

# Coronavirus disease 2019 and its vaccines: An update

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## Abstract

Coronavirus disease 2019 (COVID-19) is an infectious disease caused by coronavirus. Most of the people infected with the COVID-19 virus will experience mild-to-moderate respiratory illness and recover without requiring special treatment. Older people and those with underlying medical problems are more likely to develop serious illness. In December 2019, a novel coronavirus designated as severe acute respiratory syndrome (SARS) coronavirus 2 emerged in the city of Wuhan, China, and caused an outbreak of unusual viral pneumonia. Being highly transmissible, this novel coronavirus disease, also known as COVID-19, has spread fast all over the world. It has overwhelmingly surpassed SARS and Middle East respiratory syndrome in terms of both the number of infected people and the epidemic areas. Currently, there is no definite treatment for COVID-19 although some drugs are under investigation. Infections caused by these viruses are an enormous global health threat. Hence, the government has established fast-tracking research to develop rapid diagnostic test kits and vaccines at low cost. This review highlights the vaccines available against COVID 19 worldwide and its implications.

**Keywords:** Corona virus, COVID 19, vaccines

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## INTRODUCTION

Coronaviruses are a diverse group of viruses which infect different animals and that they can cause mild-to-severe respiratory infections in humans. The two highly pathogenic coronaviruses with zoonotic origin, severe acute respiratory syndrome coronavirus (SARS-CoV) (2002) and Middle East respiratory syndrome coronavirus (MERS-CoV) (2012), emerged in humans and caused fatal respiratory illness, making emerging coronaviruses a new public health concern in the twenty-first century. In December 2019, a novel coronavirus designated as SARS-CoV-2 emerged in the city of Wuhan, China, and caused an outbreak of unusual viral pneumonia. Being highly transmissible, this novel coronavirus disease, also known as coronavirus

disease 2019 (COVID-19), has spread fast all over the world. It has overwhelmingly surpassed SARS and MERS in terms of both the number of infected people and the epidemic areas.<sup>[1]</sup>

Coronaviruses contain a single-stranded RNA as a nucleic material and its size ranges from 26 to 32 kbs in length. The subgroups of coronaviruses family are alpha (a), beta (b), gamma (c) and delta (d) coronavirus and the International Committee on Taxonomy of Viruses named the virus as SARS-CoV-2 and the disease as COVID-19.<sup>[1]</sup>

In this review, we discuss about the vaccines available worldwide and its implications.

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## VIROLOGY

Coronavirus is an enveloped, positive single-strand RNA virus and it belongs to the Orthocoronavirinae subfamily. It is named as coronavirus because of the characteristic “crown-like” spikes on their surfaces. The exact origin and natural reservoir of the 2019-nCoV remain unclear and it is believed that the virus is zoonotic and bats may be the source of infection because of sequence identity to the bat-CoV. At the beginning of 2019-CoV outbreak, it was reported that person-to-person transmission was limited and a contaminated source from infected or sick wild animals in the wet market may be the common origin. However, more and more evidence came out with outbreaks among family confirmed the possibility of person-to-person transmission. In addition, the involvement of human angiotensin-converting enzyme 2 (ACE2) as the cellular receptor (like SARS) made droplet transmission to the lower respiratory tract possible. Furthermore, contact transmission like SARS is also likely although the survival time in the environment for the 2019-nCoV is not clear at present. Currently, there was no evidence of airborne transmission. Viral RNAs could be found in nasal discharge, sputum and sometimes blood or feces. However, whether oral–fecal transmission can happen has not yet been confirmed. Once people are infected by the 2019-nCoV, it is believed that, like SARS, there is no infectivity until the onset of symptoms. The infectious doses for 2019-nCoV are not clear, but a high viral load of up to 108 copies/mL in patient’s sputum has been reported. The viral load increases initially and still can be detected 12 days after onset of symptoms. Therefore, the infectivity of patients with 2019-nCoV may last for about 2 weeks. However, whether infectious viral particles from patients do exist at the later stage requires validation<sup>[2]</sup> [Figure 1].

