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RESEARCH ARTICLE

Current Vaccine and Efficacy of COVID-19 in Latin America: Challenges and need for updated public health policy.

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ABSTRACT
In Latin America, the COVID-19 pandemic, which initially surged and is now a constant presence, has brought about significant health challenges due to disparities and differences in regional responses. Vaccination is not only a necessity but also a responsibility as the primary tool for prevention. However, its implementation has not been consistent across countries, leading to various challenges such as global demand, initial high costs, infrastructure limitations for distribution, public hesitance, and misinformation. Other issues, like vaccine efficacy in immunocompromised patients and the use of different vaccines, were initially questioned but are now regarded as strategies to protect patients. This region, with its unique traditions, also faces several risk factors including vaccine supply shortages, lack of vaccine manufacturing, overcrowded cities, and an increasing migrant population that adds to the vulnerability of the people, challenging countries to strive for equity in prevention strategies. It is important to address individual strategies in communities to increase vaccine uptake as part of public health policy, and collaboration between countries should be encouraged to reach more people. This review will provide information about the COVID-19 vaccines available in the region, their characteristics and composition, their use across countries, and the reported effectiveness in the general population and among those with weakened immune systems.

Introduction

In Latin America, COVID-19 presented significant health challenges and starkly exposed the pre-existing disparities within the region. The urgency of the situation is evident as Latin America, despite having been a region with a significant COVID-19 mortality rate[1], has demonstrated remarkable resilience in actively combating the virus. Just as African Americans and Latinos in the United States have been disproportionately affected by COVID-19, a similar trend is observed in the region itself[2]. Vaccination, as the primary tool for prevention, is of the utmost importance[1–3]. Despite the numerous obstacles Latin American countries face in vaccinating their populations against COVID-19, including global demand, excessive costs, and infrastructure limitations, the region remains steadfast in its pursuit of herd immunity. Vaccination is a necessity in this region as 12% of all COVID-19 cases in the last 28 days were in the Americas, while the mortality rate in this region (79% of all COVID-19-related deaths) is the highest compared to others[1].

As vaccines can be designed to prevent infection, prevent disease, or serve as a treatment, it becomes crucial to clarify their purpose. Understanding these distinctions is critical to comprehend the multifaceted nature of vaccine development and use: the main objective of the COVID-19 vaccine is to prevent severe disease, mainly when local transmission is high. As long-lasting immunity is difficult to obtain in respiratory infections, most vaccines used in respiratory infections aim to lower severe disease.

Several COVID-19 vaccines have been granted emergency use by their respective countries. With at least 265 vaccine candidates, ninety-five were further studied in trials, and only twelve were finally approved by world regulations[1–3]; the development and distribution of vaccines in Latin America encountered unique challenges, including governmental hesitancy, stringent importation measures, and public health policies[4,5]. The urgency of these challenges cannot be overstated, as the vaccination percentage varies across countries and has not yet reached vulnerable populations, with additional disparities found between low- and middle-income countries[5]. A further challenge that is present in Latin America is migration. Ensuring equitable vaccine access for all, including migrants and refugees, is not just a priority but a paramount ethical responsibility in the collective fight against the pandemic, especially when population movement across borders is higher than in any other region globally.

Since overcoming these barriers is of the utmost importance to prevent more health crises, this article reviews the challenges that impact vaccination percentages in Latin America and could lead to future respiratory virus outbreaks.

Current Vaccine and Efficacy in Latin America

The four types of vaccines include mRNA vaccines, viral adenovirus vectors, inactivated viruses, and protein subunits, each with its unique characteristics and efficacy, which have different methods for creating immunity for the Spike protein, all from the original Wuhan variant. SARS-CoV-2 utilizes its surface spike glycoprotein to enter host cells. They were centered in antibodies for spike protein, as it stimulates an immune response that can neutralize the virus and prevent infection[2]. Nevertheless, the COVID-19 vaccine does not prevent infection totally, but it does prevent disease. The immune response to vaccination can vary depending on several factors, the two most important being the vaccine platform and individual immunogenicity. Immunity was thought to have two mechanisms: a persistent T-cell response that remains durable even with new variants and neutralizing antibodies that provide immediate protection against the virus[3–5]. Still, as vaccine efficacy declined, particularly regarding waning antibody titers and immune evasion, new strategies such as booster shots have been developed[6]. Current COVID-19 vaccines include primary series doses and the most recent COVID-19 booster. This last booster should have an updated XBB.1.5 Omicron variant that includes Pfizer-BioNTech, Moderna, or Novavax. This variation may lead to a heterogeneous immune response to vaccination within the community. Boosting with updated vaccines is crucial in reducing the risk of hospitalization, particularly in high-risk groups due to age or comorbidities[7]. Public health should focus on sustaining immune responses to prevent disease in high-risk groups and the community in general.

On December 31, 2021, emergency use authorization was issued for the Pfizer COVID-19 vaccine, followed by AstraZeneca/ Oxford COVID-19 on February 15, 2021, Janssen on March 12, 2021, and Moderna on April 30, 2021[2]. Initially, vaccines were rapidly rolled out in countries such as Israel, the United Kingdom, and the United States, while Latin American countries faced delays in receiving and distributing vaccines. Allocation varied, with some countries favoring vulnerable populations and others frontline workers[8].

Pfizer COVID-19 vaccine is a lipid nanoparticle formulation containing nucleoside-modified RNA against the Spike proteins of the SARS-CoV-2 virus, and Moderna is a lipid nanoparticle-encapsulated nucleoside-modified messenger RNA vaccine that encodes the prefusion spike glycoprotein of SARS-CoV-2[9]. mRNA is translated into proteins detected by human leucocyte antigen I (HLAI) and II (HLAII), leading to antigen-presenting cells to cellular and humoral cells and upregulating proinflammatory cytokines that include IL-2, IL-4, and IL-5. These interleukins cause the B-cells to differentiate into plasma cells that produce antibodies against spike proteins. This process proliferates the memory T-cells[9]. Pfizer's initial effectiveness was 67%, followed by the second dose's effectiveness, which was 90%[10]. In comparison, for Moderna, the initial effectiveness of the first dose was 74%, followed by effectiveness measures for the second dose of 93%[10]. Upon distribution of this vaccine, immediate problems arise, including a storage temperature of -70 degrees Celsius.

