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Covid-19 Vaccine Developments: A Review

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ABSTRACT: COVID-19 is an RNA virus that belongs to the family Corona viridae and is responsible for the unique SARS-CoV-2 infection. As of 23 September 2022, 771,151,224 confirmed cases of COVID-19, including 6,960,783 deaths, reported to WHO and a total of 13,513,207,331 vaccine doses have been administered. There is no specific therapy available for this disease with different spectra of pathogenicity and prevention by vaccine is the best suggested option. Therefore, research facilities all over the world are working to create an efficient vaccine against this ailment, as this is crucial in lowering mortality rates. Over 200 potential vaccines against COVID-19 have been identified. Currently, testing on humans is being done on almost 52 seeker vaccines. The majority of these vaccine candidates function by encouraging the immune system to target the shaft protein (S)or by blocking the ACE-2 receptor, which helps prevent the entry of the virus into the cells. Merits and drawbacks are associated with the various vaccine development platforms like inactivated whole virus, deficient adenovirus, recombinant protein, and viral RNA that is currently in use. The different vaccine platforms, advocates, and development strategies are discussed alongside the difficulties of developing a vaccine against SARS-CoV-2.

Keywords: Candidate vaccines, ACE-2 receptor, vaccine platforms, SARS-CoV-2.

INTRODUCTION

COVID-19 was shown to be caused by the sarcoma virus of positive sense RNA coronavirus (SARS- CoV-2), a member of the same family as the viruses that cause severe acute respiratory syndrome (SARS) and the Middle East Respiratory Syndrome (Padron-Regalado, 2020; Ortiz- Prado *et al.*, 2020).

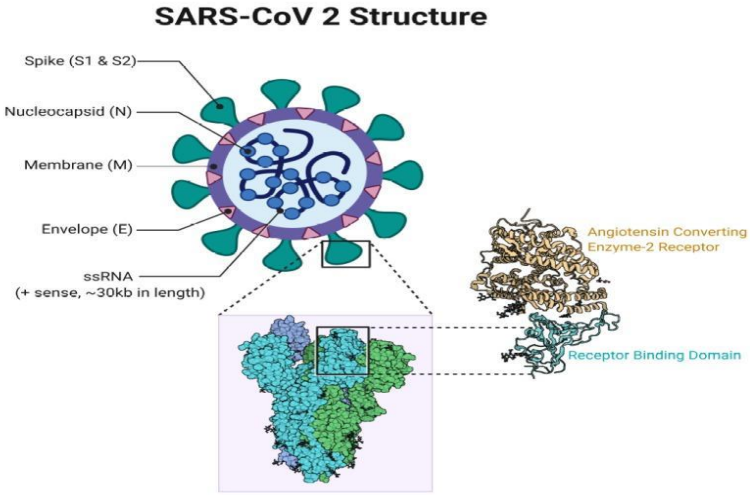
The sudden outbreak of novel Corona Virus COVID-19 creates an alarming situation throughout the world and declared as global pandemic by World Health Organization (WHO) (Tehseen *et al.*, 2021).

It is believed that new antiviral medications, masks, and a highly effective vaccination will be necessary to control the COVID-19 pandemic. Even while it's conceivable to establish herd immunity by obtaining natural immunity via illnesses, doing so would be fraught with equally disastrous mortality risks and effects (Randolph and Barreiro 2020).

In Sweden, for example, officials erroneously believed that infecting up to 60 percent of the population would be enough to cover most of the population in Sweden (Jung *et al.*, 2020). Nonetheless, this was unsuccessful, and the COVID-19 mortality rate in Sweden is at least five times higher than in Germany (Jung *et al.*, 2020). Therefore, creating an efficient vaccine is crucial, as it is the only realistic means of achieving herd immunity. The three main vaccines used in India and Sri Lanka—Covishield, Covaxin, and Sinopharm—show almost identical and extremely high vaccination efficacy against Sars-CoV-2 and delta variants. Studies now being conducted in India demonstrate that the two vaccination doses are ineffective at preventing the omicron variant. But against all COVID-19 types, including omicron, two doses, and a booster dose are quite successful (Fathima *et al.*, 2022).