## CLINICAL MANIFESTATIONS OF CORONAVIRUS DISEASE 2019

Symptoms usually begin with fever (83%–98%), dry cough (76%–82%), shortness of breath (31%–55%) and fatigue. Multiple systems may be involved, including respiratory (cough, shortness of breath, sore throat, rhinorrhea, hemoptysis and chest pain), gastrointestinal (diarrhea, nausea and vomiting), musculoskeletal (muscle ache) and neurologic (headache or confusion). Conjunctival infection was not reported in the early series and cases with age under 18 years were few. After onset of illness, the symptoms are mild and the median time to first hospital admission is 7.0 days. However, the disease progresses to short of breath (~8 days) and

acute respiratory distress syndrome (ARDS) (~9 days) and to mechanical ventilation (~10.5 days) in about 39% of patients. Patients with fatal disease develop ARDS and worsened in a short period of time and died of multiple organ failure. The 2019-nCoV virus may enter the host through respiratory tract or mucosal surfaces (such as conjunctiva). Oral–fecal transmission has not been confirmed. The virus has a preferential tropism to human airway epithelial cells, and the cellular receptor, like SARS, is ACE2. Theoretically, lungs are the major involved organ.<sup>[2]</sup>

## GENERAL TYPES OF VACCINES

There are a variety of vaccine types that are either currently in use or in development for the prevention of infectious diseases. Under ideal conditions, vaccines should trigger the innate immune system and both arms of the adaptive immune system. However, each vaccine type has both advantages and disadvantages, which can affect the stimulation of the immune system and thus limit the usefulness of the vaccine type.

Live attenuated vaccines against measles, mumps and chickenpox contain laboratory-weakened versions of the original pathogenic agent. Therefore, these vaccines produce a strong cellular and antibody responses and typically produce long-term immunity with only one to two doses of vaccine.

### Subunit vaccines

Recombinant hepatitis B vaccine includes only epitopes (specific parts of antigens to which antibodies or T-cells recognize and bind) that most readily stimulate the immune system. Because these vaccines only use a few specific antigens, this reduces the likelihood of adverse reactions; however, this specificity increases the difficulty of determining which antigens should be included in the vaccine.

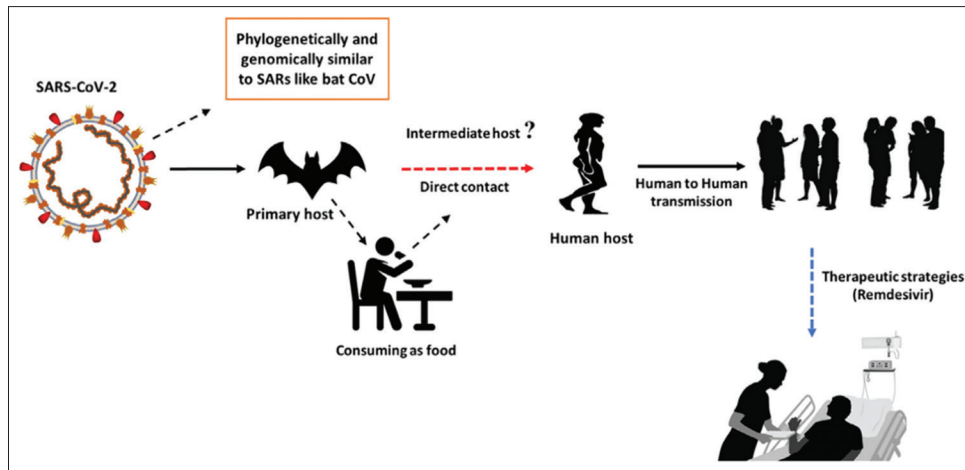
### Toxoid vaccines

Diphtheria and tetanus vaccines are produced by inactivating bacterial toxins with formalin. These toxoids stimulate an immune response against the bacterial toxins.

