

## COVID-19 VACCINES; A COMPARATIVE ANALYSIS OF THEIR DISTINGUISHING CHARACTERISTICS EFFICACY, EFFECTIVENESS AND ADVERSE EFFECTS

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### ABSTRACT

A virus is a small collection of genetic code, either DNA or RNA, surrounded by a protein coat. A virus cannot replicate alone. Viruses must infect cells and use components of the host cell to make copies of themselves. Often, they kill the host cell in the process and cause damage to the host organism. Antibiotics are ineffective against viruses as viruses do not have a cell wall but are protected by a protein coat. For counter-fight vaccines are taken into consideration in minimizing or reducing the spread of viruses. COVID 19, the highly contagious infectious disease continues to wreak havoc across the world. Like other viruses, COVID 19, cannot be killed or reduced through using antibiotics, only can stop or reduce the severe effects caused by the virus. In this review article, we are going to discuss from Moderna to Sputnik V vaccines used to control the spread of COVID-19. A number of characteristics/features of various types of vaccines available (till date) are discussed in this review article on the basis of their effects which are experienced by a large number of populations.

**KEYWORDS:** COVID-19, mRNA vaccine, Non replicating Viral Vector Vaccine, Inactivated Virus Vaccine.

### INTRODUCTION

#### History of COVID 19

The COVID-19 or SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2), the highly contagious infectious disease, has had a catastrophic effect on the world's demographics resulting in more than 2.9 million deaths worldwide, emerging as the most consequential global health crisis since the era of the influenza pandemic of 1918. It started in Dec 2019, when a person was diagnosed with pneumonia with an unknown cause in Wuhan, China. On 08 Jan 2020, the pathogen causing this outbreak was identified as a novel covid-19. Later in January, the genetic sequence became available to the WHO & public (mn908947.3) and the virus was categorized in the beta coronavirus subfamily. By sequence analysis, the phylogenetic tree revealed a close relationship to SARS virus isolates than to another coronavirus infecting humans, the MERS virus. The outbreak was declared a public health emergency of international concern on 30th Jan 2020. On 12 Feb 2020, the virus was officially named SARS-CoV-2 as WHO officially named the disease as covid-19. In March 2020, the WHO upgraded the status of covid-19 outbreak from epidemic to a pandemic, which is spreading globally at

high speed till date with the discovery of its other variants.<sup>[1]</sup> The pandemic has resulted in the loss of livelihoods due to prolonged shutdowns, which have had a rippling effect on the global economy. Even though substantial progress in clinical research has led to a better understanding of SARS-CoV-2 and the management of COVID-19, limiting the continuing spread of this virus and its variants have become an issue of increasing concern, as SARS-CoV-2 continues to wreak havoc across the world, with many countries enduring a second or third wave of outbreaks of this viral illness attributed mainly due to the emergence of mutant variants of the virus.<sup>[2]</sup>

#### Structure of COVID 19

Structurally coronaviruses are pleomorphic, enveloped viruses with a characteristic fringe of projections composed of S protein on their surface. These viruses are equipped with a positive sense ssRNA genome, which is complexed with the nucleocapsid (N) protein forming helical nucleocapsid. The genome is both capped and polyadenylated.<sup>[5]</sup>

The subfamily *Orthocoronavirinae* of the *Coronaviridae* family (order *Nidovirales*) is classified into four genera of CoVs:

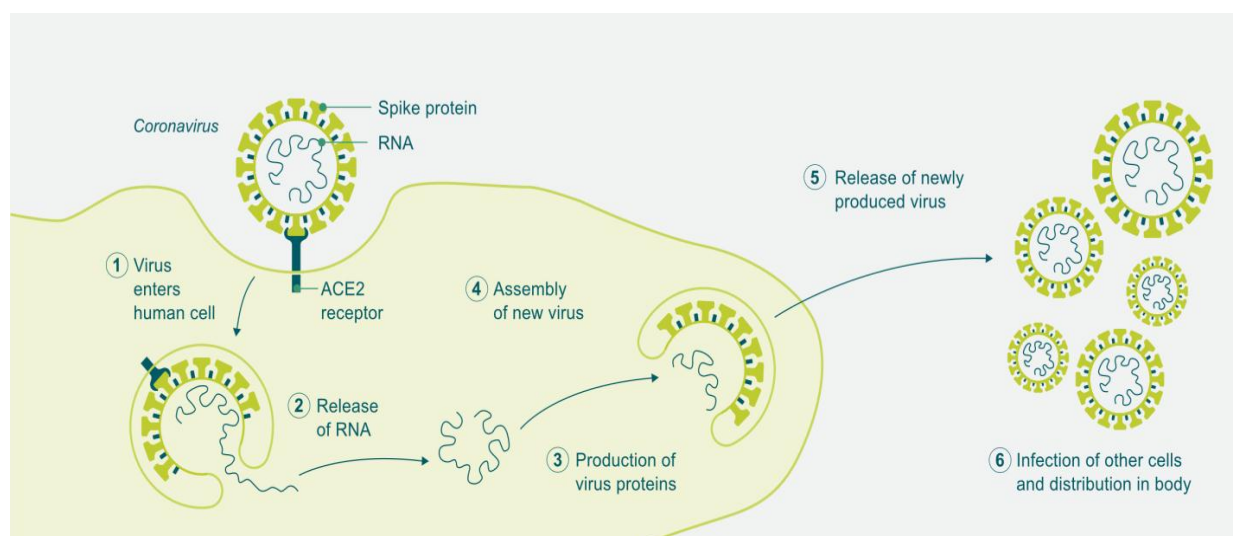
- Alpha coronavirus (alpha CoV)
- Beta coronavirus (beta CoV)
- Delta coronavirus (delta CoV)
- Gamma coronavirus (gamma CoV)

Like other RNA viruses, SARS-CoV-2, while adapting to their new human hosts, is prone to genetic evolution with the development of mutations over time, resulting in mutant variants that may have different characteristics than its ancestral strains. Several variants of SARS-CoV-2 have been described during the course of this pandemic, among which only a few are considered variants of concern (VOCs) by the WHO, given their impact on global public health. Based on the recent epidemiological update by the WHO, as of June 22, 2021, four SARS-CoV-2 VOCs have been identified since the beginning of the pandemic:

- Alpha (B.1.1.7): first variant of concern described in the United Kingdom (UK) in late December 2020
- Beta (B.1.351): first reported in South Africa in December 2020
- Gamma (P.1): first reported in Brazil in early January 2021
- Delta (B.1.617.2): first reported in India in December 2020<sup>2</sup>

### Spreading of Coronavirus inside the host cell

Coronaviruses are a large group of viruses. They consist of a core of genetic material (RNA) surrounded by a lipid envelope with protein spikes. This gives the appearance of a crown. The 'crown' in Latin is known as Corona. There are different types of coronaviruses that cause illness in animals and humans. In humans, coronaviruses can cause respiratory infections that range from the common cold to severe disorders. While coming in contact with the infected person, the coronavirus enters our body through inhalation and directly affects our lung cells. The lung cells contain an ACE II receptor, ACE is a protein inside our body, particularly in the lungs which helps in regulating blood pressure. The virus binds to this ACE II receptor by modifying its cell structure (as shown in Fig 1). The virus enters the cell in a form of a vesicle. Our cell contains lysozyme enzymes that attack the vesicle containing the virus and dissolve the proteins present on the envelope of the virus thereby releasing the RNA into the cytoplasm of our cell. As it is a positive single-stranded RNA, it uses human cell ribosomes to produce various proteins like proteases. It also replicates its own RNA by using an enzyme called RNA-dependent RNA polymerase. Here, the assembly of virus and viral proteins takes place and copies itself inside the cell. At some stage, the cell bursts, and the virus cells are released thereby, infecting other cells of the body.



**Fig1: The process of spreading coronavirus inside the host cell (<https://biontech.de/covid-19-portal/covid-19-disease>).**

### Stopping the spread of the virus through vaccination

There are quite a few ways to reduce the spread of SARS-COV-2 infections, which include social distancing measures, wearing a properly fitted mask, cleaning hands frequently with alcohol-based hand rub or soap and water, and last but not the least getting vaccinated as soon as it's your turn. More than 1, 00,000,000 people are either fully or partially vaccinated in India whereas the rest of the population remains unvaccinated. No antibiotics are effective against

COVID 19 virus, only the vaccines are safe and trusted in minimizing or reducing the infection of this virus amongst the human population. During this tough time, the vaccination is like a ray of light after dark. They are looked upon as a most critical tool to end the pandemic and to save lives and livelihoods. Equitable access to safe and effective vaccines is crucial along with other measures like wearing masks, washing hands, ensuring good ventilation indoors, physical distancing, and avoiding crowds.<sup>[4]</sup>