The four fundamental characteristics of an ideal vaccination are security, immunogenicity, protective effectiveness, and stability. But it's also crucial to consider if the vaccine can be produced commercially (Poulinlu *et al.*, 2021). To develop a vaccine for COVID-19, a critical trimeric envelope glycoprotein (S Protein) produced on the surface of SARS-CoV-2, is the primary target of vaccines due to its ability to interact with host cells. S1 and S2 of the S-protein are responsible for controlling the receptor repertoire and membrane emulsion, respectively, as reported by Tse *et al.* (2020). The S protein undergoes a dramatic conformational change as the viral and cellular membranes are drawn together and fused (Graham, 2020). Evidence of the diversity of coronavirus S proteins can be seen in the fact that SARS CoV and MERS CoV S proteins only share 44 of the inheritable

sequence (Tse *et al.*, 2020). The S1 subunit, comprised of the N-terminal sphere (NTD) and the receptor-binding sphere (RBD), is the primary contributor to the S protein's remarkable diversity. The fact that SARS-CoV and MERS-CoV use different receptors to enter host cells explains the diversity in their RBDs. However, MERS- -CoV uses the dipeptidyl peptidase 4 (DPP4) receptor (Tse *et al.*, 2020; Wrapp *et al.*, 2013), whereas SARS-CoV and SARSCoV-2 use the angiotensin-converting enzyme 2 (ACE2) receptor. Due to the similarity in RBD sequences between the SARS CoV and the SARS CoV-2, monoclonal antibodies against the RBD of the SARS CoV were tested for cross-reactivity to the RBD of the SARS CoV-2. However, no records were found that matched SARS CoV- 2 RBD (Wrapp *et al.*, 2020).



The SARS CoV-2 genome codes for a variety of structural proteins, including those involved in making their "shaft, ""envelope, ""membrane," and "nucleocapsid" (Du *et al.*, 2009). The purpose of COVID-19 seeking vaccines is to prevent infection by preventing the virus from binding to the fatal ACE2 receptor. To do this, the vaccines use viral antigens or genome sequences to create antibodies against the viral shaft protein (S) (In vivo Gen, 2020). Either an attenuated or inactivated whole virus is used to stimulate an immune response against multiple viral antigens in the hopes of producing a heterologous polyclonal immune response. Recent advances have made it possible for several public and international medical regulatory organizations to quickly grant emergency use authorizations (EUAs) for various SARS-CoV-2 vaccination programs since the public was given access to the SARS-CoV-2 genome on January 11, 2020.

According to the World Health Organization's Drought Geography of COVID-19, as of January 5, 2021, 63 seeker vaccinations had completed deadly clinical trials, while more than 172 campaigners were in preclinical research. Of the sixty vaccines for which clinical estimates are available, thirteen market leaders are either in the midst of or planning to launch Phase 3 clinical trials. Several research institutions have used platform technology to create vaccine campaigners. To be among the first to enter Phase 3 clinical trials, candidates must employ cutting-edge strategies like quick deployment, the use of a videlicet nucleic acid platform, the use of non-replicating viral vector systems, the use of inactivated virus, and the use of recombinant subunit vaccines. While downgraded contagion vaccines and other traditional approaches to vaccine development have historically led to successful vaccines against viral conditions (Minor, 2015; Hendriks & Blume 2013), they require extensive cell culturing processes to achieve downgraded strains. SARS-CoV-2 vaccines of the next generation may show they may elicit more powerful and longer memory responses after a single immunization, which would be a significant advance (Jeyanathan *et al.*, 2020).

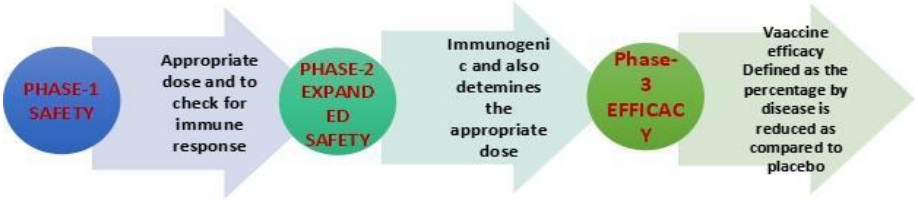
COVID-19 VACCINE DEVELOPMENT

The process of creating a new vaccination has historically been lengthy, often taking 10 to 15 times as long as it should have (Han 2015). The mumps vaccine took around 5 times as long to develop and be licensed for use as any other vaccination. Making a vaccine against COVID-19 within the next 12 to 24 months is, therefore, an extremely difficult task. To identify natural or synthetic antigens that could serve as vaccination candidates, researchers need to do early bench-level tests and utilize computer modeling. In the alternative phase, a beast model, as well as cell-culture or towel-culture systems, are used to test the immunogenicity of the seeker vaccine and its safety for human use. Once efficacy, safety, and immunogenicity have been determined in animals, human clinical trials, which examine these factors in both small and large groups across three stages, can initiate.