The AstraZeneca/Oxford COVID-19 vaccine contains a replication deficiency chimpanzee adenoviral vector delivering the SARS-CoV-2 structural surface glycoprotein antigen gene[9]. DNA gets released into the cytoplasm and later migrates into the cell nucleus; it gets translated into mRNA and proteins expressed in cell membranes, which HLAI and HLAII detect[2,9]. The first dose's initial effectiveness was 69%, followed by an 89% effectiveness measure in the second[10]. Although using a viral vector, Janssen is a non-replicating recombinant human adenovirus type 26, containing a full-length SARS-CoV-2 Spike protein[10]. Its effectiveness in preventing severe disease is around 66%. In general, these vaccines are easier to store and, therefore, to distribute.

Other available vaccines include Sputnik V, distributed in Argentina, Bolivia, Venezuela, Paraguay, and Mexico. This vaccine uses two different human adenoviral vectors (Ad26 and Ad5) to stimulate a stronger and longer immune response with a calculated efficacy of 91.6%[2]. Sinovac uses an inactivated, non-replicative virus with an adjuvant to boost the immune system and stimulate antibodies for spike protein and nucleocapsid. Although unable to replicate, this virus vaccine can still generate an immune response with an efficacy calculated near 65% for symptomatic and 87.5% for preventing hospitalizations[2]. The full list of vaccines with mechanisms of action is available in Table 1.

Table 1. Different vaccines are categorized by mechanism and dose.

Vaccine Company	Name	Mechanism	Doses
Pfizer	BNT162b2 Comirnaty	mRNA of spike protein in lipid nanoparticle.	30 ug (2 doses)
Moderna	mRNA-1273 Spikevax	mRNA of spike protein in lipid nanoparticle.	100 ug (2 doses)
CanSino	Ad5-nCoV Convidecia	Non-replicating Human Adenovirus 5 encoding spike protein	0.5 x 1011 VP
AstraZeneca/ Oxford	ChAdOx1 nCoV-19 AZD1222 Vaxzevria	Non-replicating Chimpanzee Adenovirus Y25 encoding spike protein	0.5 x 1011 VP
Janssen	Ad26.COV2.S Jcovden	Non-replicating Human Adenovirus 26 encoding spike protein	0.5 x 1011 VP
Gamaleya	Gam-COVID-Vac *Sputnik V*	Non-replicating Human adenovirus 26 (first dose) and Human adenovirus 5 (second dose) encoding spike protein.	0.5 ml (2 doses)
Novavax	NVX-CoV2373	A trimeric full-length spike was produced as a recombinant protein in insect Sf9 cells using a baculovirus expression system and mutations to stabilize it. Adjuvant matrix-based adjuvant.	5 ug SARS-CoV-2 rS + 5- ug Matrix M1 adjuvant (2 doses)
Sinovac	CoronaVac	Inactivated COVID-19 virus by beta-propiolactone with adjuvant aluminum hydroxide	3 ug (2 doses)
Sinopharm	BBIBP-CorV Covilo	Inactivated COVID-19 virus by beta-propiolactone with adjuvant aluminum hydroxide	4 ug (2 doses)
Bharat	BBV152 Covaxin	Inactivated COVID-19 virus by beta-propiolactone with adjuvant aluminum hydroxide	3 ug (2 doses)
Abdala	CIGB-66	A receptor-binding protein was produced as a recombinant protein that uses the yeast *Pichia pastoris*.	

VP: Viral particles.

The initial COVID-19 vaccines, originally developed against the ancestral (Wuhan) strain, can have some efficacy for current variants, but an update is warranted. Effectiveness against virus variants varies. Pool effectivity for the Alpha variant was 84%, while for the delta variant, it was 64%[10,11]. Initially, receiving only two doses of the COVID-19 vaccine was believed to be sufficient to provide immunity against the virus. However, over time, it has become apparent that a third booster shot is necessary to improve and maintain immunity against the evolving variants of the virus. Beta and Delta showed our vulnerability to variants in the vaccinated population[12]. Initial strategies to strengthen immunity and breakthrough infections, including the administration of booster shots, have become critical, and it has become evident that new vaccines targeting these variants have become crucial. Omicron, first detected in South Africa in November 2021, has more mutations in its genome than any other variant. The mutations in the RBD have led to increased transmissibility, immune escape, and potentially reduced effectiveness of existing COVID-19 vaccines[3,12]. The updated vaccine had 20-fold neutralizing titers against the Omicron variant. This reduced susceptibility also applies to subvariants that include BQ.1, BQ.1.1, XBB, and XBB.1. The bivalent Omicron-containing vaccine elicited higher spike binding antibodies to ancestral and Omicron subvariants[13]. The current circulating variants are mostly JN.1, followed by JN.1.13 and JN.1.18, subvariants of Omicron. Prior variants are not detected. Pfizer and Moderna upgraded their vaccines, including variant updates based on Omicron[12].

Although many different types of vaccines are available, they are not continuously available in all countries, and it is important that as efficacy declines over time and variants, this could leave vulnerable individuals within a community. In Table 2, COVID-19 vaccines are organized according to country. Individual immune status also affects the immune response evoked by vaccines. As most vaccines are designed to prevent severe infection, it is important to establish thorough vaccination.

Table 2. Available Vaccines in Latin American Countries.