### Conjugate vaccines

Haemophilus influenzae type B vaccine is a special type of subunit vaccine. In a conjugate vaccine, antigens or toxoids from a microbe are linked to polysaccharides from the outer coating of that microbe to stimulate immunity (especially in infants).

Naked DNA vaccines use DNA specific for microbial antigens to stimulate immunity. This DNA would be administered by injection and then body cells would take



**Figure 1:** Transmission of COVID 19 to humans<sup>[1]</sup>

up the DNA. These body cells would then start producing the antigen and displaying it on their surfaces which would then stimulate the immune system.

Recombinant vector vaccines are experimental vaccines that use either an attenuated virus or microbe to introduce microbial DNA into body cells. These viral vaccines would readily mimic a natural infection, thus stimulating the immune system. Attenuated bacteria could also have genetic material for antigens from a pathogenic microbe inserted. These antigens from the pathogenic microbe would then be displayed on the harmless microbe, thus mimicking the pathogen and stimulating the immune system. Both bacterial and viral-based recombinant vector vaccines for HIV, rabies and measles are in the experimental stages. In addition to these vaccines, there have been studies examining the possibility of improving vaccine adjuvants which would target the innate immune system. These adjuvants would fall into two classes, either delivery systems (such as cationic microparticles) or immune potentiators (such as cytokines or porcine reproductive and respiratory syndrome). The delivery systems would possibly be used to concentrate and display antigens in repetitious patterns, to assist in localizing antigens and immune potentiators and to target the antigens in the vaccine to the antigen-presenting cells. However, the immune potentiators would be used to activate the innate immune system directly.<sup>[3]</sup>

## TYPES OF COVID VACCINES

### Pfizer-BioNTech

It is an mRNA vaccine that codes for the virus's spike protein and is encapsulated in a lipid nanoparticle. Once injected, the cells churn out the spike protein, triggering the body's immune system to recognize the virus. In Phase III trials, it demonstrated 95% efficacy. The Pfizer-BioNTech vaccine requires storage at about  $-94^{\circ}\text{F}$ , which requires

specialized freezers. Lab data suggest "quite effective" against the UK variant as well as the South African and Latin American variants.<sup>[4,5]</sup>

### Moderna

On November 16, 2020, Moderna issued a preliminary data readout of its COVID-19 vaccine, suggesting an efficacy rate of 94.5%. It was authorized by the Food and Drug Administration (FDA) on December 19. Like the Pfizer-BioNTech vaccine, it is an mRNA vaccine. Unlike that vaccine, however, the Moderna vaccine is stable at  $36$  to  $46^{\circ}\text{F}$ , about the temperature of a standard home or medical refrigerator, for up to 30 days and can be stored for up to six months at  $-4^{\circ}\text{F}$ . Lab data suggest "quite effective" against the UK variant as well as the South African and Latin American variants.<sup>[4,6]</sup>

### Sinovac Biotech

On January 13, 2021, China-based Sinovac Biotech reported that its COVID-19 vaccine had a 50.38% efficacy in late-stage clinical trials in Brazil. The company's clinical trials are demonstrating dramatically varying efficacy rates. In Indonesia, a local trial demonstrated an efficacy rate of 65%, but the trial had only 1620 participants. Turkey reported an efficacy rate of 91.25% in December 2020.<sup>[4]</sup>

### Covishield

On November 23, 2020, AstraZeneca and the University of Oxford announced high-level results from an interim analysis of their COVID-19 vaccine, AZD1222. The analysis was from the trials in the UK and Brazil and demonstrated efficacy of up to 70% overall. The vaccine was effective at preventing COVID-19, with no hospitalizations or severe cases in people receiving it. The AstraZeneca vaccine can be stored, transported and handled at normal refrigerated conditions, about  $36^{\circ}\text{F}$ – $46^{\circ}\text{F}$  for at least

six months and administered within existing health-care settings. The AstraZeneca and University of Oxford's vaccine uses technology from an Oxford spinout company, Vaccitech. It deploys a replication-deficient chimpanzee viral vector based on a weakened version of a common cold virus (adenovirus) that causes infections in chimpanzees. It contains the genetic materials of the spike protein. After vaccination, the cells produce the spike protein, stimulating the immune system to attack the SARS-CoV-2 virus.<sup>[4]</sup>