Phase 1- Safety Evaluating the vaccine in humans is the initial step in the vaccine development process.

Phase 2- Expanded Safety Phase 2 trials establish the vaccine's safety and immunogenicity and help pinpoint the optimal treatment for use in Phase 3 studies.

Phase 3- Efficacity Here, thousands of people are being vaccinated to determine the vaccine's effectiveness. Vaccine efficacy (VE) is the probability that the vaccinated group will experience fewer complaints than the placebo group (Singh and Mehta 2016).



Sample size considerations are affected by the prevalence of complaints during Phase 3 studies. After the vaccine has been tested on humans and found to be safe and effective, it will be tested on humans. Investigation and approval Regulatory bodies must examine the results of clinical studies before approving a vaccine for general use. The FDA in the USA and the EMA in Europe are two examples of regulatory bodies for pharmaceuticals. Control During Production and After Release to the Market. This is done after the vaccine has been tested for safety and effectiveness in numerous populations and made available to the public. They also document any unintended consequences that may arise from widespread vaccination.

VACCINE DEVELOPMENT STRATEGIES AND PLATFORMS

Although conventional approaches to vaccine development have been shown to be effective against a variety of pathogens, more cutting-edge methods involving recombinant DNA technology are slowly taking their place (Plotkin, 2014). Table 1 lists the benefits and drawbacks of each technique. In spite of this, there are two primary goals that must be met by any vaccine strategy: vaccine safety and the generation of strong adaptive vulnerable responses that provide lifelong protection against multiple pathogen strains with a single vaccine cure.

Table 1.

Vaccine development strategies	Advantage	Disadvantage	Licensed vaccines that use this strategy
Attenuated live pathogen vaccines	In most cases, just one injection is all that's needed to provoke a robust immune response—long-lasting, potentially permanent immune reactions.	Concerns about the health of immunocompromised patients. The difficulty in weakening tensions. Development time. Must be refrigerated.	Varicella, measles, mumps, rotavirus, rubella, and vaccinia, in addition to BCG and oral polio vaccine.
Inactivated pathogen vaccines	Safety because the pathogen has died. Movement and storage.	The pathogen has to be treated in massive numbers. When an antigen is inactivated, its immunogenicity may be diminished. Antibody levels decline with time. Several doses of boosters will be required. Don't make your cells react.	Rabies, Polio, Hep A
Protein Subunit vaccines	Production-line security. Safe for use in patients with compromised immune systems. There is no need to deal with any kind of infectious material.	Antigens of a small size are less likely to be taken up by APCs. Low immunogenicity. Several adjuvants and booster shots are required. Avoid stimulating cell reactions. Verification of antigen integrity is essential. Antigen manufacturing scalability is an obstacle for production.	Human papillomavirus (HPV), hepatitis B and hepatitis C, influenza, acellular pertussis, and other vaccines.
Polysaccharide vaccines	An alternative to immunizations against bacteria and other pathogens whose antigens are mostly polymers.	Increasing the dosage almost never improves the results. Consequently, antibody-mediated effector functions are restricted to only the IgM and IgG2 isotypes. Poor ability to recall information. Poor results with young clients.	Polysaccharide vaccines against Neisseria meningitidis and pneumococcal disease (PPSV or PPV-23) (meningococcal vaccine)
Conjugate vaccines	T-dependent responses are induced, which improves the subpar immunologic responses often seen after receiving a polysaccharide vaccination.	No cellular reactions were observed. Booster and adjuvant doses are required.	Meningococcal conjugate vaccine, pneumococcal conjugate vaccine, streptococcus pneumoniae conjugate vaccine, and typhoid vaccine. Type B influenza virus vaccination
Virus-like particles vaccines	They're safe like subunit vaccinations but just as effective as attenuated ones. The ability to increase production quickly and	The particles might be difficult to form.	HPV, Hep B

