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REVIEW ARTICLE

Future health policy perspectives for COVID-19 infection

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ABSTRACT
COVID-19 is a global public health disaster, a pandemic that is spreading and worsening at frightening rates. Existing broad-spectrum antiviral medicines, previously utilized medications, and antibiotic combinations were employed to treat symptoms. Vaccines were manufactured on a war footing all across the world, and vaccination campaigns began in various countries in 2021. Vaccination is the most effective strategy to prevent illness and severity related to COVID-19. Nonetheless, many people, particularly in undeveloped and underdeveloped nations, still lack access to even the first dose of vaccine. This article provides an overview of the types of WHO-approved vaccines, the many types of SARS-CoV-2, and how effectively vaccines perform. We also examined the success and failure of vaccination programs in major countries, where vaccination and administration have become new challenges for governments. Several factors contribute to the success of vaccination programs, including novel variants, differences, storage, transportation, acceptance and attitude differences between races, and limits in children. We also looked at WHO's COVID-19 response strategy for 2021 and 2022. With a discussion on a global COVID-19 Vaccination Plan, this article aims to contribute to the ongoing discourse, offering perspectives that could shape future health policies and potentially save millions of lives worldwide.
Keywords: *COVID-19; vaccines; subunit vaccines, mRNA-based vaccines, Virus-like particles.*

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INTRODUCTION

The coronavirus-2, often known as severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), is a positive-sense, and single-stranded RNA virus that is highly infectious. It is rapidly spreading around the world. The infection that is caused by this is known as coronavirus disease 2019 (COVID-19), and it can cause a variety of symptoms, including a cough, fever, chest pain, and even respiratory distress syndrome in extreme cases[1, 2]. Vaccines that are both efficient and secure are absolutely necessary in order to put a stop to the COVID-19 epidemic[3, 4]. Earlier research has revealed the progress that has been made in the development of vaccines against SARS-CoV and Middle East respiratory syndrome coronavirus (MERS-CoV)[5-7]. The preclinical findings of these candidate vaccines helped to save some time in the development of the SARS-CoV-2 vaccines that are already in the market and would provide platforms for the potential widespread use of SARS-CoV-2 vaccines in the future. Inactivated vaccines live attenuated vaccines, vector vaccines, RNA vaccines, DNA vaccines, protein subunit vaccines, and virus-like particle (VLP) vaccines are the different types of COVID-19 vaccines that are categorized by the World Health Organization (WHO) as having been analyzed or approved for clinical trials. This article provides a concise overview of the global response to COVID-19 immunization, covering topics such as the WHO-approved vaccinations available, the appearance of SARS-CoV-2 variations, and the efficacy of the available vaccines. It examines the WHO's strategy for combating COVID-19 and emphasizes the successes and challenges seen by different nations in their vaccination programs. Last but not least, it lays forth a plan for a nationwide vaccination campaign against COVID-19 that could save millions of lives around the world.

Approaches for COVID-19 vaccines

Vaccines are made utilizing a complete virus or bacteria, genetic material, and a microbe that induces an immune response. Live and non-live vaccines were the only types previously. Nowadays, nucleic acid-based DNA and RNA vaccines, viral vectors, etc.[8]. Living vaccinations multiply enough to boost the immune system but not enough to induce disease. Adjuvants are usually added to non-live vaccinations to boost immune response. Recently licensed adjuvants include oil-in-water emulsions and liposome-based adjuvants[9]. The entire virus, Spike (S), Nucleocapsid (N), and Membrane (M) proteins are vaccine candidates. COVID-19 vaccines are intramuscular, causing a systemic response (i.e., the antibodies are generated in blood and circulate to all body organs). COVID-19 intranasal vaccinations are promising, along with intramuscular ones. A variety of approaches is used for COVID-19 vaccine development.

Vaccines approved by WHO

Efforts in the COVID-19 vaccine program are precedented and led to several breakthroughs. Intense R&D activity worldwide has led to the development of more than 200 vaccines on diverse platforms including inactivated viruses, live attenuated viruses, recombinant proteins, viral vectors, peptides, and nucleic acids (DNA & RNA). There are several vaccines in the world market which has got emergency use authorization (EUA) from different countries and WHO has given emergency use approval to 11 vaccines, while others are under review process. Among these vaccines, only the BioNTech Pfizer vaccine is approved for the age group 12 years and above[10]. Various WHO EUA-approved COVID-19 vaccines and their development platforms are summarized in Table 1.