### Several different types of potential vaccines for COVID-19 are:

- **Inactivated or weakened virus vaccines:** Inactivated vaccines are produced by growing SARS-CoV-2 in cell culture then chemically inactivating the virus. The inactivated virus is often combined with alum or another adjuvant in the vaccine to stimulate an immune response. Inactivated vaccines are typically administered intramuscularly. They require a biosafety level 3 facility for production. Immune responses to a SARS-CoV-2 inactivated vaccine would target not only the spike protein but also other components of the virus.
- **Live attenuated vaccines:** Live attenuated vaccines are produced by developing genetically weakened versions of the wild-type virus; these weakened viruses replicate in the recipient to generate an immune response but do not cause disease. Attenuation can be achieved by modifying the virus genetically or by growing it in adverse conditions so that virulence is lost but immunogenicity is maintained. A live attenuated COVID-19 vaccine would hopefully stimulate both humoral and cellular immunity to multiple components of the whole attenuated virus. Another advantage of live vaccines is that they can be administered intranasally, as with the live attenuated influenza vaccine, which might induce mucosal immune responses at the site of viral entry in the upper respiratory tract. However, safety concerns with live attenuated vaccines include reversion to or recombination with the wild-type virus.
- **Recombinant protein vaccines:** Recombinant protein vaccines are composed of viral proteins that have been expressed in one of the various systems, including insect and mammalian cells, yeast cells, and plants. These vaccines are typically administered intramuscularly. They do not require replication of the live virus, which facilitates the production, although production yields depend on the ability to express the spike protein, which is variable. Recombinant COVID-19 vaccines in development include recombinant spike protein vaccines, recombinant receptor-binding domain vaccines, and virus-like particle (VLP) vaccines.
- **Vector vaccines**

**Replication-incompetent vector vaccines:** Replication-incompetent vector vaccines use a different vector virus that has been engineered to not replicate *in vivo* and to express the viral protein that is the intended immune target. Many replication-incompetent vector vaccine candidates use adenovirus vectors, but other vectors include modified vaccinia Ankara (MVA), human par influenza virus, influenza virus, adeno-associated virus (AAV), and Sendai virus. One drawback to vector vaccines is that pre-existing immunity to the vector can attenuate the immunogenicity of the vaccine. This can be avoided by using viral vectors that are uncommon in

humans, vectors derived from animal viruses, such as a chimpanzee adenovirus, or vectors that do not induce self-immunity, such as AAV. Most SARS-CoV-2 replication-incompetent vector vaccines are administered intramuscularly and are engineered to express the spike protein, with a resultant host immune response to that protein.

**Replication-competent vector vaccines:** Replication-competent vectors are derived from attenuated or vaccine strains of viruses. Using replication-competent vectors often results in a more robust immune response than with replication-incompetent vectors, since they replicate within the vaccinated individual and trigger an innate immune response. Among COVID-19 vaccine candidates, replication-competent vectors have been engineered to express the spike protein in measles vaccine strain vectors, influenza virus-based vectors, vesicular stomatitis virus (VSV)<sup>2</sup> and Newcastle disease virus (NDV). NDV-based vectors propagate to high titers in eggs and could be produced using the global influenza vaccine production pipeline; they could also be given intranasally to stimulate mucosal immunity at the site of viral entry.

**Inactivated virus vector vaccines:** Inactivated virus vectors are engineered to express the target protein but have been inactivated and are thus safer since they cannot replicate, even in the immunocompromised host.

- **DNA vaccines:** DNA vaccines consist of plasmid DNA that contains mammalian expression promoters and the target gene so that the target protein is expressed in the vaccine recipient. Large quantities of stable plasmid DNA can be generated in *Escherichia coli*, which is a major production advantage. However, DNA vaccines are often of low immunogenicity and need special delivery devices, such as electroporators, which limit their use. Further, DNA vaccines must reach the nucleus to be transcribed to messenger RNA (mRNA) so proteins can be generated to stimulate an immune response.
- **RNA vaccines:** RNA vaccines were the first vaccines for SARS-CoV-2 to be produced and represent an entirely new vaccine approach. Once administered, the RNA is translated into the target protein, which is intended to elicit an immune response. The mRNA remains in the cell cytoplasm and does not enter into the nucleus; mRNA vaccines do not interact with or integrate into the recipient's DNA. These vaccines are produced completely *in vitro*, which facilitates production. However, some of the vaccines must be maintained at very low temperatures, complicating storage.<sup>[6]</sup>