	easily is called scalability. Due to their compact size, they can be easily carried by APCs.		
Viral-vectored vaccines	capable of eliciting robust humoral and cellular responses following a single dosing. A high standard of safety.	The immune response can be dampened if the human host already has immunity to the viral vector. It is recommended that certain candidates be kept at 20 °C.	Ebola
Nucleic-acid vaccines	Scalability. Rapid iteration and creation. Extremely safe. Negligible contact with infectious materials is needed. Affects both the humoral and cellular immune systems.	There is not yet a licensed nucleic acid vaccination. DNA vaccines need an alternative method of administration. mRNA vaccines are unstable and should be kept at 20°C.	--

GLOBAL CURRENT VACCINE CANDIDATES

Nucleic acid vaccines mRNA vaccines mRNA-1273(Moderna/ US NIAID)

Only 63 days after the genome sequencing of the virus, clinical trials of the first SARS-CoV-2 vaccine candidate were initiated by the Boston-based company Moderna Rectifiers and the National Institute of Allergy and Infectious Diseases (NIAID). The vaccine consists of a lipid nanoparticle (LNP) vector that enhances uptake by host cells that are vulnerable to SARS-CoV-2 infection and an mRNA patch that contains the instructions for fusing the stabilized prefusion form of the Shaft (S) protein of SARS-CoV-2. Instructing the host cell's recap and restatement ministry to produce the viral antigen, which is then displayed in T lymphocytes and also directly honored by host B lymphocytes, the delivered mRNA initiates an adaptive susceptible reaction towards the virus's S protein. In a press release dated November 18, 2020, Moderna, Inc. reported that the primary efficacy target for its immunization seeker had been met after analyzing the first interim analysis of its Phase 3 clinical study.

BioNTech/ Fosun/ Pfizer A second mRNA-based immunization encoding the SARS-CoV-2 RBD sphere is currently in development by the American pharmaceutical giant Pfizer and the German start-up BioNTech. A vaccine candidate called BNT162 is currently in Phase 3 trials for boosting an inadequate immune response through the use of modified mRNA and a T4 fibritin-deduced trimerization sphere. (Mulligan *et al.,* 2020).

NON-REPLICATING VIRAL VECTOR VACCINES

AstraZeneca/ University of Oxford

The University of Oxford and the British pharmaceutical company AstraZeneca developed a nonreplicating chimpanzee viral vector vaccine formerly known as ChAdOx1 and now known as AZD1222. As part of Operation Warp Speed, the leading candidate, AZD1222, is now completing Phase 3 clinical testing. Studies at Pirbright 2021 showed a robust antibody response in gormandizer mice prior to clinical trials. Results from the Phase 1/2 research were published in the Lancet. Researchers in the UK recruited 1077 healthy actors aged 18 to 55 for a randomized, single-blind study (Folegatti *et al.,* 2020).

Can Sino Biological Inc./ Beijing Institute of Biotechnology. The Ad5 adenovirus is used as a non-replicating viral vector in the CanSino Ad5- nCoV vaccine to deliver the SARSCoV-2 gene into human cells. CanSino has a proven track record of contributing to the development of an Ebola vaccine. Ad5- nCoV vaccine phase 1 trial showed no adverse reactions after 28 days of immunization, according to findings published in the Lancet (Zhu *et al.,* 2020).

Inactivated Vaccines. The Wuhan Biological Products Research Institute Two inactivated vaccines are currently being developed by Sinopharm at its Beijing biological products research centre in conjunction with the Beijing Institute of Biological Products and the Wuhan Institute of Biological Products. Both of these vaccine believers are currently enrolled in advanced studies. Preliminary results from two randomized, blinded Phase 1 and Phase 2 clinical studies conducted by the Wuhan Institute of Biological Products were published in JAMA (Xia *et al*., 2020).