Country (%)	**Number of vaccines and Vaccine**	**Boosters available and vaccine:**	**Production vaccines:**	**Government Page**
Argentina (76.54%)	9: Moderna, Pfizer/BioNTech, CanSino, Gamaleya, Gamaleya, Oxford/ AstraZeneca, Serum Institute of India, Sinopharm, Sinovac	Booster to all over 18 years with Moderna.	Sputnik (Richmond), Oxford/ AstraZeneca (mAbxience), Sinopharm (Sinergium Biotech)	(1)
Bolivia (53.4%)	6: Pfizer/BioNtech, Gamaleya, Janssen, Serum Institute of India, Sinopharm, Sinovac	No recommendation was found and not specified.	Does not produce	Not Found
Brazil (82.3%)	7: Pfizer/BioNtech, Gamaleya, Janssen, Oxford/ AstraZeneca, Serum Institute of India, Sinopharm, Sinovac	Booster to high-risk groups and not specified.	Sputnik (Uniao Química), Oxford/ AstraZeneca (Fiocruz), Pfizer (Eurofarma), Sinovac (Butantan)	(2)
Chile (92.6%)	6: Moderna, Pfizer/BioNTech, CanSino, Gamaleya, Oxford/ AstraZeneca, Sinovac	Booster to high-risk groups with Moderna.	Does not produce	(3)
Colombia (72.4%)	6: Anhui Zhifei Longcom Moderna, Pfizer/BioNtech, Janssen Johnson & Johnson, Oxford/ AstraZeneca, Sinovac	Booster to all over 18 years with Pfizer/BioNTech.	Does not produce	Not Found
Costa Rica (84.1%)	2: Pfizer/BioNtech, Oxford/ AstraZeneca	Booster to all over 18 years with Moderna or Pfizer/BioNTech	Does not produce	(4)
Ecuador (80.6%)	5: Pfizer/BioNtech, CanSino, Gamaleya, Oxford/ AstraZeneca, Sinovac	Booster to high-risk groups with Moderna.	Does not produce	(5)

Country (%)	Number of vaccines and Vaccine	Boosters available and vaccine:	Production vaccines:	Government Page
El Salvador (67.5%)	3: Pfizer/BioNTech, Sinovac, Oxford/ AstraZeneca,	No recommendation was found, and Pfizer/BioNTech was used.	Does not produce	(6)
Guatemala (41.7%)	4: Moderna, Pfizer/BioNTech, Gamaleya, Oxford/AstraZeneca	Booster to all over 18 years with Moderna and Pfizer/BioNTech.	Does not produce	(7)
Guyana (48.3%)	6: Moderna, Pfizer/BioNTech, Gamaleya, Oxford/ AstraZeneca, Serum Institute of India, Bharat Biotech,	The booster is for all over 18 years, but the vaccine is not specified.	Does not produce	(8)
Mexico (64.1%)	10: Centre for Genetic Engineering and Biotechnology, Moderna, Pfizer/BioNTech, CanSino, Gamaleya, Janssen, Oxford/ AstraZeneca, Bharat Biotech, Sinopharm, Sinovac	No recommendation was found, but Abdala, Sputnik V, and Pfizer/BioNTech being applied	CanSino (Drugmex), Oxford/ AstraZeneca (Liomont), Sputnik (BIRMEX)	(9)
Nicaragua (89.3%)	8: Centre for Genetic Engineering and Biotechnology, Instituto Finlay de Vacunas Cuba, Pfizer/BioNtech, Gamaleya, Oxford/ AstraZeneca, Serum Institute of India, Sinopharm	No recommendation was found, but Pfizer/BioNTech was used.	Does not produce	Not Found
Panama (73.3%)	4: Pfizer/BioNtech, Gamaleya, Oxford/ AstraZeneca, Sinovac	Booster to all over 18 years with Pfizer/BioNTech.	Does not produce	(10)
Peru (86.1%)	4: Pfizer/BioNtech, Janssen, Oxford/ AstraZeneca, Sinopharm	Booster to all over 18 years with Pfizer/BioNTech.	Does not produce	(11)
Uruguay (83.3%)	3: Pfizer/BioNtech, Oxford/ AstraZeneca, Sinovac	Booster to high-risk groups with Pfizer/BioNTech.	Does not produce	(12)
Venezuela (52.6%)	7: Centre for Genetic Engineering and Biotechnology, Instituto Finlay de Vacunas Cuba, Vector State Research Centre of Virology and Biotechnology, Gamaleya, Sinopharm, Sinovac	Booster to all over 18 years with Pfizer/BioNTech.	Does not produce	Not Found

Percentage of vaccination obtain from Statista.com: Anhui Zhifei Longcom (Zifivax), Moderna (Spikevax), Pfizer/BioNtech (Comirnaty), Janssen Johnson & Johnson (Jcovden), Oxford/ AstraZeneca (Vaxzevria), Sinovac (Coronavac), Centre for Genetic Engineering and Biotechnology (Abdala), Instituto Finlay de Vacunas Cuba (Soberana 02), Vector State Research Centre of Virology and Biotechnology (EpiVacCorona), Gamaleya (Sputnik Light), Gamaleya (Sputnik V), Sinopharm (Covilo), Serum Institute of India (Covishield), CanSino (Convidecia), Bharat Biotech (Covaxin),
(1) https://www.argentina.gob.ar/noticias/refuerzo-vacuna-covid#
(2) https://agenciabrasil.ebc.com.br/es/saude/noticia/2023-11/vacuna-contra-el-covid-estara-en-el-programa-nacional-de-inmunizacion
(3) https://www.chileatiende.gob.cl/fichas/86047-vacunaci%C3%B3n-covid-19
(4) https://www.ministeriodesalud.go.cr/index.php/prensa/61-noticias-2024/1780-cnve-aprobo-inclusion-de-vacuna-monovalente-contra-covid-19
(5) https://www.salud.gob.ec/centros-de-salud-habilitados-para-la-vacuna-covid-19/
(6) https://www.vacunacioncovid19.gob.sv/
(7) https://registrovacunacovid.mspas.gob.gt/mspas/consulta/vacunacion
(8) https://covid19communicationnetwork.org/es/covid19resource/covid-19-booster-shot-promotion/
(9) https://vacunacovid.gob.mx/preguntas-frecuentes/
(10) https://panama.iom.int/es/todo-lo-que-necesita-saber-sobre-la-covid-19
(11) https://www.gob.pe/21301-coronavirus-esquema-de-vacunacion-contra-la-covid-19
(12) https://www.gub.uy/ministerio-salud-publica/comunicacion/noticias/esquema-vacunacion-contra-covid-19

It is important to note that while vaccination is effective, its efficacy decreases with newer variants, leaving a vulnerable population. Additionally, everyone's immune response is unique, resulting in a community of vaccinated individuals with varying immunity[14]. As the immunity of some people may wane faster due to certain factors, continuous vaccination programs are necessary for maintaining efficacy. Several factors, such as age, gender, type of vaccination, and date of vaccination, can influence an individual's immune response. Studies indicate that patients previously infected with the virus tend to show higher levels of anti-spike IgG titers than those without. Furthermore, female patients tend to have a stronger humoral response, which decreases with age. When comparing different types of vaccines, mRNA vaccines were found to elicit a stronger immune response than viral vectors. Understanding these differences can aid in developing more effective vaccination strategies[15].