SARS CoV-2 variants and vaccine effectiveness

Virus mutagenesis is causing SARS-CoV-2 to evolve quickly, expanding the pandemic and endangering public health. Despite the fact that CoV NSP14 acts as a 3′-5′ exoribonuclease, SARS-CoV-2 spreads swiftly over the world, resulting in increasing mutations in the viral genome[11, 12]. In most cases, virus variations have no effect on virus function. Some SARS-CoV-2 variants, particularly those in the spike protein, have gained attention due to their effect on ACE2 binding, TMPRSS2 cleavage, or evasion of immunity, altering transmissibility, antigenicity, morbidity, clinical symptoms, and implications, or decreasing responses to potential treatments[13]. The variants were classified as variants of concern (VOCs) and variants of interest (VOIs). VOCs are SARS-CoV-2 variations having changed phenotypic traits, such as greater transmissibility or virulence, the capacity to circumvent an immune response caused by spontaneous infection or vaccination, or the ability to avoid neutralization by monoclonal antibodies. VOIs are variants that have been found in many countries and have mutations with phenotypic consequences[14]. The WHO designated and monitored these variants (Figure 1). To better understand VOCs and VOIs, consider the following characteristics: They speed up transmission, they are invisible to conventional diagnostic techniques, the severity of clinical symptoms worsens; It is possible to overcome both innate immunity and vaccine-induced immunity, and therapies have a lower likelihood of working. Until August 2021, four VOCs (Alpha to Delta) and six VOIs (Epsilon to Lambda) were detected. WHO recognized a novel SARS-CoV-2 variant as Mu and classed it as VOI on August 30, 2021[14]. The variant categorization system was changed in September 2021 and categorized as VOCs (Alpha to Delta), VOIs (Lambda and Mu), and Variants Under Monitoring (VUM). When compared to the native Wuhan strain, all of these strains have demonstrated genetic change inside the Spike (S) gene[15]. The bulk of vaccinations generated are used to treat the early strain of the virus that spreads globally. As a result, a few vaccines proved to be less efficient in guarding against newly generated SARS-CoV-2 virus strains. However, according to the US FDA (Food and Drug Administration), all FDA-approved vaccinations remained effective against the circulating SARS-CoV-2 strains until February 2021. Currently, available vaccines are intended to stimulate neutralizing antibodies against the Spike (S) protein in the wild-type SARS-CoV-2 strain. COVID-19 protection is strongly linked to antibodies against the S protein[16]. Neutralizing antibodies against the wild-type S protein strain may not recognize the mutant S protein, reducing vaccine effectiveness. Variations that can re-infect, circumventing immunity, can overwhelm healthcare systems, as witnessed in Brazil in the fourth quarter of 2020. These variances may affect emergency therapeutic and prophylactic mAb therapies. The Alpha N501Y change does not appear to impair serum neutralizing capacity after immunization[17, 18]. Muik and colleagues conducted the investigation with sera from 16 volunteers who received the mRNA-based Pfizer-BioNTech vaccine (BNT162b2) against the original strain and the pseudovirus S only portion of Alpha [19]. Sera neutralized both the Alpha S protein and the wild-type virus equally well in this investigation. The 69-70 deletion has been associated to lower neutralization by SARS-CoV-2 human convalescent serum generated from convalescent people and viral escape in immune-compromised persons[20]. Alpha can still be neutralized by convalescent and vaccination serum, albeit to a lesser extent[21-23]. A post-hoc study of the protein-based Novavax (NVX-CoV2373) safety and efficacy trial found that the vaccine was 86.3 percent