Sinovac. Phase 3 clinical trials have begun on CoronaVac, an inactivated aluminum adjuvant vaccine developed by Sinovac. As of August 2020, all of its Phase 3 studies have been conducted outside of China, in Brazil and Indonesia, according to Clinicaltrials.gov. To meet the demand for its seeker vaccine, Sinovac is increasing production with the goal of delivering 40 million boluses to Indonesia by March 2021 and beginning international distribution in the first half of 2021. CoronaVac/Sinovac allegedly got urgent authorization for restricted usage in China in July.

BBIBP- CorV (Beijing Institute of Biotechnology China National Biotech Group- Sinopharm). An alternative inactivated influenza vaccine was developed as a joint effort between Sinopharm and the Beijing Institute of Biological Products. Inactivation of SARSCoV- 2 strain 19nCoV- CDC- Tan- HB02 by β-propiolactone in a Vero cell 88 replication system adjuvanted with aluminum hydroxide yielded BBIBP-CorV. Aluminum hydroxide stimulates the inflammasome's NLRP3 receptor component and encourages the storage of high levels of IL-1 and IL-18, both of which play a role in escalating the immune system's proinflammatory response (He *et al.,* 2015).

Protein subunit vaccines NVX- CoV2373(Novavax). Maryland- grounded The Beijing Institute of Biological Products and Sinopharm worked together to develop a different inactivated vaccination against the pandemic. Vaccines based on protein subunits typically don't elicit cell-mediated susceptible responses, but the saponin-based Matrix M1 adjuvant can assist (Rajput *et al.,* 2007).

ZF2001(Anhui Zhifei Longcom Biopharmaceutical/ Chinese Academy of Medical lores). Anhui Zhifei Longcom Biopharmaceutical and the Institute of Microbiology of the Chinese Academy of Medical Lores have produced an adjuvanted RBD-dimeric antigen as the most current subunit vaccination candidate to enter Phase 3 clinical testing. China Daily 2020 reported in December that a phase 3 clinical investigation will begin in China and Uzbekistan, with further locations in Indonesia, Pakistan, and Ecuador. (Clinical Trial Identifier NCT04646590 and Registration Number ChiCTR2000040153).

Sanofi Pasteur/ GlaxoSmithKline). The Flu Blok quadrivalent vaccination made by Sanofi was an inspiration for this seeker's layout. To mass-produce the S protein of SARS-CoV2, Sanofi used a baculovirus expression strategy to introduce the immunogen's heritable information into lepidopteran nonentity cells (Cox & Hollister 2009). GSK's squalene-based AS03 (Adjuvant System 3) adjuvant is used in the Pandemrix vaccination for pandemic influenza A. This adjuvant has been utilized successfully in a variety of GSK vaccines (Yin *et al*., 2011; Nikolaos *et al*., 2021).

Virus-like particle vaccine

CoVLP (Medicago). Flyspeck vaccines, also known as contagious disease vaccines, are being developed to merge the potency of suppressed pathogen vaccines with the superior safety profile often obtained by subunit injections. The VLP is sized to be recognized and then taken up by antigen-presenting cells, and its surface is covered with many copies of the target antigen. This sets the way for powerful adaptive responses by facilitating dendritic cells' ability to phagocytose, process, and donate. Medicago, a based company in Quebec, developed the only commercially available SARS-CoV-2 vaccine. The SARS-CoV-2 S-protein prefusion trimeric component is attached to the surface of VLPs produced in the infected tobacco plant, *Nicotiana benthamiana*, and subsequently used for vaccination (Nikolaos *et al.*, 2021).