Recent research explores the role of the intestinal microbiome, which is influenced by various factors such as behavior, environment, nutrition, and perinatal and intrinsic host factors. These factors affect baseline immunity and have been found to impact the immunogenicity of different vaccines. Low- and middle-income countries face various challenges, such as poor organization, industrialization, and high-fat diets, which can reduce microbial diversity, increase *Prevotella* species and decrease *Bacteroidaceae*. These changes in the microbiome can also affect vaccine immunogenicity, not only for COVID-19 but also for other vaccine-preventable diseases[16].

The investment in COVID-19 vaccines has led to multiple vaccines with different mechanisms of action. While most of these vaccines effectively protect against the disease, they do not guarantee immunity against infection, and the immunity can wane over time. Breakthrough variant infections with increased cases and hospitalization have been detected, leading to doubts about the efficacy of vaccination. Booster doses were initially administered to lower risks, but new variants continue to emerge, and countries with vaccine shortages have had to implement mixing vaccines to overcome the shortages. While the vaccine mechanisms are different, they generally end with the same immune response, with mRNA vaccines having a slightly higher efficacy rate. Mixing vaccinations is a strategy that can be used for shortages, safety, and efficacy. Currently, newer variants require updated vaccines to continue providing protection.

Low- and middle-income countries are still struggling to achieve complete protection against COVID-19. Chile currently has the highest vaccination percentage at around 70%, while some countries have less than half of their population fully vaccinated. The lack of healthcare infrastructure to support vaccination in some countries could be a reason for this. Due to the strain on healthcare infrastructure and personnel, some individuals seek medical attention from other sources, such as pharmacies and drug stores. However, collaboration between countries with higher vaccination rates could help increase the percentage of vaccinated individuals. Collaboration has played a significant role in increasing the vaccination percentage in India[17]. National organizations such as NGOs have collaborated to reach communities that are not easily accessible [17]. Collaboration can also occur on an international level by partnering with countries that have the capability to store vaccines at the required conditions and distribute them nearby with shorter travel time and less cost. This method results in more outreach and helps more people get vaccinated[17]. This collaboration within the country administers at least 14 million doses, with 6 million being in the most vulnerable and marginalized communities in India[17]. This model can be applied to many countries in Latin America, making vaccines available for the farthest and most marginalized communities.

Countries with low vaccination rates are at a higher risk of complications caused by COVID-19. Although vaccination can be costly, it is still more cost-effective than treating severe diseases caused by the virus. The cost of COVID-19 was not only calculated in the price of treatment, but cost also should calculate decreased productivity, years of life lost, cost of insurance, and medical expenditures[18]. Many studies on the cost of COVID-19 are conducted in high- and middle-income countries, which have more data available[18]. However, data is scarce in low-income countries. One study found that the average indirect cost of COVID-19 per case is $1,101, while the cost per death attributable to COVID-19 is $90,820[19]. Universal vaccination would have an average cost of $55,705 per averted death[19]. This is a substantial cost saving compared to other measures, especially when considering the benefits for younger age groups. Although this cost saving may not apply to all countries, especially low-income countries, the benefit of savings is clear. It should not be a barrier for local health systems to acquire vaccines.

Covid-19 Vaccination in Immunocompromised Individuals

Immunocompromised individuals, such as those with HIV/AIDS, cancer, or organ transplants, are at higher risk of infections due to the lower efficacy of their immune system[5,20,21]. Healthcare providers often misunderstand the possibility of vaccinating this population, leading to reduced vaccination rates. Concerns were initially raised about flares and adverse events related to the COVID-19 vaccine among immunocompromised patients, resulting in cautious approaches to vaccinating this population. Immune dysregulation occurs in patients with autoinflammatory conditions, resulting in a blunted immune response to vaccines. As in any other condition, treatments shown in Table 3 have proven to have a negative effect on humoral response[22–28]. However, the benefit of vaccination outweighs the risk, and live attenuated or vector vaccines should be avoided. It is important to have a range of vaccine mechanisms available when vaccinating a vulnerable population with a suboptimal immune response due to exogenous immunosuppression[5].

Table 3. Medicine associated with Lower Response to Vaccine

Medicine	Dose	Effect	Strategy
Methotrexate	0.4 mg/ kg/ week	Reduce humoral response	Continue as the benefits outweigh the risk If the viral vector skips interval dosing and resumes 4 weeks after
Prednisone equivalent	7.5 -10 mg daily	Reduce humoral response	Continue as the benefits outweigh the risk If the viral vector skips interval dosing and resumes 4 weeks after
Azathioprine	3 mg/ kg/ day	Reduces immunogenicity of vaccines	Continue as the benefits outweigh the risk If the viral vector skips interval dosing and resumes 4 weeks after
Leflunomide	Any dose	Lower humoral response	Continue as the benefits outweigh the risk If the viral vector skips interval dosing and resumes 4 weeks after
Mycophenolate mofetil	Any dose	Reduces immunogenicity of vaccines	Continue as the benefits outweigh the risk If the viral vector skips interval dosing and resumes 4 weeks after
Cyclophosphamide	Any dose	Reduces immunogenicity of vaccines	Continue as the benefits outweigh the risk If the viral vector skips interval dosing and resumes 4 weeks after
Tumor necrosis factor inhibitor	Any dose	Mixed results	Continue as the benefits outweigh the risk If the viral vector skips interval dosing and resumes 4 weeks after
JAK kinases	Any dose	Mixed results	Continue as the benefits outweigh the risk If the viral vector skips interval dosing and resumes 4 weeks after
Rituximab	Any dose	Lower humoral response in general. Sustain T cell response to mRNA vaccines despite lower humoral.	Vaccination 2 weeks prior to the next dose

Many vulnerable populations have been studied for their seroconversion rates in comparison to healthy controls in different clinical scenarios (seroconversion rate from 97-100%). For instance, patients undergoing dialysis have a seroconversion rate of 88.5%, while those who have undergone a kidney transplant have a rate of 27.2%[9,29–31]; While patients with hematologic cancer and solid tumors have a general seroconversion rate of 65% and 94%, respectively[29]. Despite having higher efficacy, patients with a third booster dose are still at a higher risk than the general population[20,32]. This applies to clinical scenarios affecting immunology, such as hematologic cancer and solid tumors[29]. The aging population is another vulnerable group that experiences immunosenescence, reducing the ability to respond to infections and less long-term immune memory. This population also has a higher prevalence of chronic pulmonary obstructive disease, diffuser interstitial disease, and respiratory infections. Specifically, this population shows a lower T-cell response with the worst memory response and CD8+ T-cell[33]. Immunogenicity is lowered in this population upon additional doses[34]. Not only are the number of doses applied in this population, but cohort studies with delayed interval vaccination could have a 3.5-fold higher antibody response. These findings suggest that vulnerable populations must be carefully considered in vaccination efforts[35], either with additional doses or timing.