effective against the virus's Alpha form[24]. As a result, past infection or immunization against the wild-type virus still protects against the Alpha version. Wang and colleagues, on the other hand, have shown that the mAbs currently used to treat Alpha NTD may be ineffective [21]. Numerous in vitro laboratory experiments have found the E484K alteration in S protein as a way to avoid neutralization by both convalescent serum and monoclonal antibodies [15, 25]. Both the Beta and Gamma versions, as expected, are resistant to neutralization by both convalescent serum and antibodies from COVID-19 vaccines[21]. In neutralization studies using sera from AstraZeneca (AZD1222/ChAdOx1) vaccine recipients, activity levels against the Beta version were undetectable, resulting in immunological escape [26]. Serum from recipients who received the Moderna (mRNA-1273), Pfizer-BioNTech (BNT162b2), and Sinopharm (BBIBP-CorV) vaccinations had significantly lower levels of neutralization of the Beta version[27]. Covaxin (BBV152), an inactivated virus-based vaccination, likewise had a lower neutralizing antibody titre when compared to D614G[28]. Despite being at a lower level than Alpha or D614G, data from the Novavax (NVX-CoV2373) trial show that the vaccination still protects successfully against the Beta variant (60%)[29]. When only the E484K alteration was present in the virus, serum neutralization dropped considerably (2.8-fold) compared to viruses carrying all of the Beta changes, which decreased dramatically (8.6-fold)[22]. Pfizer-BioNTech (BNT162b2) and Moderna (mRNA-1273) vaccines revealed 6.7- and 4.5-fold declines in activity in gamma variant effectiveness and viral neutralization experiments, respectively[27]. While Gamma variations are comparable to Beta variants in several ways, they are less resistant to neutralization[30]. Certain neutralizing antibodies, including the currently used therapeutic mAb, Bamlanivimab, have been shown to be resistant to the Delta variant in studies[31]. The Delta variant's L452R alteration is discovered in a region of the RBD known to be resistant to mAbs [32]. Planas and colleagues also investigated the effect of serum from people who had received the Pfizer-BioNTech (BNT162b2) and AstraZeneca (AZD1222/ChAdOx1) vaccines on the Delta variant. Serum from people who had only received one dosage of the vaccine scarcely suppressed the virus [31]. The Delta variation has continued to mutate and acquire new problematic mutations, such as the K417N substitution discovered in the Beta version. The Omicron VOC contains twice as many mutations as the Delta VOC [33], raising concerns that this variant may impair the efficacy of current vaccinations and monoclonal antibody treatments. Pulliam and colleagues conducted a retrospective study of epidemiological data and discovered that the Omicron variation is related with a greater ability to circumvent immunity from earlier SARS-CoV-2 infection[34]. According to computational projections, the structural alterations may reduce antibody interaction but not totally avoid neutralizing antibodies [35]. BNT162b2 (Pfizer-BioNTech) preliminary data show that a third dosage of the BNT162b2 vaccine neutralizes the Omicron form, whereas just two doses have a much lower neutralization titer. When compared to merely two doses, three doses boosted the neutralization titer by 25-fold[36]. Similarly, In South Africa, plasma from BNT162b2 vaccinated individuals was reduced 41-fold against the Omicron variant, while prior infection and vaccination boosted neutralization. Since the Omicron variant's amino acid modifications do not modify the S protein's CD8+ T-lymphocyte epitopes, two doses may protect against severe illness. In vitro, Omicron showed greater immunological escape than Beta, although it was still protected by past SARS-CoV-2 infection and vaccination[37].

Correlation between SARS-CoV-2 infection & Immunity

The surface of SARS-CoV-2 consists of a ton of spike-like projections[38, 39] that, when viewed under an electron microscope, resemble a solar corona, from which they derive their name. The spike glycoprotein of SARS-CoV-2 consists of two subunits, S1 and S2, which are divided by a furin cleavage site (PRRAR). This site modulates the sugar spike's fusogenic activity. SARS-CoV-2 attaches to host cells via the receptor-binding domain (RBD) and N-terminal domain (NTD) of the S1 subunit, while SARS-COV-2 fuses to host cell membranes via the S2 subunit[40-42]. There are three major types of adaptive immune responses triggered by spike glycoproteins on enveloped viruses. These types of cells include B cells (humoral immunity), CD4+ and CD8+ T cells (cell-mediated immunity) [43, 44]. Antigen-specific antibodies are produced by activated B cells in response to viral infection. The virus has also developed immune escape strategies, including antigenic shielding by adding complex glycans[45, 46], secreting truncated viral glycoproteins for subverting the immune response[47], preventing complement activation and neutralization. In contrast, activated B cells from secondary lymphoid organs produce antigen-binding memory B cells that undergo population expansion, somatic hypermutation, and selection for improved antigen binding. Virus variants and other pathogens are regularly protected by these evolutionary strategies[48-50].

Seroprevalence, natural infection and vaccination

Infectious disorders, such as COVID-19, have an indirect impact on the economic, political, and social sectors in addition to directly harming health systems. Natural immunity[51, 52] and vaccine-induced immunity [53-55] can both lower mortality/ morbidities, but appropriate management is still being

debated. UNITY Studies and partners issued a preprint in December 2021 as part of the greatest significant meta-analysis ever undertaken on SARS-CoV-2 seroprevalence studies. The meta-analysis includes 92 countries, including 53 low- and middle-income countries and nearly half of the countries included by the COVID-19 Global Humanitarian Response Plan[56]. The meta-analysis revealed several noteworthy conclusions, including:

- In April 2021, 26% of the world's population had SARS-CoV-2 antibodies, indicating that the great majority were still susceptible to infection.
- SARS-CoV-2 seroprevalence ranged from 0.3% in WHO's Western Pacific Region to 57% in high-income Americas countries.
- Infants under nine and seniors over sixty had lower seroprevalence than adults aged 20 to 29.
- According to projections of seroprevalence to confirmed cases in the third quarter of 2020, COVID-19 surveillance and reporting in low-income countries grossly understates infection and immunity.