INDIAN VACCINE CANDIDATES

Covaxin. The first indigenous COVID-19 vaccine, Covaxin, was created through a collaboration between Bharat Biotech and the Indian Council of Medical Research, a government-run organization that provides funding for medical research in India (Thiagarajan, 2021). In June 2020, Covaxin received approval to begin human clinical trials from the DCGI, and by July of that year, the initial testing was complete (Zhang *et al.*, 2020). At 12 different hospitals and medical facilities throughout India, 365 healthy patients participated in Covaxin's phase I trials (Belete, 2021). Some of these included the All-India Institute of Medical Sciences (AIIMS) in New Delhi, the All-India Institute of Medical Sciences (AIIMS) in Patna, and the Post Graduate Institute of Medical Sciences (PGI) in Rohtak. Because the inactivated virus cannot do any harm, this vaccination is safe to use. The SARS-CoV-2 virus's modified protein capsid contains RNA that has undergone some kind of modification that prevents it from reproducing. This approach makes use of the SARS-CoV-2 virus in a fully pathogenic state. The vaccine has 0.5 milliliters of phosphate buffer saline, 2.5 milligrams of TM 2- phenoxyethanol, and 15 grams of TLR7/8 agonist (imidazoquinolinone). It also contains 250 grams of aluminum hydroxide gel as an adjuvant. Multidose vials of the vaccine are shelf-stable between 2 and 6 °C (Gharate *et al.*, 2021). The vaccine is not affected by subzero storage or reconstitution. An increased immune response to the vaccine's antigen is one way in which adjuvants improve the efficacy of vaccinations. When an alkali is added to the product of an aluminum swab, crystalline aluminum oxyhydroxide is formed; this is the basis for the adjuvant used in Covaxin (Liang, *et al.*, 2020).

Covishield. The Serum Institute of India (SII), Pune is working on developing Covishield (ChAdOx1- nCOV or AZD1222), a recombinant, replication-deficient chimpanzee adenovirus vector that encrypts the SARS-CoV-2 S glycoprotein (Singh *et al.*, 2021; Malabadi *et al.*, 2020). Both the United Kingdom and India approved the AZD1222 COVID-19 vaccine on December 30, 2020, and on January 2, 2021, respectively (Voysey *et al*., 2021). SARS-CoV-2 and adenovirus (the virus responsible for the seasonal flu) strains that have been altered genetically and attenuated are included. There are 5 × 1010 ChAdOx1- S (recombinant) contagion patches in a single dose (0.5 ml) of the medication. The vaccine donor formulation contains hAdOx1- S(recombinant), magnesium chloride hexahydrate, L- histidine, L- histidine hydrochloride, disodium edetate dihydrate, sodium chloride, ethanol, sucrose, polysorbate 80, and water for injection. Storage and transit temperatures for vaccines range from 2 to 8 degrees Celsius (Thiagarajan *et al.* 2021; Misra *et al*., 2021). Covaxin and Covishield are two boluses used for immunization; intramuscular injections of Covaxin are recommended every 28 days, while Covishield (0.5 ml in each cure) is administered every 4 to 6 weeks (Misra *et al.*, 2021).

Sputnik V. The Russian Ministry of Health and the Gamaleya Research Institute have developed a non-replicating viral vector vaccine called Sputnik V, and it is currently in phase 3 clinical trials. The Sputnik V anti-SARS-CoV-2 vaccine was developed by the Gamaleya Institute in Moscow and given a license by Russia on August 11, 2020 (Kashte, *et al.*, 2021). An adenoviral vector is used to deliver the antigen, much like Covishield. In addition, a single immunization results in cellular and humoral impunity, while two immunizations result in a double and prolonged vulnerable response. (Jones & Roy 2021). This is a vector vaccine using a combination of rAd types 26 and 5. They both have a full set of SARS-CoV-2 glycoprotein S genes. They are both 21 days apart and administered intramuscular injections. In August 2020, the first and secondary stages of this vaccine's clinical testing in India were finished (Logunov *et al.*, 2021).

Biological E vaccine. India has created a new vaccine called Corbevax, which is a biotechnological E vaccine similar to Novavax. By the end of the horizon, it will have been distributed nationally. This vaccination strategy employs two doses of a protein subunit vaccine

administered at different periods. The Bio-E vaccine, created in India and claimed to be 90% effective against COVID-19 variants, has the potential to be a game-changer in the effort to halt the virus's spread. In India, the Serum Institute of India will manufacture Novavax. They previously produced Covishield (Pagliusi *et al.*, 2020).

ZyCoV- D vaccine. The Ahmedabad-based Zydus-Cadila company developed the ZyCov-D vaccine. Vaccines, Novel Biologicals, NCEs, and Biosimilars were the main topics of study and development. In order to guard against the new coronavirus, a DNA vaccine called zocovirus-D was created that blocks the viral membrane protein that the virus needs to enter human cells. This approach relies on plasmid DNA patches, which are used in inheritable engineering and are tiny, indirect, and extra chromosomal bacterial DNA patches. This is great news for India because it will be the first time a COVID-19 vaccine has been tested in a population of adolescents (12-18). The effectiveness of the intradermal vaccination ZyCoV- D against the virus has been demonstrated in three separate studies separate studies (Sharun & Dhama (2021).