### Russia's sputnik V vaccine

Around November 11, 2020, Russia's National Research Center for Epidemiology and Microbiology claimed that sputnik v vaccine had a efficacy rate of 92% after the second dose. On December 14, 2020, they reported efficacy of 91.4%. Russia's Gamaleya Research Institute appears to be focused on potentially marketing their vaccine worldwide. Even the name of the vaccine has emphasized the idea of a race. The organization has indicated that a dose of the vaccine will cost no more than \$10, about half the cost of the Pfizer vaccine. On February 2, 2021, the lancet published Phase III data demonstrating a 91.6% efficacy against the original strain of the virus.<sup>[4,7]</sup>

### BBIBP-CorV (Sinopharm)

Sinopharm is a Chinese state-owned biotech company based in Beijing. Reuters reported in September that Phase III trials for the Sinopharm shot had been conducted in 10 countries worldwide. The vaccine has been granted authorization in China and several other countries. Once inside the body, given through intramuscular injection, some of the inactivated viruses are engulfed by antigen-presenting cells. The antibodies also attach to viral proteins, such as the spike proteins that populate the viral surface.<sup>[8,9]</sup>

### EpiVacCORONA

On July 24 2020, the Russian Health Ministry authorized vector research center to conduct clinical trial of its vaccine on volunteers. The testing ended on September 30. On October 14, Russian President Vladimir Putin announced that Vector's vaccine had been registered. Furthermore, on November 16, the Health Ministry granted permission for the EpiVacCorona post-registration studies on 150 volunteers aged over 60 years and on November 18 for testing on 3000 volunteers above 18 years of age. The peptide-based vaccine is the second to be licensed for use in Russia.<sup>[10,11]</sup>

### CanSino Biologics

CanSino Biologics vaccine was codeveloped with the Chinese military. It has an efficacy rate of 65.7%

at preventing symptomatic cases. This is based on a multicountry analysis first posted on Twitter by Faisal Sultan, Pakistan's health adviser, on February 8, 2021. The Phase III trial includes 30,000 participants and demonstrated 90.98% efficacy in preventing severe disease. It only requires a single shot. It has agreed to supply 35 million doses to Mexico and is in talks with Malaysia for 3.5 million shots. Pakistan is running one of the largest trials and has contracted for 20 million shots. It is also working with the WHO for approval for the vaccine through the Covax program. It is also planning a trial with Russia to determine if swapping the second dose of Russia's Sputnik V vaccine with CanSino would produce the same or better protection.<sup>[4]</sup>

### Covaxin

Covaxin is a whole virion, inactivated SARS-CoV-2 vaccine, two doses of which have to be administered 28 days apart. The vaccine candidate received Drugs Controller General of India nod for restricted EUA in clinical trial mode in early January. The phase II trials are currently being conducted on 25,800 volunteers aged over 18 years at 25 sites across the country. The company expects the interim efficacy data from the phase II study to be available over the next couple of weeks.<sup>[12]</sup>

### (Sinopharm) Wuhan Institute

Sinopharm's research institute in Wuhan, Central China's Hubei Province on Wednesday said that their inactivated COVID-19 vaccine shows an efficacy of 72.51% after two shots in phase III clinical trials. The institute said on its website that they applied to Chinese drug management authorities for emergency use approval on February 21, which has been officially accepted. Phase III clinical trials on the vaccine kicked off on July 16, 2020, in several countries, such as the United Arab Emirates. So far, data from the trials show that the vaccine can trigger high-titer antibodies in recipients. The neutralizing antibody-positive conversion rate reached 99.06% after two shots, according to the institute.<sup>[13]</sup>