A variety of aspects of natural and vaccine-induced immunity to COVID-19 are being studied, including antibody type, cellular type, relapse after infections and/or vaccinations, immuno-logical memory, reinfection frequency and severity, comparison of vaccination and unvaccinated populations in terms of immunity developed, and potential adverse effects of vaccination. In 2020, COVID-19 natural immunity trials indicated different duration lasting immunity[57-59]. Antibodies had been present for 8 months throughout the first half of 2021[60, 61]. Two investigations including COVID-19 patients were conducted until September 2021 to describe long-term humoral and cellular immunity following the initial SARS-CoV-2 infection. Over a year following infection, SARS-CoV-2-specific T cells and antibodies were discovered[62, 63]. Other authors have emphasized the survival of neutralizing antibodies one year after SARS-CoV-2 infection in people through the end of 2021[64]. Spikes (S), membranes (M), envelopes (E), and nucleocapsids (N) are the four structural proteins found in this virus (N). According to the research, S and N proteins are the most immunogenic. Protein S appears to particularly generate a "protective" host cellular/ humoral immune response. This is because protein S stimulates the generation of neutralizing antibodies (nAbs), which are essential for virus pathogenicity. Most investigations with follow-ups after healing discovered protective antibodies and memory B cells, and their presence was even more prolonged with extended observation intervals. According to a Swedish study, those who did not receive further immunizations were 95% protected from infection and hospitalization after spontaneous infection for up to 20 months[65]. The cellular response is initiated and stays active even in the absence of an antibody response, according to biochemical and immunological findings. SARS-CoV-2 recovery has been shown to produce T CD4+ and CD8+ cells up to 18 months after infection. Natural immunity degraded faster than vaccine-induced immunity (post-COVID-19), but the latter is the sole type of immunity stimulated by cross-reactivity against additional infections[66].

Vaccination strategy adopted by different countries

The COVID-19 pandemic has not only created a global health crisis, but has also changed the lives of people around the world[67]. Within a year of COVID-19 being declared a pandemic, many COVID-19 vaccines were developed and approved for emergency use[67-70]. Developed and high-income countries have strategically monitored the vaccination of their citizens. However, a major problem for developed countries has been the adoption of vaccines against COVID-19 and the resulting population distribution. As far as vaccinations are concerned, priority must be given to the most clinically vulnerable people, in line with the WHO roadmap for Prioritization [71]. Fluctuating and unpredictable vaccine supplies have been a major obstacle to planning and preparing large-scale vaccination programs. In many countries, it has not been worth the effort because vaccine supplies are unpredictable due to high demand than production. One of the problems throughout the pandemic was people's lack of belief in the vaccines[72]. According to the Centers for Disease Control and Prevention (CDC), vaccine confidence is the conviction that vaccines are effective, safe, and an essential component of a healthy healthcare system. People won't take steps toward getting themselves or their children vaccinated if they lack some amount of confidence. The professionals, teachers, and others had shared their vaccination experiences on social media and/or through schools. Children, teenagers, parents, and guardians have seen an increase in vaccine confidence because of the schools and childcare facilities. In order to boost vaccine confidence and uptake, evidence-based methods were adopted nationally in the USA[73-75]. Furthermore, vaccines used in vaccination programs during the pandemic were poorly regulated and were not properly validated and tested for QC[76-78] (Figure 2). Regulators have struggled to provide clear and timely guidance on using tools to ensure a rapid and flexible pandemic response[67]. There have been a number of adverse reactions to vaccination around the world[79-85]. Many countries did not have adequate surveillance for such side effects as well[86]. Vaccine safety monitoring and prompt regulatory action are essential to protect public health. If a vaccine is found unsafe then the vaccination in the community is to be paused immediately[87]. In Japan, the strategy for

