After President Joe Biden took office, his administration purchased over a billion additional doses, the majority of which have been donated to other countries.

Another way researchers have quickened the process is by focusing on new vaccine approaches. RNA- and DNA-based vaccines can be developed far faster than conventional vaccines, which require months at a time of growing antigens in animal or insect cells.

How are COVID-19 treatments helping?

Dozens of treatments have been developed or repurposed. (Treatments would not preven someone from being infected with COVID-19 but could help reduce the severity and duration of illness.) Among them is the antiviral drug remdesivir, which was developed by U.S.-based Gilead Sciences and approved by the FDA; studies of the drug have shown fast rates of recovery from COVID-19 and lower risk of hospitalization. Additionally, dexamethasone, a common steroid, has been found to reduce the risk of death in severely COVID-19 patients. The FDA has authorized emergency use of convalescent plasma, or bl plasma of previously infected people who have created COVID-19 antibodies. While plasr donations have been used in many patients, research is ongoing to determine the treatme effectiveness.

Additionally, scientists have developed oral antiviral treatments that can be administered home. Paxlovid and molnupiravir, pills developed by Pfizer and Merck, respectively, were first such treatments to be authorized for emergency use by the FDA, in late 2021. A stud by the U.S. Department of Veterans Affairs found that taking Paxlovid within the first fev days of infection could reduce the risk of long COVID, or a wide range of symptoms that continue after the infection is gone.

Can vaccines end the pandemic?

Even with a variety of vaccines with at least limited approval, there remains the tremend challenge of making enough and distributing them to the global population. Though multilateral initiatives such as COVAX and individual governments are investing billions dollars to expand production plants, current global manufacturing capabilities remain fa below what's needed.

This task has not only motivated countries to scale up production, but also pitted them against one another amid a limited vaccine supply. Wealthy countries including Australia Canada, and the United States struck deals with manufacturers early on to provide their countries with more than enough doses, leaving lower-income countries unable to immu but a small proportion of their citizens. China and India have large vaccine industries, w allowed them to reserve some of their vaccine supplies for their own populations. Expert including CFR's Thomas J. Bollyky have warned that vaccine nationalism leads to inequit distribution and, ultimately, fails to eliminate the risk of new outbreaks. Beijing's decisio rely entirely on domestically made vaccines, for example, drew heightened criticism in 20 as the government faced a record caseload, an underimmunized populace, and mass prot against its zero-COVID strategy.

After wealthier countries were well supplied, global cooperation increased. On the sidelin of the 2021 UN General Assembly, Biden announced an ambitious goal to vaccinate 70 percent of the world's population by fall 2022. (Countries fell short of this target.) Additionally, dozens of countries at the World Trade Organization have backed a patent waiver for COVID-19 vaccines to scale up global production, though some countries oppo the idea and negotiations are likely to be slow. With vaccine-makers such as Moderna refusing to share their intellectual property, some lower-income countries are working to develop their own mRNA vaccines with the help of the WHO.

Meanwhile, new strains of the coronavirus, particularly omicron and its subvariants, have raised concerns among scientists and health officials about increased transmission, wanin immunity, and reduced vaccine effectiveness. In response, countries including China and United States have encouraged eligible people to receive booster shots, though WHO and other health officials have emphasized that initial doses for unvaccinated people should b prioritized.

On top of these challenges are the public's concerns about sped-up vaccines and side effe
A 2021 study on COVID-19 vaccine acceptance across twenty-three countries found that o
quarter of those surveyed were vaccine hesitant. "We've not done a really good job of say
'Here's what happens if you get this vaccination and here's what happens if you don't,'" sa
Georges C. Benjamin, executive director of the American Public Health Association. "We'
not married those two stories in a compelling way for a lot of people who are fundament
hesitant."

Recommended Resources

For *Nature*, CFR's Amy Maxmen looks at the radical plan for vaccine equity. With Think Global Health, Maxmen gives a behind-the-scenes look at her reporting on the mRNA vaccine technology transfer hub.

This In Brief explains how to tell when COVID-19 becomes endemic.

In this report, Ginkgo Bioworks' Ryan Morhard outlines how global health security governance can keep pace in the DNA age.

CFR's Thomas J. Bollyky, the Institute for Health Metrics and Evaluation's Olivia Angelino and Joseph L. Dieleman, and Bilkent University's Simon Wigley write in the *Lancet* that trust made the difference for democracies during the COVID-19 crisis.

The WHO breaks down how vaccines protect against dozens of life-threatening diseases.

This timeline looks at major epidemics since the start of the twentieth century.

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