It is important to continue studying the effectiveness of vaccines in immunocompromised individuals and vulnerable populations. These groups may not have the same ability to generate an immune response as the general population and may lose immunity faster. Several strategies have been implemented, but further research is needed to improve the immune response. Increasing the vaccine dosage and defining the vaccine interval may improve immunogenicity. Standardizing vaccination policies is also crucial. Further studies are needed to evaluate different subgroups, and vaccination schedules must be updated as new drugs become available.

Heterogenous Individual Vaccination to Heterogeneous Vaccination in a Country

As mentioned earlier, the primary goal of the vaccine is to prevent severe disease. Its secondary objective is to achieve herd immunity and reduce the number of infections. Public health experts are concerned about the possibility of a resurgence of infections among the unvaccinated population. This concern is also relevant for people with incomplete vaccination or whose immunity has weakened over time. Administering vaccines to the entire community is not enough to achieve herd immunity, especially when immunity eventually wears off. Various community factors, such as spatial distribution, population density, and movement, can affect vaccination strategies, resulting in a diverse immune community rather than uniform herd immunity[36].

The shortage of COVID-19 vaccines has led to the development of newer methods, such as heterologous vaccine schedules, which offer flexibility to vaccination programs based on the country's supply. Heterologous vaccines involve administering primary doses of one type of vaccine followed by another type of vaccine as a booster. Studies have shown that heterologous vaccination is safe[37]. However, its efficacy remains a focus of research. While this approach may provide a more robust antibody response and enhanced effectiveness, it has not yet been established as a policy.

The effectiveness of mixed vaccines depends on the variant of COVID-19. Initially, a decline in efficacy of 21% was thought to occur, which was later calculated to be 29% during the Omicron era. According to Zhang et al. (2022), the odds ratio for infection for those who received three doses of mRNA vaccine was 0.076, while the odds ratio for those who received two doses of inactivated vaccine with one dose of mRNA vaccine was 0.045[37]. The effectiveness of two doses of adenovirus vaccine with one dose of mRNA vaccine was comparable to three doses of mRNA. Only one study has calculated the odds ratio for four doses of mRNA vaccines, which is 0.058 [38].

Comparing the odds ratios of vaccinated patients who received two adenovirus vaccines boosted with mRNA, it was found that the odds ratios for non-delta and non-omicron cases were both 0.06 for asymptomatic and hospital admissions. However, the odds ratios were 0.23 for asymptomatic (infection prevention) and 0.08 for admission (disease prevention) for delta and omicron cases. Similarly, for three mRNA vaccines, the odds ratios for symptomatic and hospital admission were 0.07 (infection prevention) and 0.04 (disease prevention), respectively, for non-delta and non-micron cases. In contrast, the odds ratios for delta and omicron cases were 0.24 (infection prevention) and 0.07 (disease prevention), respectively[38].

Notably, heterologous vaccinations have also demonstrated safety and immunogenicity in vulnerable populations, including those with immunosuppression[39]. With the limitation of a surplus vaccine, choices were made depending on its existence, leaving the population no choice in the vaccine being applied. Due to the different efficacy and clinical scenarios, communities experience a heterogeneous immunity that could represent a risk of infection or disease. As more heterogenous immunity exists in a community, the interplay of different immune systems could be a factor in developing vaccine breakthrough variants of concerns, with events like what happened in South Africa with Beta, India with Delta, and South Africa with Omicron. Many infectious disease models assume that the community is homogeneous or everyone has a similar risk of getting infected. However, population heterogeneity can cause a backward bifurcation, which means the disease can persist even if the reproduction number is below one. Therefore, stakeholders should consider this point when deciding the types of vaccinations to offer the community[14].

A community can be split into two groups: those who are vaccinated and those who are not. However, it is important to note that even among those who are vaccinated, there may be differences in their immune responses. This results in a heterogeneous vaccinated population. Other factors to consider are the varying levels of immunogenicity provided by different COVID-19 vaccines and the risk of a false sense of herd immunity[40]. Although most of the general population may end up with heterogeneous vaccination status, the significance of this will likely decrease once everyone has received the latest vaccine version that targets the current variant of concern.

It is important to consider the concept of a heterogeneous community. This means that the protection provided by vaccines may wane faster in some individuals than in others, especially with the presence of unvaccinated individuals within the community. These unvaccinated individuals could be migrants fearing administrative repercussions or hesitant individuals. This could lead to backward bifurcation, where viral transmission continues despite a low number of cases. This could pose a local risk to public health authorities.

Additional Factors that Affect Viral Transmission

Understanding the dynamics of viral spread in Latin America involves multiple factors that contribute to high transmission rates. With 30% of the population living in poverty and 60% working in informal jobs, living conditions often lack basic sanitation and may include overcrowded housing, which increases the risk of transmission. The same factors that drive higher transmission rates are also associated with higher mortality rates. This increase in mortality has also been observed in more marginalized populations[41]. Latin America's lack of physical activity, unhealthy diet, air pollution, inadequate healthcare facilities, low testing, and poor adherence to protective measures have made it a region with increased transmission during the different COVID-19 waves. Public health measures were harshly criticized, and some areas were unable to adapt due to a lack of resources. While vaccination has been the prevention measure people have been waiting for, other public health measures were implemented to stop transmission while treatment and vaccination were being developed[41]. Social distancing and wearing masks have proven effective in reducing viral and bacterial infections in children and adults in the initial steps, but an increase in cases of COVID associated with lifting these restrictions and a decrease in the total number of routine vaccinations being administered. This highlights the importance of vaccinating against COVID-19 and maintaining regular vaccination schedules to prevent the resurgence of other infectious diseases[42].