monitoring the safety of COVID-19 vaccines by the Ministry of Health, Labor and Welfare, and the Pharmaceutical and Medical Devices Agency is evaluated to be working well[84]. In 2021, the Japanese Joint Council reviewed thrombosis, pericarditis, myocarditis, anaphylaxis, thrombocytopenia syndrome, and death. Such monitoring of the adverse effects of vaccines resulted in the appropriate regulatory actions in terms of revision of package inserts with warnings about their adverse effects. Japan's experiences could serve as a lesson for other nations with low vaccination rates, and they could also serve as a catalyst for worldwide discussions on better COVID-19 vaccine safety monitoring[84]. Many reports from different countries suggested that mRNA vaccines may increase the risk of myocarditis and pericarditis in younger men[79-84]. On October 15, 2021, the Japanese joint committee found that mRNA vaccines, specifically mRNA-1273, put men in their teens and early 20s at risk for pericarditis and myocarditis. Myocarditis and pericarditis were included in the list of clinically severe adverse reactions under "ADVERSE REACTION" in future updates to mRNA-1273 and BNT162b2 vaccination package inserts on December 3, 2021[88, 89]. Medical personnel in Japan report unfavorable events voluntarily. This lets governments quickly examine, share, and analyze COVID-19 vaccination safety. Many developed countries actively monitor signals using massive computerized medical databases (including immunization data) in addition to volunteer reporting mechanisms[84].

Vaccination in under-developed countries

It's amazing that so many effective COVID-19 vaccines were created in less than a year. Global population protection depends on vaccine dosages and government immunization programs. Vaccination, not vaccinations, saves lives, the adage goes. By February, Israel had vaccinated 50% of its population, leading several high-income countries (HICs)[90]. The WHO, the Global Alliance for Vaccine Access (Gavi), and the Coalition for Epidemic Preparedness Innovations lead the COVAX (COVID-19 Vaccines Global Access) Facility, which assists a large number of low- and middle-income countries (LMICs). As part of its efforts to achieve its goal of providing equal access to COVID-19 vaccines, COVAX has been making use of donor funds in its advanced market commitments. In some of these low- and middle-income countries, vaccination campaigns have already begun [91]. Vaccines have been shipped from the COVAX facility to more than 150 different countries as of this moment; however, distribution is still restricted due to production and supply limitations. In addition, the African Union has begun distributing vaccines to the continent's 54 member states by establishing the Africa CDC Vaccines Platform (AVATT)[92]. The vaccination against COVID-19 has proven difficult in a number of HICs. Challenges such as vaccine skepticism and a lack of available doses have been foreseen, and various solutions such as demographic group prioritizing and mass media interventions have been presented as viable remedies [93, 94]. These initiatives may have improved vaccination uptake and efficiency, but they have not solved all difficulties. HICs commencing the vaccination process have raised new administrative challenges and suggested new approaches to overcome supply constraints, such as increasing the period between vaccine doses[93, 95]. Low-resource countries struggle to distribute COVID-19 vaccines. These countries have weak healthcare infrastructure and few vaccines and medical resources, making immunization distribution and administration problematic. The latest research on COVID-19 vaccine introduction in LMICs demonstrated challenges to herd immunity. HICs buy most vaccinations, including unmade ones [96, 97]. Both studies stressed that low- and middle-income countries are unable to afford the price of COVID-19 vaccines for their populations[98, 99]. Recent findings from the study indicate that one of the most significant barriers is the poor manufacturing of vaccines[100]. The elderly, educated, rural, or semi-urban people were more likely to refuse or delay getting vaccinated[101]. According to the results of a poll done in Ghana on a total of 2,734 people living in all sixteen regions of the country, 82.8% were eager to receive the COVID-19 vaccine, while 9.7% were cautious. Fear of unfavorable side effects, confusion about vaccinations, a lack of information, and a lack of trust in both the government and pharmaceutical companies are among the most common reasons for hesitating[102]. Vaccine adoption was found to be associated with social norms, perceived risk of COVID-19, trust in the efficacy of vaccines, perceived safety of vaccines, and supposed availability of vaccines in a study conducted in five LMICs, including Bangladesh[103].

Roadmap by WHO to combat SARS CoV-2

WHO has developed a strategic plan to guide the global response to the COVID-19 pandemic[104]. This plan, which was updated in 2021, includes a roadmap that lays out a series of actions to be taken by WHO and its partners to control the outbreak and eventually bring it to an end. The WHO issued recommendation according to the SARS CoV2 time to time. WHO proposal includes several main components: Surveillance and response are the first steps, which include identifying, investigating, and responding to cases and outbreaks, as well as building health systems to detect, investigate, and respond to epidemics. Laboratory testing comes next: This includes increasing the availability of diagnostic testing, assisting in the development of novel tests, and providing guidance on the right use of tests. The third option is vaccination.