Scientific name of the vaccines	mRNA-1273	mRNA-BNT 162b2	AZD1222 (ChAdOx1)	NVX-CoV 2373	JNJ-7843-6735	Corona Vac	BBV152	BBIBP-CorV	Gam-COVID-Vac
Common name	Moderna	Pfizer-BioNTech COVID-19	Covishield vaccine	Novavax (in India under the brand name Covovax)	Johnson & Johnson's Janssen COVID-19 Vaccine	Sinovac COVID-19 vaccine	Covaxin vaccine	Sinopharm COVID-19 vaccine or BIBP vaccine	The Sputnik V vaccine
Manufacturer	Moderna, NIAID	Pfizer, Inc., and BioNTech	<u>AstraZeneca, Serum Institute of India</u>	<u>Novavax and the Coalition for Epidemic Preparedness Innovations (CEPI)</u>	Janssen Pharmaceutical Companies of Johnson & Johnson	<u>Sinovac Biotech</u>	<u>Bharat Biotech</u>	Sinopharm's Beijing Institute of Biological Products.	<u>Gamaleya Research Institute</u>
Country of Origin	Cambridge, Massachusetts	Germany	England	Gaithersburg in the United States	Leiden, Netherlands	China	India	China	Russia.
Manufacturing	Genetically engineered								
Efficacy	94% (95% CI 89-97) after median of 2 months follow-up <sup>6</sup>	In individuals 16 years and older: 95% (95% CI 90-98) after median of 2 months follow-up  91% (95% CI 89-93) after median of 6 months follow-up  In adolescents 12 to 15 years old: 100% (95% CI 75-100)  In children 5 to 11	70% (95% CI 55-81) after median of 2 months follow-up <sup>[6]</sup>	A two-dose regimen of the NVX-CoV2373 vaccine administered to adult participants conferred 89.7% protection against SARS-CoV-2 infection <sup>7</sup>	67% (95% CI 59-73) against moderate to severe COVID-19 after median of 2 months follow-up <sup>[6]</sup>	A large phase 3 trial in Brazil showed that two doses, administered at an interval of 14 days, had an efficacy of 51% against symptomatic	COVAXIN® demonstrated 81% interim efficacy in preventing COVID-19 in those without prior infection after the second dose. <sup>[9]</sup>	A large multi-country Phase 3 trial has shown that 2 doses, administered at an interval of 21 days, have an efficacy of 79%	Sputnik V COVID-19 vaccine shows 97.6% efficacy. <sup>[11]</sup>

		years old: 91% (95% CI 68-98) <sup>[6]</sup>				ic SARS-CoV-2 infection, 100% against severe COVID-19, and 100% against hospitalization starting 14 days after receiving the second dose. <sup>[8]</sup>		against symptomatic SARS-CoV-2 infection 14 or more days after the second dose. Vaccine efficacy against hospitalization was 79%. <sup>[10]</sup>	
<b>FDA Approval</b>	Authorized under EUA	On August 23, 2021, FDA announced the first approval of a COVID-19 vaccine. The vaccine has been known as the Pfizer-BioNTech COVID-19 Vaccine, and will now be marketed as Comirnaty, for the prevention of COVID-19 in individuals 16 years of age and older. <sup>[12]</sup>	WHO EUA qualified	WHO EUA qualified	WHO EUA qualified	WHO EUA qualified	WHO EUA qualified	WHO EUA qualified	Awaited
<b>Targeted Site</b>	Full-length, SARS-CoV-2 spike protein <sup>6</sup>	Full-length, SARS-CoV-2 spike protein <sup>[6]</sup>	Based on a replication-incompetent chimpanzee adenovirus vector that expresses the spike	It is a recombinant protein nanoparticle vaccine composed of trimeric spike glycoproteins and a potent Matrix-M1 adjuvant <sup>6</sup>	Based on a replication-incompetent adenovirus 26 vector that expresses a stabilized	An aluminum hydroxide adjuvant <sup>6</sup>	An aluminum hydroxide and a toll-like receptor agonist adjuvant. <sup>[6]</sup>	Based on two different SARS-CoV-2 isolates from patients	Uses two replication-incompetent adenovirus vectors that express a full-length spike glycoprotein <sup>[6]</sup>