### Johnson and Johnson

Johnson and Johnson announced on November 15 that it initiated a second global Phase III trial of its Janssen COVID-19 vaccine. They expect to enroll up to 60,000 volunteers worldwide. Whereas all of the other three vaccine candidates require two doses about 28 days apart, the J and J vaccine only requires a single dose. Interim results from its Phase I/IIa trial demonstrated a single dose of the vaccine induced a robust immune response and was generally well tolerated. The ENSEMBLE 2 study evaluated a two-dose regimen as well. The

Phase III ENSEMBLE trial demonstrated that the single-shot vaccine is 66% effective overall in preventing moderate-to-severe COVID-19, 28 days after vaccination. However, it demonstrated 100% efficacy and preventing severe disease after day 49. The vaccine uses the company's AdVac technology platform, which it used to develop its approved Ebola vaccine and its Zika, *respiratory syncytial virus* and HIV investigational vaccine candidates. It revolves around the use of an inactivated common cold virus, similar to what the AstraZeneca-University of Oxford program utilizes.<sup>[4,14]</sup>

### CoviVac

The CoviVac shot is administered in two doses, 14 days apart. It is transported and stored at normal fridge temperatures of 2°C–8°C. CoviVac is made of a coronavirus that has been inactivated or stripped of its ability to replicate.<sup>[15]</sup>

### UPCOMING VACCINES (NOVAVAX AND COVOVAX)

#### Novavax

On January 28, 2021, Novavax announced that its COVID-19 vaccine, NVX-CoV2373, hit the primary endpoint with a vaccine efficacy of 89.3% in its Phase III trial in the UK. The vaccine is a protein-based COVID-19 vaccine candidate. It also has data from the South Africa Phase IIb trial and several Phase I, II and III trials. It has demonstrated high clinical efficacy against the UK and South Africa variants as well. The vaccine contains a full-length, prefusion spike protein made using the company's recombinant nanoparticle technology and its proprietary saponin-based Matrix-M adjuvant. It is stable at 2°C–8°C and shipped in a ready-to-use liquid formulation. This vaccine will be available possibly in March or February 2021 in the UK; possibly Q1 2021 or later in the U.S.<sup>[16]</sup>

#### Covovax

Serum institute of India plans to launch new vaccine by June under brand name covovax. It is being developed by American company Novavax. The vaccine was found to be 89.3% effective in a UK trial and was nearly as effective in protecting against the UK variant. It contains a full-length, prefusion spike protein made using their recombinant nanoparticle technology and the company's proprietary saponin-based Matrix-M adjuvant. It is stable at 2°C–8°C (refrigerated) and shipped in ready-to-use liquid formulation<sup>[17]</sup> [Table 1].

### EFFECTIVENESS OF VACCINES AGAINST NEW STRAINS

Of the multiple variants, the three new variants being

tracked are;

- UK strain: The United Kingdom variant spreads more easily and quickly than others. Currently, there is no evidence that it causes more severe illness or increased risk of death
- Brazil strain: The Brazil variant contains more mutations than the UK strain that may affect its ability to be blocked by therapeutic antibodies or a vaccine
- South African strain: The South African variant shares some mutations with the Brazil variant and is a similar threat.

Pfizer vaccine claims to be effective against the UK strains, whereas Moderna is said to be effective against UK and South African strains. Sinovac says that it is effective against the Brazil strain. Sputnik-V also suggests that it will have high efficacy against the UK strain. However, none of the currently available vaccines have claimed their efficacy so far.<sup>[20-22]</sup>

### SIDE EFFECTS OF COVID-19 VACCINE THAT MAY BE A CAUSE FOR CONCERN

The side effects experienced with a vaccine are mild or moderate, last for 2–3 days and can be easily managed. In the case of COVID vaccines, the side effects are a possible reaction to the immune system's natural response against the many spike proteins which are created in the body, when the body identifies a potential threat. Therefore, any chills and pains you experience could be just an indicator of the vaccine training your body to recognize pathogens in the future. Low-intensity muscle pain and joint aches are systematic responses generated when a vaccine is administered in the body. This is also one of the most common side effects experienced by people who have received the vaccine dose right now (reported in over 43% cases).