This includes expediting COVID-19 vaccine development, production, and distribution, as well as providing immunization instructions. The fourth category is therapeutics, which includes accelerating pharmaceutical development, production, and distribution as well as making therapeutic usage recommendations. The fifth priority is health systems, which encompasses both strengthening health systems to respond effectively to the pandemic and resolving the epidemic's consequences on health systems. The sixth approach is Research, which comprises increasing research to better understand the virus and the pandemic, as well as developing new pandemic-fighting tools. The next step is to improve countries' capacity to detect, investigate, and respond to epidemics, as well as to strengthen health-care systems' resilience. Finally, communication requires providing reliable and timely information to the public as well as correcting misinformation and disinformation. WHO is working closely with GAVI, CEPI, UNICEF, and regional and national governments during these times to guarantee that immunizations are widely available in every country [105]. The group will also keep tabs on the virus's progress and report on the newest findings when they become available. In the wake of the COVID-19 pandemic, WHO amended its operational planning criteria to balance the preservation of critical health services, protection of healthcare professionals, and minimization of the risk of system failure[104]. WHO has provided interim contact tracing guidelines as a follow-up to their earlier advice on examining cases and clusters. WHO developed the "WHO Academy App" and the "WHO Info App" to help COVID-19 patients get better care and protect themselves[106]. The WHO has published suggestions for countries to incorporate a gender focus into their COVID-19 responses in order to ensure that public health policies and activities to combat the pandemic take gender into account and how it interacts with other disparities [107]. Given that Member States were dealing with a variety of transmission scenarios, the WHO developed four annexes to public health and social measures for workplaces, schools, and mass gatherings, as well as public health criteria to change these measures[108]. New doctor guidance in a WHO article on medications of COVID-19 includes a conditional recommendation against using remdesivir in hospitalized COVID-19 patients of any severity [109]. Between December 2020 and May 2021, the International Federation of Red Cross and Red Crescent Societies (IFRC), WHO Global Outbreak Alert and Response Network (GOARN), and the United Nations Children's Fund (UNICEF) released COVID-19 Global Risk Communication and Community Engagement Strategy Recommendations[110].

Strategy for 2023

The COVID-19 pandemic is not ended so far, new mutation of the SARS-CoV-2 is still a great risk for the world[67]. It is now apparent that it may not be possible to eradicate the SARS-COV-2 completely and the virus may continue to circulate within the community long-term, resulting in endemic outbreaks[111]. COVID-19, in addition to wreaking havoc on people's lives and economies, also disrupted education systems around the world. Individuals around the world have been vaccinated or have acquired natural immunity or a combination of both. But the plasticity of the virus suggests that the risk remains to all as the virus is mutating continuously which may lead to the emergence of more virulent and transmissible variants than previous ones. Moreover, aged people, new birth cohorts, immunocompromised individuals and patients with HIV, cancer or other conditions will be particularly at risk from these new variants. Thus, we have to have a long-term strategy in place with respect to deployment of resources that would help to minimize the risk of severity and deaths[112].

FUTURE PROSPECTS

The world has seen from mild endemic to severe pandemic scenarios of COVID-19[113-115]. As the SARS-COV-2 in earlier waves of pandemic had its different behavior in different regions of the world varying geographically as well as demographically, in future too such scenarios may occur at different times or places. Thus, there is a need of new strategy that can manage not only the uncertainty the unstable virus but also the long-term risks associated with this. WHO states – "If the vaccine isn't everywhere, this pandemic isn't going everywhere"[116]. Therefore, a fair distribution of vaccines is a needed under WHO's supervision. Future strategies to combat COVID-19 in the long term include the development of multivalent vaccines capable of conferring immunity to all strains of SARS-CoV-2 as the antibody cocktail therapy has been shown to be an effective way to reduce the development of SARS-CoV-2 mutations[117]. In the future, seasonal immunization against the SARS-CoV-2 may be necessary too, following the example of the decades-long successful use of influenza vaccination[118]. A universal vaccine, one that protects against SARS-COV-2 irrespective of the virus subtype, antigenic shift or shift, and doesn't need to be modified each year, has been argued to be necessary for the world. Such a vaccine would offer defense against all virus strains and viruses belonging to a particular virus family[119-121]. Universal vaccination development requires greater resources and often fails due to breakthroughs and discoveries. A universal vaccine may not prevent future pandemics, and it is unclear how long SARS immunity would last. When vaccinations are