			protein <sup>[6]</sup>		spike protein <sup>[6]</sup>			in China; they each have an aluminum hydroxide adjuvant. HB02 is also known as BBIBP-CorV <sup>[6]</sup>	
Coadministration of COVID-19 vaccines with other vaccines	COVID-19 vaccines may be administered without regard to timing of other vaccines. If multiple vaccines are administered at a single visit, administer each injection in a different injection site. For people ages 11 years and older, the deltoid muscle can be used for more than one intramuscular injection administered at different sites in the muscle. For children ages 5–10 years, if more than two vaccines are injected in a single limb, the vastus lateralis muscle of the anterolateral thigh is the preferred site because of greater muscle mass. This includes simultaneous administration of COVID-19 vaccine and other vaccines on the same day. It is not known if the reactogenicity of COVID-19 vaccines is increased with coadministration, including with other vaccines known to be more reactogenic, such as adjuvanted vaccines. When deciding whether to administer an(other) vaccine(s) with a COVID-19 vaccine, vaccination providers should consider whether the patient is behind or at risk of becoming behind on recommended vaccines, their risk of vaccine-preventable disease (e.g., during an outbreak or occupational exposures), and the reactogenicity profile of the vaccines. <sup>13</sup>								
<b>Routes of Administration</b>	intramuscular injection into the deltoid muscle.								
<b>Vaccine Type</b>	mRNA	<u>mRNA</u>	Non-Replicating Viral Vector	<u>Subunit</u> vaccine	<u>Viral Vector</u>	<u>Inactivated virus COVID-19 vaccine</u>	Inactivated virus COVID-19 vaccine	Inactivated virus COVID-19 vaccine	Non-Replicating Viral Vector
<b>Adverse Effects</b>	Anaphylaxis (approximately 5 per million)  Myocarditis/pericarditis (approximately 16 per million among 16-39 year olds) <sup>6</sup>		Very rare thrombotic complications associated with thrombocytopenia: Cerebral venous	NA	Thrombotic complications associated with thrombocytopenia: For females 30-39 years old: 12.4 cases/million	NA	NA	NA	NA

			<p>sinus thrombosis (169 of <math>\approx</math> 34 million)</p> <p>Splanchnic vein thrombosis (54 of <math>\approx</math> 34 million)</p> <p>Guillain-Barre syndrome (227 cases/51 million)<sup>6</sup></p>		<p>For females 40-49 years old: 9.4 cases/million</p> <p>For females in other age ranges and males: 1.3 to 4.7 cases/million</p> <p>Guillain-Barre syndrome (approximately 8 cases/million)<sup>[6]</sup></p>				
<b>Dosage</b>	<p>Primary series - For individuals 18 years and older: Two 0.5 mL (100 mcg) doses 4 weeks apart<sup>Δ</sup></p> <p>Booster dose<sup>§</sup> - For individuals 18 years or older: One 0.25 mL (50 mcg) dose 6 months following primary</p>	<p>Primary series: For individuals 12 years and older: Two 0.3 mL (30 mcg) doses 3 weeks apart<sup>Δ</sup></p> <p>For individuals 5 to 11 years old: Two 0.1 mL (10 mcg) doses 3 weeks apart<sup>◊</sup></p> <p>Booster dose<sup>§</sup> - For individuals 12 years or older: One 0.3 mL (30 mcg) dose 5 months following primary series<sup>[6]</sup></p>	<p>2 doses: 4 to 12 weeks apart (manufacturer recommendation) 8 to 12 weeks apart (WHO recommendation)<sup>[6]</sup></p>	<p>2 doses (0.5 ml) given intramuscularly. The two doses should be administered with an interval of 3-4 weeks. SAGE recommends that severe and moderately immunocompromised persons should be offered an additional dose of vaccine. This is due to the fact that this group is less likely to respond</p>	<p>Primary series - For individuals 18 years and older: One 0.5 mL (<math>5 \times 10^{10}</math> viral particles) dose</p> <p>Booster dose<sup>§</sup> - For individuals 18 years or older: One 0.5 mL (<math>5 \times 10^{10}</math> viral particles) dose 2 months</p>	<p>2 doses (0.5 ml) given intramuscularly. WHO recommends an interval of 2-4 weeks between the first and second dose. SAGE recommends that a third, additional dose of the</p>	<p>SAGE recommends the use of BBV152 vaccine as 2 doses (0.5 ml) given intramuscularly. The vaccine can be administered with an interval of 4 weeks. It is recommended that all vaccinated individuals receive two</p>	<p>SAGE recommends the use of BIBP vaccine as 2 doses (0.5 ml) given intramuscularly. WHO recommends an interval of 3-4 weeks between the first</p>	<p>2 doses, The second dose should be taken after 21 days / 3 weeks gap of the first dose.<sup>17</sup></p>