Nasal spray vaccine. The Nasal COVID-19 Vaccine Hyderabad, India's Bharat Biotech is responsible for creating BBV154. No additional immunizations are given through hysterectomy. Nasal immunizations against COVID-19 are more successful than more hyped-up vaccinations in the region where incontinent individuals take vaccines via the nose. After being exposed to the virus, BBV154, when administered as an IV injection, evokes a broad range of immunological responses. Immune reactions at the injection site are essential for halting COVID-19 infection and dissemination i.e., the nose mucosa (Chavda *et al*., 2021).

DISCUSSION

A number of research organizations and pharmaceutical firms across the globe are currently working to develop an effective COVID-19 vaccine. Multiple vaccine candidates using various platforms have been developed, and it now appears that a SARS-CoV-2 vaccine is being rushed into use and approved. On December 2, 2020, the UK granted emergency use approval for the Pfizer/BioNtech vaccine. Since then, emergency use approvals for the Moderna and Oxford/AstraZeneca vaccines have been granted by a number of drug regulatory organizations, and vaccination programs have begun in a number of countries. To keep up with the expanding worldwide demand for vaccinations, massive immunization efforts are needed. It's unprecedented in the annals of vaccine development for pharmaceutical companies to take the chance of ramping up production without knowing whether or not their candidate will gain licensure. This implies that governments have had to establish prioritization schemes ever since the first candidates were approved for widespread usage. Pharma firms and other associated institutions are continually forging new strategic relationships to enhance SARS-CoV-2 vaccine manufacturing sites across the globe and maximize the vaccine's output on a global scale.

An essential deciding element in the broad usage and supply of various platforms is the maintenance of a cold chain for them. Nucleic acid and viral vector platforms may be more difficult to disseminate and use, especially in underserved areas, because of the long-term storage at 70 °C required from manufacture to administration. There is no evidence linking these vaccine candidates to a decreased risk of COVID-19 or SARS-CoV-2 infection. Understanding the specifics of T cell responses that lead to subclinical or mild illness, or antibody titers that afford protection, is essential. In order to protect ourselves against infections and debilitating diseases, it is crucial to understand the factors that correspond with immunity. More study is required to evaluate the duration and strength of immunity provided by each vaccine. Although it is well known that infection by human coronaviruses generates humoral memory cells that last for months to years, there is currently a dearth of long-term data on SARS-CoV-2 immunity. The current clinical studies did not involve vulnerable groups including children, pregnant women, or other vulnerable groups. They won't be able to take part in future, more restricted clinical studies until the first generation of vaccinations has been authorized for use on adults. Properties such as antibody generation, memory cells, and cell-mediated immunity all contribute to a vaccine's effectiveness as given in Table 2 (Swarnali *et al.*, 2022).

Covishield's efficacy was approximately 90% in the third phase of the Indian trial, whereas Covaxin's was only about 80%". The two vaccine formulations developed in India have shown great efficacy against several mutant variants of SARS-CoV-2, however, Covishield's efficacy may be lowered in the future if there are significant changes to the structure of the spike (S) protein. Since Covaxin induces the creation of multiple antibodies against different epitopes, it has the potential to be effective against such variants (Swarnali *et al.*, 2022).

There were 153 vaccines in clinical development and 196 in pre-clinical stages as of April 1st, 2022 (https://www.who.int/publications/m/item/draftlandscape-of-covid-19-candidate-vaccines). Serum Institute of India's Covishield (Oxford/Astra Zeneca formulation), Bharat Biotech's Covaxin (BBV152), Sinopharm's Covilo, Sinovac's CoronaVac, Pfizer/BioNTech's Comirnaty (BNT162b2), Moderna's Spikevax (mRNA-1273), Janssen's Ad26.COV2.S, Oxford/AstraZeneca's, Serum Institute of India: COVOVAX (Novavax formulation), Novavax: Nuvaxovid (NVX-CoV2373) Pfizer/BioNTech: Comirnaty(BNT162b2), are some of the vaccinations that the WHO has authorized for use in emergencies(https://covid19.trackvaccines.org/agency/who/) (Ndwandwe & Wiysonge 2021; Rashedi *et al.*, 2022).