Latin America has faced many challenges in the battle against COVID-19. However, despite these difficulties, the region has significantly progressed in vaccinating its population. Currently, there are ten different vaccines available in Latin America, including AstraZeneca, Pfizer, Covishield, Sinovac, Moderna, Bharat, Sinopharm, CanSino, and Sputnik [42]. Table 2 displays the vaccines that are available in the region. Achieving herd immunity is crucial to protecting vulnerable groups from the virus. To achieve herd immunity, at least 60-70% of the community must be fully vaccinated. However, reaching this goal has been complicated as vaccines do not completely block transmission but significantly reduce severe infection[43]. There is a risk of new COVID-19 variants emerging due to low vaccination rates, limited access to vaccines, inadequate healthcare infrastructure, and a high prevalence of comorbidities. These risk factors make it essential to continue efforts to increase vaccination rates across the region [3,44,45].

Vaccine-preventable diseases continue to cause significant levels of morbidity and mortality worldwide. The burden of these diseases varies from country to country, but vaccination still has economic advantages[46]. While COVID-19 treatment costs vary from country to country, they are generally higher in low-income countries due to limited healthcare infrastructure, inadequate access to medical resources, and higher rates of comorbidities. Vaccination is cost-saving and health-improving, with yearly savings from complete vaccination estimated to range from $266,754,782 in Argentina to $9,689,633,010 in Mexico. These estimates consider factors such as avoided deaths, health outcomes, quality-adjusted life years, life years gained, critical care burden, days of hospitalization, and treatments per year[47]. While these are merely estimates, the savings still exceed the cost of treatment.

Including various diseases in vaccination strategies is important, not just COVID-19. Apart from the vaccine itself, other measures such as vaccine education, access to vaccines, avoiding interruptions, partnering with local communities and organizations, and targeted outreach to vulnerable populations should be implemented[48]. Ignoring vaccination for other preventable diseases can leave the population vulnerable to other illnesses. Although public health spending on infrastructure and treatment is essential, vaccination provides significant benefits, including higher savings than treatment costs. Therefore, the budget analysis should include programs that aim to reach vulnerable populations.

Adverse Events as a Reason for Hesitancy

Adverse events are a common occurrence with all vaccines. Typically, these events are mild and related to reactions at the vaccine site. Since the beginning, local and systemic adverse events have been reported, which have caused some doubt and hesitancy. Although most adverse events are mild, at least 10% can limit daily activities. Although the vaccine type may affect adverse events, the safety profile is similar across all vaccines. Common adverse events with mRNA vaccines include pain, redness, swelling, and itching[49,50]. These were slightly more common with Moderna than with

Pfizer. Other common adverse events include fatigue, headache, and muscle pain, while less common events include fever, chills, and joint pain[49,50]. Adverse events were seen as more common in heterogenous vaccination and younger adults.

One adverse event that has raised concern is myocarditis[51–53]. However, mild vaccinations are generally halted and not recommended until completely resolved. According to current estimates, the likelihood of myocarditis occurring after receiving an mRNA booster is 1 in 41,500. This risk is greater in young males aged 18 to 24 compared to those aged 25 to 29[53,54]. The clinical presentation of myocarditis includes new chest pain, shortness of breath, and palpitations that typically occur within the first week after vaccination[51]. A rare adverse event associated with adenoviral vector vaccines is vaccine-induced immune thrombotic thrombocytopenia[55,56]. This event is characterized by developing anti-PF4 antibodies and prothrombotic syndrome. The syndrome is more common in younger patients and females and can result in thrombosis in the cerebral veins, deep veins of the leg, pulmonary arteries, and splanchnic vessels[55–58]. Another concern about vaccination is related to thrombotic events like vaccine-induced immune thrombotic thrombocytopenia (VITT). The most frequent thromboembolic complications that have been reported in the literature are cerebral venous sinus thrombosis and deep vein thrombosis/pulmonary embolism, mainly with the AstraZeneca vaccine[59]. Nevertheless, despite the concern about these adverse events, thrombotic complications are more common with COVID-19 infection itself than from vaccination; therefore, the benefit of vaccination far outweighs the risk[60]. Elias et al. (2023) found that vaccination after a multisystem inflammatory system in children was safe, and any mild adverse events were resolved with acetaminophen[61].

Drivers of Acceptance and Hesitancy

The acceptance of vaccines varies across the world. In 2021, the acceptance rate in Latin America was 80%, which changed over time[62]. The early high mortality rate and the number of cases were thought to be the main drivers behind the high vaccination rates. However, vaccine hesitancy and refusal played a key role in later affecting the rates. Vaccine hesitancy refers to the delayed acceptance or refusal of vaccination despite availability [63,64]. In Colombia, Brazil, and Peru, vaccine hesitancy was common during the initial vaccination campaigns. Lastly, there was a significant non-acceptance of vaccines in Ecuador due to doubts about their efficacy[65]. The percentage of vaccine hesitancy varied by country, ranging from 10.4% in Peru to 26.4% in Mexico[66]. This is in line with the response of Latin American countries to COVID-19, which can be categorized according to their public health measures[62].

To effectively combat vaccine hesitancy, it is crucial for stakeholders and policymakers to have a comprehensive understanding of the underlying issues. It is important to note that these issues may vary from country to country. Internal factors are the primary causes of hesitancy in the population, but external factors are also becoming increasingly prevalent[67]. Internal factors include unequal access, limited availability, delivery concerns, fear of adverse events, misinformation, conspiracy theories, and a lack of support from local authorities. In general, it was found that hesitancy towards vaccines was associated with individuals in each country who shared concerns about possible adverse events, safety issues, conspiracy theories, the belief that their immune system is stronger than the vaccine, religious beliefs, the perception that the risk of acquiring COVID-19 is low, and a general avoidance of vaccines. External factors like the migration crisis also contribute to vaccine hesitancy. This trend is observed globally, with the six main reasons for vaccine hesitancy being a low perceived benefit, low perceived risk, health concerns, lack of information, systemic mistrust, and spiritual beliefs[68].