	series for individuals 18 years or older <sup>[6]</sup>			adequately to vaccination following a standard primary vaccination series and are at higher risk of severe COVID-19 disease. <sup>[14]</sup>	following primary series <sup>[6]</sup>	Sinovac vaccine be offered to persons aged 60 and above as part of an extension of the primary series. Current data does not indicate the need for an additional dose in persons under 60 years of age <sup>[8]</sup>	doses. <sup>[15]</sup>	and second dose. <sup>[10]</sup>	
<b>Side Effects</b>	<p>In the arm where you got the shot: Pain, Redness, Swelling Throughout the rest of your body: Tiredness, Headache, Muscle pain, Chills, Fever, Nausea These side effects happen within a day or two of getting the vaccine. They are normal signs that your body is building protection and should go away within a few days.<sup>[18]</sup></p>								
<b>Who all are eligible for vaccine</b>	for individuals 18 years of age and older, as a third primary series dose for individuals	for individuals 5 years of age and older, as a third primary series dose for individuals 5 years of age and older who have been determined to have certain kinds of immunocompromise, and as a single	The Covisheild vaccine is recommended for people aged 18 years and older. <sup>[21]</sup>	The Novavax vaccine is recommended for people aged 18 years and older. Vaccination is recommended for people living with conditions that have been	The J&J/Janssen COVID-19 Vaccine is recommended for people 18 years and older. The vaccine is safe and	The sinovac COVID-19 Vaccine is recommended for people 18 years and older. WHO	COVAXIN® has been approved for restricted use in emergency situation in individuals 18 years of age and	The sinopharm COVID-19 Vaccine is recommended for people 18	The Sputnik V COVID-19 Vaccine is recommended for people 18 years and older. <sup>[17]</sup>



	<p>18 years of age and older who have been determined to have certain kinds of immunocompromise, and as a single booster dose for individuals 18 years of age and older at least five months after completing a primary series of the vaccine. The Moderna COVID-19 Vaccine is also authorized for use as a heterologous (or “mix and match”) single booster dose for individuals 18 years of age and older</p>	<p>booster dose for individuals 12 years of age and older at least five months after completing a primary series of the vaccine. The Pfizer-BioNTech COVID-19 Vaccine is also authorized for use as a heterologous (or “mix and match”) single booster dose for individuals 18 years of age and older following completion of primary vaccination with a different available COVID-19 vaccine. For example, Moderna and Janssen COVID-19 vaccine recipients 18 years of age and older may receive a single booster dose of the Pfizer-BioNTech COVID-19 Vaccine.<sup>[20]</sup></p>		<p>identified as increasing the risk of severe COVID-19, including cardiovascular disease, respiratory disease, diabetes, liver disease, obesity and neurodevelopmental and neurodegenerative conditions. the vaccine can be offered to people who have had COVID-19 in the past. WHO recommends the same use of Novavax (NVX-CoV2373) vaccine in breastfeeding and non-breastfeeding women<sup>22</sup></p>	<p>effective in people with known medical conditions associated with increased risk of severe disease, such as hypertension, chronic lung disease, significant cardiac disease, obesity, and diabetes. WHO recommends a second dose of the Janssen Ad26.COV2.S (COVID-19) vaccine for immunocompromised persons aged 18 years and older, given 1–3 months after the first dose in order to increase protection as quickly as possible.</p>	<p>recommends the use of the COVID-19 vaccine Sinovac-CoronaVac in lactating women as in other adults. WHO does not recommend discontinuing breastfeeding after vaccination. Persons living with human immunodeficiency virus (HIV) are at higher risk of severe COVID-19 disease. Such persons were not included in the clinical trials informing</p>	<p>older<sup>15</sup></p>	<p>years and older.<sup>10</sup></p>	
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	following completion of primary vaccination with a different available COVID-19 vaccine. For example, Pfizer-BioNTech COVID-19 Vaccine and Janssen COVID-19 vaccine recipients 18 years of age and older may receive a single booster dose of the Moderna COVID-19 Vaccine. <sup>[19]</sup>				This vaccine can be offered to a breastfeeding woman who is part of a group recommended for the vaccination (e.g. health workers); discontinuing breastfeeding after vaccination is not currently recommended. <sup>[23]</sup>	SAGE’s review, but given this is a non-replicating vaccine, persons living with HIV and part of the recommended group for vaccination may be vaccinated. <sup>[8]</sup>			
<b>Who shouldn’t get the vaccine</b>	<p>If you have had a severe allergic reaction (anaphylaxis) or an immediate allergic reaction, even if it was not severe, to any ingredient in the COVID-19 vaccine (such as polyethylene glycol), you should not get this vaccine.</p> <p>If you had a severe or immediate allergic reaction after getting the first dose of a COVID-19 vaccine, you should not get a second dose of either of this vaccine.</p> <p>Anyone with a body temperature over 38.5°C should postpone vaccination until they no longer have a fever.</p> <p>The vaccine is not recommended for persons younger than 18 years of age pending the results of further studies in that age group.</p>								
<b>Ingredients</b>	Nucleoside modified mRNA encoding the viral spike (S) glycoprotein	Nucleoside modified mRNA encoding the viral spike (S) glycoprotein of SARS-CoV-2, lipids ((4-hydroxybutyl)azanedi	Recombinant, replication-deficient chimpanzee adenovirus vector	Active ingredient (main ingredient) SARS-CoV-2 rS (NVX-CoV2373) Other ingredients (inactive ingredients) •	recombinant, replication-incompetent adenovirus type 26 expressing the SARS-	Inactivated SARS-CoV-2 Virus (CZ02 strain) (the active	6µg of whole-virion inactivated SARSCoV-2 antigen (Strain: NIV-2020-	Active ingredient: inactivated antigen of SARS-CoV-2	The active components are a modified replication-defective <u>adenovirus</u> of a different serotype