Table 2: Different vaccine candidates and their effectiveness.

Vaccine	Type	Approval	Protection	Age	Dose	Ist Booster and 2nd Booster Dose
Pfizer/BioNTech	mRNA	WHO	95.6%	5 years and up	2	5 months, Pfizer or Moderna 4months Pfizer or Moderna
Moderna	mRNA	WHO FDA EMA	93%Biological Forum – An International Journal (SI-AAEBSSD-2021) 13(3b): 25-30	Adults(FDA) 6 and up(EMA)	2	5 months, Pfizer or Moderna 4months Pfizer or Moderna
Oxford/AstraZeneca	Vector	WHO EMA	76%	Adults	2	4-6 months, Pfizer or Moderna 4months Pfizer or Moderna
Sputnik V	Vector	OTHERS	92%	Adults	2	3 months, Pfizer or 4months4months Pfizer or Moderna
Johnson & Johnson	Vector	WHO FDA EMA	66%	Adults	1	2 months, Pfizer or Moderna, 4months Pfizer or Moderna
Covishield	Vector	WHO	62%	Adults	2	3 months Covishield,TBD
CanSinoBio/Convidecia	Vector	WHO	58%	Adults	1	TBD ,TBD
Sinopharm	Inactivated	WHO	79%	Adults (who) 3 and up (Others)	2	3 months, Sinopharm or, Pfizer 4months Pfizer or Moderna
Coronavac/Sinovac	Inactivated	WHO	51%	Adults (who) 5 and up (Others)	2	Mix and Match, 4 months Pfizer or Moderna
Covaxin	Inactivated	WHO	77.8%	Adults	2	Covaxin TBD
Novavax	Subunit	WHO EMA	90.4%	Adults	2	Novavax TBD

CONCLUSIONS

Since the first SARS-CoV-2 illness case was reported in 2019, more than 230 vaccine candidates are now being developed, with the majority of them already having received Emergency Use Authorizations (EUAs). In an effort to increase the rate at which new vaccines can be introduced to the market, ethical review boards are tightening their approval criteria, and pharmaceutical companies are entering into potentially riskier strategic alliances with vaccine development organizations. The COVAX project and other coalitions have been supported by over 150 countries to ensure equitable distribution and supply. Attempts to restore normalcy have been aided by certain governments' upfront payments for vaccination doses. Many questions remain about COVID-19 immunity, but data from Phase 3 trials should help us draw more definitive conclusions about the factors that predict safety from infection with COVID-19 and about various vaccine candidates. There are likely to be a number of different vaccine candidates using a variety of vaccine delivery methods needed to combat the COVID-19 pandemic. More vaccines that have been given the green light means more vaccine doses may be manufactured in less time, which might be used to vaccinate a large population. However, different vaccine platforms will produce vaccine candidates for varying degrees of defense against populations with altered immune responses, such as kids, pregnant women, people with co-morbidities, and people who are immunosenescent (those whose immune systems have lost the capacity to function properly after the age of 65). Clinical studies helped verify the vaccines' effectiveness and determine the extent to which they protected against COVID-19.

CURRENT PERSPECTIVE OF WHO

The COVID-19 vaccination should be available to everyone, everywhere. The COVID-19 vaccine response has made significant progress, and it is crucial to keep making it, especially for individuals who are most at risk of acquiring the disease.

WHO recommends a simplified single-dose regime for primary immunization for most COVID-19 vaccines which would improve acceptance and uptake and provide adequate protection at a time when most people have had at least one prior infection. Available data suggest the monovalent Omicron XBB vaccines provide modestly enhanced protection compared to bivalent variant-containing vaccines and monovalent index virus vaccines.

When monovalent XBB vaccines are not available, any available WHO emergency-use listed or prequalified vaccine, bivalent variant-containing or monovalent index virus vaccines, may be used since they continue to provide benefits against severe disease in high-risk groups.

The Strategic Advisory Group of Experts on Immunization (SAGE) is charged with advising WHO on overall global policies and strategies, ranging from vaccines and technology, research and development, to delivery of immunization and its linkages with other health interventions. SAGE is also responsible for the COVID-19 vaccine interim recommendations.

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