Initially, the vaccination rates in Latin America were affected by unequal access, availability, and delivery of vaccines. However, currently, the decision not to get vaccinated is more likely due to hesitancy. When asked about their preferences, people expressed a desire for vaccines with high efficacy and a low incidence of major adverse events. They also preferred vaccines that were domestically produced and endorsed by medical organizations. Recommendations from family, friends, and healthcare providers played a significant role in vaccine acceptance or refusal[69].

Many people are skeptical about the COVID-19 vaccine and believe in conspiracy theories that involve complex plots, for example, the implantation of chips during vaccination[70]. These beliefs have affected the adherence to other protective measures. Countries like Peru have high beliefs in conspiracy theories, while countries like Chile have lower beliefs[70]. The lack of clear information about vaccine safety and efficacy, limited access to healthcare facilities, and insufficient communication contribute to vaccine hesitancy and hinder equitable distribution [37]. Healthcare workers have also shown hesitancy to the COVID-19 vaccine due to discrimination and low-risk perception[62]. To increase acceptance, healthcare workers can defer these ideas and deliver vaccines at the first level or specific vaccine centers[62,67]. Promoting vaccination should also include providing accessible vaccination sites, implementing outreach and education campaigns targeting vulnerable populations, addressing language and cultural barriers, and ensuring equitable distribution of vaccines across all communities [67].

Vaccine hesitancy can be addressed through clear communication and providing accurate information. Other negative factors contributing to vaccine hesitancy include being a younger adult, having a low income, and having no history of receiving other seasonal vaccines, such as the influenza vaccine. It is worth noting that vaccine uptake can vary depending on the region, with some rural areas having a higher uptake due to better availability[71]. In healthcare workers, factors such as previous infections, Latin ethnicity, and lower education levels can lead to vaccine hesitancy[72]. In some cases, executive dismissal of the severity of the disease and discouragement can also contribute to population hesitancy, as seen in Mexico and Brazil[73]. However, population surveys have shown that people are equally effective as medical experts in promoting vaccine uptake. To improve vaccine hesitancy, it is crucial to continuously ensure people's safety and efficacy and communicate this in understandable terms. Community leaders, government officials, and role models can help avoid false information and promote trustworthy sources[66].

Hesitancy, a delay in getting vaccinated due to internal and external factors, can be addressed by a multi-step algorithm. This is not new, with many vaccines being questioned for efficacy and safety. However, due to the media attention surrounding the COVID-19 pandemic, it has been more prevalent with COVID-19 vaccines. Moreover, local authorities have been skeptical of the vaccine in some places, leading to lower vaccination uptake. Peru, which had a high number of deaths from COVID-19, currently has a high vaccination percentage among its citizens. Conversely, Mexico has a 65% complete vaccination rate, which could be due to incomplete registries or high vaccine hesitancy rates. Addressing hesitancy from local to national reasons, studying facilitators and different strategies to improve vaccination should be first in health policies [63,65,72]. While getting vaccinated is a social responsibility, enforcing it and making it obligatory could lead to distrust and further separation from the healthcare system. There are also ethical concerns related to coercion. Empowering the population can start with simple processes such as electronic vaccine health records that remind patients of the next doses[74]. This requires having enough vaccines for this process.

Development as a Barrier for Equity

Some Latin American countries like Chile and Uruguay were proactive in controlling the spread of the virus by implementing strict measures such as widespread testing, contact tracing, and strict lockdowns. They also focused on initiating and completing vaccination schemes and distributing vaccines through stadiums, universities, and newly established vaccine centers. Other countries like Colombia and Ecuador prioritized completing vaccination schemes rather than giving one dose to the entire population. However, these countries faced challenges due to the lack of vaccine accessibility, which resulted from the limited cooperation between public and private institutions. Although domestic vaccine production in Latin America is limited, mobile and permanent vaccine centers were established to ensure a steady supply[73]. Unfortunately, the lack of vaccination centers and supplies led to mistrust and hesitancy in the population to seek vaccination[48,75], which, in turn, created a lack of trust in government policies[4,76].

Latin America has historically faced challenges in developing vaccines. However, producing vaccines locally could help address the COVID-19 vaccine shortage. As a region that depends on public health policies to acquire vaccines, individuals are not given the opportunity to choose their preferred vaccine. Several vaccines, including Abdala and Soberana from Cuba, ButanVac and ButanCorona from Brazil, and Patria from Mexico, are now locally approved but have not yet received full approval for widespread use. However, they have been proven effective against the original strain of COVID-19. Unfortunately, this region has experienced slow vaccine uptake due to skepticism about the severity of the infection[73]. Table 2 shows the disproportionate number of vaccines acquired compared to those produced within the region.

Vaccination In Migrants

It is often more difficult to reach vulnerable populations in rural settings than in urban areas, especially those who do not seek medical attention. COVID-19 has highlighted the healthcare needs and shortcomings of those with acute illnesses. Health crises, food insecurity, unemployment, and economic difficulties are the main drivers of migration in Latin America[77–79]. Many people migrate from Central America, where there are droughts, violence, and poverty, to the North, where restrictive measures prevent them from entering. However, migration can also occur towards the south, such as in Chile, which currently receives migrants from Venezuela, Peru, Colombia, and Haiti[77–79]. Sanitation crises have been exacerbated by COVID-19. Border restrictions are in place, but COVID-19 has made crossing borders even more difficult, increasing the number of migrants in certain areas and leading to overcrowding. Economic crises often lead to poor working conditions, usually lacking legal representation, resulting in fear of absenteeism[77,79]. These migrants also have to face administrative issues with the additional lack of information leading to vaccine hesitancy. Migrants often arrive carrying chronic conditions such as diabetes and hypertension. Unfortunately, they may face a lack of medicine and have uncontrolled chronic comorbidities, making them more susceptible to severe diseases compared to the general population[77]. While they may initially seek medical attention, the fear of deportation and unknown processes can lead them to seek attention from pharmacies or drug stores. Although not common, a language barrier can still exist, further complicating seeking medical attention[77–79].