	<p>of SARS-CoV-2, lipids (SM-102, polyethylene glycol [PEG] 2000 dimyristoyl glycerol [DMG], cholesterol, and 1,2-distearoyl-sn-glycero-3-phosphocholine [DSPC]), tromethamine, tromethamine hydrochloride, acetic acid, sodium acetate trihydrate, and sucrose<sup>[24]</sup></p>	<p>yl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate), 2 [(polyethylene glycol)-2000]-N,N-ditetradecylacetamide, 1,2-Distearoyl-sn-glycero-3-phosphocholine, and tromethamine hydrochloride, sucrose, and sodium chloride<sup>25</sup></p>	<p>encoding the SARS-CoV-2 Spike (S) glycoprotein. Produced in genetically modified human embryonic kidney (HEK)293 cells<sup>27</sup>. L-Histidine, L-Histidine hydrochloride monohydrate, Magnesium chloride hexahydrate, Polysorbate 80, Ethanol, Sucrose, Sodium chloride, Disodium edetate dihydrate (EDTA), Water for injection.<sup>[26]</sup></p>	<p>Matrix-M adjuvant, which contains: • Quillaja Saponaria saponins fraction A • Quillaja Saponaria saponins fraction C • cholesterol • phosphatidyl choline • monobasic potassium phosphate • potassium chloride • Dibasic sodium phosphate heptahydrate<sup>[28]</sup></p>	<p>CoV-2 spike protein, citric acid 2 monohydrate, trisodium citrate dihydrate, ethanol, 2-hydroxypropyl-β-cyclodextrin (HBCD), polysorbate-80, sodium chloride.<sup>[29]</sup></p>	<p>ingredient). The vaccine does not contain the live COVID-19 virus itself. • Aluminum hydroxide (the adjuvant), • and the following ingredients: • disodium hydrogen phosphate, • sodium dihydrogen phosphate, • sodium chloride • water.<sup>[30]</sup></p>	<p>770), and the other inactive ingredients such as aluminum hydroxide gel (250 µg), TLR 7 /8 agonist (imidazoquinolinone) 15 µg, 2-phenoxyethanol 2.5 mg, and phosphate buffer saline up to 0.5 ml. The vaccine (COVAXIN®) thus has been developed by using inactivated/killed virus<sup>[31]</sup></p>	<p>WIV04 strain. Adjuvant: aluminum hydroxide. Auxiliary materials: sodium chloride, disodium hydrogen phosphate, sodium dihydrogen phosphate<sup>[32]</sup></p>	<p>(Serotype 26 for the first component and serotype 5 for the second), modified to include the protein S-expressing gene of the SARS-CoV-2 virus. The <u>ingredients</u> include Tris-(hydroxymethyl)-aminomethane, Sodium chloride, Sucrose, Magnesium chloride hexahydrate, Disodium EDTA dihydrate, Polysorbate 80, Ethanol, and Water.<sup>[33]</sup></p>
<p><b>Benefits</b></p>	<ul style="list-style-type: none"> <li>• <i>Based on what we know about vaccines for other diseases, experts believe that getting a COVID-19 vaccine may help keep you from getting seriously ill even if you do get COVID-19.</i></li> <li>• <i>COVID-19 vaccines are being carefully evaluated in clinical trials and will be authorized or approved only if they make it substantially less likely you'll get COVID-19.</i></li> <li>• <i>Getting vaccinated may also protect people around you, particularly people at increased risk for severe illness from COVID-19.</i></li> </ul>								