Headache is also currently the second most commonly recorded symptom with the vaccines being inoculated in India and abroad. The Centers of Disease Control observations also show that the presence of headaches is more common after the second shot.

While a lot of people with COVID-19 experience chronic fatigue and exhaustion, experiencing bouts of fatigue after getting a vaccine shot may also mean that the body is building required protection against the virus. Fatigue can also be accompanied by feelings of chills and minor aches. This is one of the reasons doctors are now advising patients to take ample rest after the vaccine shot. Fatigue could also make some people faint. Hence, people above the age of 55 years should be more careful of this.

**Table 1: Summary of approved vaccines**<sup>[4,15,18,19]</sup>

Name	Vaccine type	Primary developers	Country of origin	Efficacy (%)	Storage (°C)
Comirnaty (BNT 162b2)	mRNA-based vaccine	Pfizer, BioNTech; Fosun Pharma	Multinational	95	-94
Moderna COVID-19 vaccine (mRNA-1273)	mRNA-based vaccine	Moderna, BARDA, NIAID	US	94.5	2-7
Corona vaccine	Inactivated vaccine (formalin with alum adjuvant)	Sinovaccine	China	50.38-91.25	2-8
COVID-19 vaccine AstraZeneca (AZD1222); also known as Covishield	Adenovirus vaccine	BARDA, OWS	UK	70	2-8
Sputnik-V	Nonreplicating viral vector	Gamaleya Research Institute, Acellena Contract Drug Research and Development	Russia	91.6	2-8
BBIBP-Corona vaccine	Inactivated vaccine	Beijing Institute of Biological Products; China National Pharmaceutical Group (Sinopharm)	China	86	2-8
Epi vaccine corona	Peptide vaccine	Federal Budgetary Research Institution State Research CENTER of Virology and Biotechnology	Russia	Not known yet	-70
CONVID icea (Ad5-nCoV)	Recombinant vaccine (adenovirus type 5 vector)	CanSino biologics	China	65.7	2-8
Covaxin	Inactivated vaccine	Bharat Biotech, ICMR	India	70%	2-8
Sinopharm (Wuhan)	Inactivated vaccine	Wuhan Institute of Biological Products; China National Pharmaceutical Group (Sinopharm)	China	72.51	2-8
JNJ-78436735	Nonreplicating viral factor	Jansen Vaccines (Johnson and Johnson)	The Netherlands, US	66	2-8
COVID vaccine	Inactivated vaccine	Chumakov Federal Scientific Center for Research and Development of Immune and Biological Products	Russia	Not known yet	2-8

COVID-19: Coronavirus disease 2019, nCoV: Novel coronavirus, mRNA: Messenger RNA, OWS: Operation warp speed, BARDA: Biomedical advanced research and development authority, ICMR: Indian council of medical research, NIAID: National institute of allergy and infectious disease

According to many, rashes and redness are not the most common side effects but can sometimes take up to a week's time to come up. It could also be more common in the patients who may be suffering from an allergy or might be sensitive to the vaccine's makeup. Swelling, bleeding, delirium or chronic fainting spells should also not be ignored.<sup>[23]</sup>

## CONCLUSION

The COVID-19 viral infection has affected numerous countries worldwide in various walks of life. The loss in economy and livelihood has pushed scientists throughout to work on vaccinations, which can be the only possible hope for eradication of the virus. Vaccines take years to even decades to make. Due to emergency situations, vaccines are being approved and large numbers of people are getting vaccinated at the Stage III Clinical trials phase. Based on the assessment of efficacy so far, Pfizer, Moderna and Sputnik are on top of the list with their efficacy >90%. To conclude, people should opt for vaccines with high efficacy, effective against new strains and less side effects.

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## Conflicts of interest

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