unavailable for variants that spread quickly and avoid vaccine protection, social distancing, wearing a mask in public, and basic personal hygiene are the best ways to manage COVID-19[122]. Apart from achieving equitable access to available vaccines, it is a must to monitor the dynamic virus and accordingly develop newer diagnostics, therapeutics, and prophylactics as well. However, certain cases would require a special approach such as oxygen, enhanced diagnostic capacity, PPE etc. The diagnostic tools are either based on detecting 'specific viral proteins' or 'specific targets in the viral genome'[123]. A mutation in the variants can alter these specific targets, which can affect the sensitivity of diagnostic tests. Therefore, it is important to develop new diagnostic tools[124] capable of detecting all variants of SARS-CoV-2 [125]. The genomic surveillance of variants [126] is a reliable strategy to obtain evidence of whether the variants are virulent, antigenically different, more infectious, or resistant to vaccines in use currently before they spread globally [127]. Major pandemics and epidemics including the plague, cholera, flu, MERS, and SARS-CoV had already severely impacted humanity before COVID-19 [128]. Infectious diseases will change along with societies, and in the ensuing decades, an increase in the frequency of epidemics and pandemics is anticipated [129]. As infectious diseases are evolving, we must monitor and strengthen our capacity to counter it.

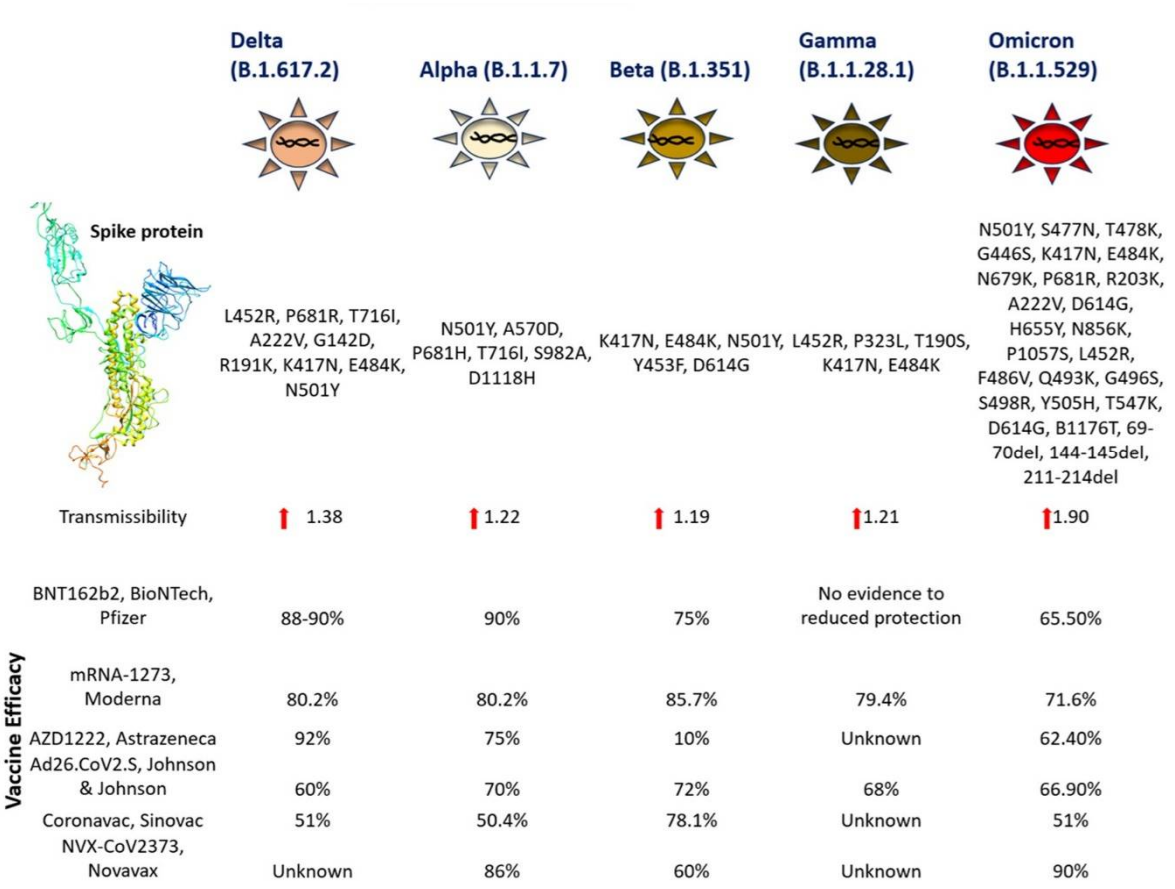

Figure 1: The WHO designated and monitored these variants

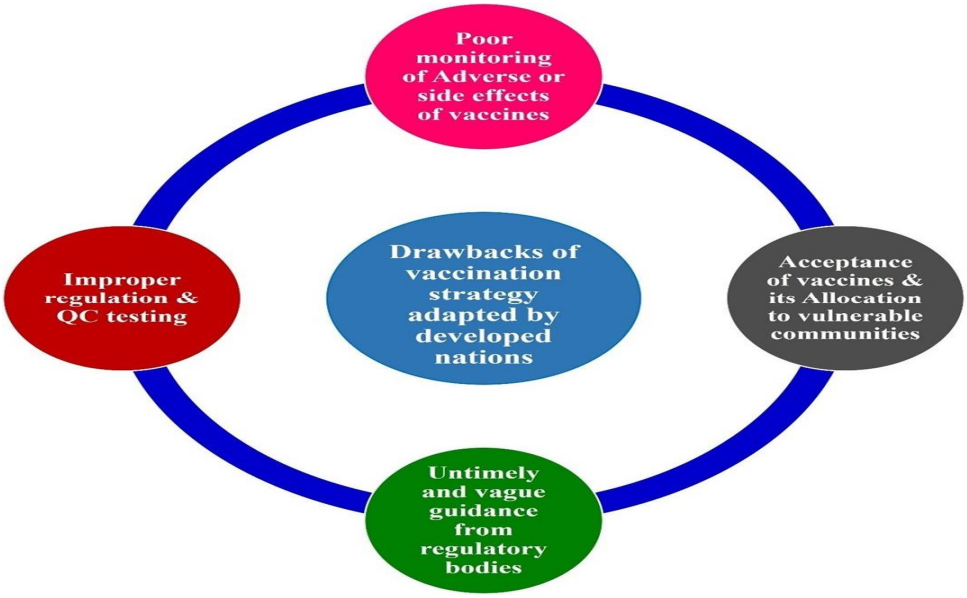

Figure 2: vaccines used in vaccination programs during the pandemic

Table 1. EUA approved COVID-19 vaccines by WHO

S. No.	Vaccine	Manufacturer	Platform	NRA
1.	BNT162b2/Comirnaty	BioNTech, Pfizer	Nucleoside modified mRNA	EMA
2.	mRNA-1273/ Spikevax	Moderna	mRNA encapsulated in lipid nanoparticles	EMA
3.	AZD1222 Vaxzevria	Astrazeneca	Recombinant Adenoviral vector encoding spike protein antigen of SARS-CoV-2	EMA, MFDS Korea, Japan MHLW, Australia TGA
4.	Ad26.CoV2.S/ Jcovden	Janssen, Johnson & Johnson	Ad26 vector vaccine encoding spike protein	EMA