<b>Effectiveness in observational studies when Delta variant prevalent</b>	Symptomatic infection: 85 to 88%  Severe disease/hospitalization: 89 to 96% <sup>[6]</sup>	Symptomatic infection: 41 to 88% Severe disease/hospitalization: 86 to 95% <sup>[6]</sup>	Symptomatic infection: 51 to 96% Severe disease/hospitalization: 60 to 73% <sup>[6]</sup>	NA	Symptomatic infection: 51 to 96%  Severe disease/hospitalization: 60 to 73% <sup>[6]</sup>	NA	NA	NA	NA
<b>Pricing</b>	Rs 2,348 to Rs 2,715 per dose	Rs 1,431 per dose	Rs 200 per dose (for first 100 million doses), Rs 1,000 per dose thereafter at private outlets	Rs 1,114 per dose	Rs 734 per dose	Rs 1,027 per dose	Rs 206 per dose	less than Rs 5,650 per dose	less than Rs 734 per dose

## CONCLUSION

A detail comparison of all the available vaccines is done in the Table 1. However, if we compare at large Moderna and Pfizer BioNTech COVID 19 Vaccine is a genetically engineered mRNA vaccine Every cell in the body uses mRNA to provide real-time instructions to make the proteins necessary to drive all aspects of biology, including human health and disease. These vaccines consist of mRNA which is encapsulated by a lipid bilayer. The mRNA in the vaccine is encoded by a spike protein. The vaccine enters the cell in a form of a vesicle, just like the virus does. A Lysozyme enzyme attacks the vesicle and dissolves the proteins present on the envelope thereby releasing the mRNA into the cytoplasm of our cell. The cell then expresses/targets the full-length, SARS-CoV-2 spike protein and the immune response is generated. Covishield, Janssen and Sputnik V are genetically engineered Non-Replicating Viral Vector vaccines that consist of dsDNA encoding for the spike protein is protected in a safe virus. The infected cell expresses the spike protein which leads to an immune response. Sinovac, Covaxin, and Sinopharm are inactivated virus vaccines. SARS CoV<sub>2</sub> is chemically inactivated (with a chemical called beta propiolactone) so it cannot replicate and all the proteins remain intact. Novavax is a subunit vaccine in which nanoparticles are coated with synthetic spike protein. An additional element called an adjuvant is added which allows to a boost of an immune response.

All the available vaccinations are FDA approved and individuals above 18 years of age are eligible. However, Sputnik V is waiting for its FDA approval and only Pfizer BioNTech COVID 19 is eligible for individuals of 5 years of age.

As far as targeting site is considered, for Moderna and Pfizer BioNTech COVID 19 Vaccine its full length, SARS CoV 2 spike protein is targeted to elicit the immune response. For Covishield, the targeting site is based on a replication-incompetent chimpanzee adenovirus vector that expresses the spike protein, Janssen vaccination uses an adenovirus 26 vector that expresses a stabilized spike protein and Sputnik V uses two replication-incompetent adenovirus vectors that express a full-length spike glycoprotein. Sinovac, Covaxin, and Sinopharm uses an aluminum hydroxide adjuvant for eliciting an immune response. Novavax uses a recombinant protein nanoparticle vaccine composed of trimeric spike glycoprotein and a potent Matrix M1 adjuvant.

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