5.	Covishield	Oxford/ Astrazeneca & Serum Institute of India	Recombinant Adenoviral vector encoding spike protein antigen of SARS-CoV-2	DCGI, India
6.	Convidecia	CanSino	Non-replicating viral vector	NMPA, China
7.	Covaxin	Bharat Biotech India	Whole virion inactivated Vero cell	DCGI, India
8.	Covilo/ InCoV (Vero cell)	Sinopharm	Inactivated virus	NMPA
9.	Coronavac	Sinovac	Inactivated virus	NMPA
10.	Covovax	Novavax& Serum Institute of India	Protein subunit (Recombinant nanoparticle)	EMA, DCGI
11.	Nuvaxovid	Novavax	Protein subunit (Recombinant)	EMA

NRA: National Regulatory authority; EMA: European Medicines Agency; MFDS: Ministry of Food and Drug Safety; NLSW: Ministry of Health, Labour and Welfare; TGA: Therapeutics Good Administration; DCGI: Drugs Controller General of India; NMPA: National Medical Products Administration

CONCLUSION

In conclusion, the COVID-19 pandemic has presented numerous challenges to global public health. While vaccination remains the most effective strategy for preventing the spread of the disease, access to vaccines remains a significant obstacle, particularly in developing nations. Future efforts must focus on increasing vaccine availability and addressing issues such as new variants, storage and transportation, and acceptance among different populations. The WHO's plan to fight COVID-19 provides a roadmap for such efforts, and a global COVID-19 Vaccination Strategy can save millions of lives. Various studies shows that vector-based vaccines are more popular in underdeveloped nations, whereas, mRNA-based vaccines are more w popular in wealthy countries like the United States. Thus, it is a matter of scientific explanation which sort of vaccination platform can solve problems faced by both underdeveloped countries and developed countries, have the least amount of side effects, and address antigenic variation subjected to virus evolution. This primary question has to be investigated by scientists.

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CONFLICTS OF INTEREST
"The authors declare no conflict of interest."

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