Migrants have limited access to medical services, and even when they do, they tend to underutilize them compared to local individuals. This is primarily due to the fear of experiencing discrimination or racism from healthcare workers, as well as being reported to local authorities and being deported. According to recent statistics, Colombia has the lowest rate of medical attention seeking by migrants, followed by Ecuador, Panama, and Peru. In contrast, at least 54% of migrants in Mexico and 82% in Chile seek medical attention[77].

The ongoing migrant crisis has highlighted the plight of a vulnerable population that lacks access to adequate healthcare, including COVID-19 vaccination. Migrants and refugees are particularly susceptible to the virus and are at a higher risk of experiencing severe outcomes[77]. It is crucial to implement healthcare strategies that account for the needs of this population, ensure fair access to vaccinations, and safeguard the entire community's health[80]. Initially, when countries devised their vaccination plans, the inclusion of migrants was not prioritized. Instead, frontline workers and high-risk patients were given priority. In some cases, migrants were included in vaccination plans simultaneously with non-migrants. However, most guidelines did not specifically address the vaccination needs of migrants. Despite this, all individuals, regardless of their migration status, were eligible for vaccination[81,82]. Furthermore, migrants find themselves in poverty, social exclusion, and working in hazardous environments. It is essential to ensure that effective and adequate healthcare and prevention measures are accessible to them without any economic or social barriers. These measures must not be conditional to their job status or fear of deportation[77,78].

Vaccine Opportunities and Improving Vaccination Uptake

Due to the pandemic, countries worldwide have developed various vaccination strategies to increase the uptake of vaccines. Some of these strategies involve making vaccinations mandatory for certain activities, such as school immunization and travel vaccines[3]. Unfortunately, just like in the United States, where African Americans and Latinos have been disproportionately affected by COVID-19, a similar trend is being observed in Latin America. Moreover, not all patients have the option to travel to get vaccinated. According to UNICEF, at least 12 million children have left school due to the pandemic, which means that a similar number of children might remain unvaccinated if school immunization was the primary vaccination strategy. Although young adults are less likely to experience severe COVID-19, they can still spread the virus within the community. When deciding on vaccination policies, it is important to consider the possible variants of the virus. The Omicron variant appears to have a lower hospitalization risk than previous variants, such as Delta. Booster shots were found to be effective in reducing the risk of hospitalization during the Delta variant's prevalence. It is important to note that not only an individual's risk of hospitalization but also the effectiveness of vaccination in preventing the spread of the virus and reducing the number of severe cases is crucial to avoid overwhelming healthcare systems[54].

Regular booster shots are a way to improve the efficacy of vaccination. Just like primary vaccination, this approach involves providing access to information for the community and its leaders to support vaccination efforts. With the emergence of newer variants, getting booster shots becomes optional as a country strategy, but it is necessary to maintain community immunity. Also, the vaccines used for these booster shots should be updated to ensure their effectiveness against the latest variants. As with any healthcare strategy, ethical concerns must be addressed. Lastly, it is not acceptable to use coercion to force people into getting booster shots.

Due to the high number of patients seeking medical attention, there were instances where some patients missed their scheduled vaccines and treatments. Patients often visit pharmacies and drug stores for their medical needs, but inadequate health records can cause them to miss regular doses and boosters. Vaccinations are usually given at primary healthcare centers, and patients who have been treated at second or third-level hospitals must seek vaccination at after-discharge primary health centers. It is crucial for countries to have easily accessible and understandable vaccination strategies. Some Latin American countries have implemented electronic vaccine records, and it would be ideal for other countries, such as Canada and the United States, to establish similar systems with regular alerts reminding individuals to seek missing vaccines. Even though healthcare systems cannot constantly remind patients to get vaccinated, it is the shared responsibility of the patient to keep track of their vaccination schedule.

Improvements In Public Health Vaccination Policy

Hesitation towards vaccination can leave vulnerable individuals unprotected and increase the risk of new variants. It is important to consistently promote the message that vaccines are safe and effective at protecting against infectious diseases. To achieve this, public health policies should incorporate the following measures:

- The public health response to the pandemic must have four pillars to support it: mitigation measures, testing, healthcare resources, and financial evaluation. Prevention measures, such as testing and contact tracing, are crucial in identifying cases. Vaccination is one of the most effective strategies against COVID-19, as it stops the disease and reduces the risk of infection, even when the protection for infection wanes with time.
- Vaccination campaigns should be a top priority for health ministries and run throughout the year. The focus should be directed towards those who are hesitant about getting vaccinated. The reasons for their hesitancy should be addressed by educating them about the safety of vaccines, the need for boosters, where to get vaccinated, and dispelling myths surrounding vaccines. While many people currently use local web pages to access vaccine information, additional strategies such as reminders during primary care visits, pharmacies, calls, or messages should be used. Electronic vaccine records can be helpful, but illiterate patients may be excluded from this method. Hence, alternative methods should be considered for such patients. Even if the vaccine cannot be made mandatory, it should be presented as a social responsibility to keep the community safe.
- When it comes to spreading information about vaccinations, it is important that the information is accessible to both those who are in favor of vaccinations and those who are against them. This information should be relevant to the specific context, involve people in the process, prioritize the population's needs, and be self-reflective. Additionally, it is crucial to view vaccination not as a singular solution but as a part of a larger effort to meet the population's healthcare needs[83].
- It is crucial to have enough vaccines available to ensure everyone has access to them. If there are not enough vaccines, people may miss out on the opportunity to get vaccinated, leading to decreased motivation to vaccinate in the future. In order to ensure fairness, it is important to identify at-risk populations based on criteria such as age, race, medical conditions, occupation, and socioeconomic status. This includes migrant citizens, who are at a higher risk if left out of the vaccination program. We must ensure that campaigns to promote vaccination also address their inclusion in the program.
- Equity in vaccination means that vaccines should be distributed nationwide without considering the economic status of individuals. However, promoting vaccination has been inconsistent due to the financial burden and public health programs. To address this, the COVAX program was established in 2020 by CEPI, Gavi, and WHO to ensure equity in vaccination. Increasing vaccination rates can reduce mortality and lower hospitalization rates and ICU admissions. In addition to increasing vaccine acquisition through sales, local production can also help improve distribution. It is important to fast-track and support the removal of importation and trade barriers to facilitate this[84].
- Although it may not be feasible to produce vaccines locally due to the high cost of implementation and production requirements, establishing a manufacturing center that allows for easy exportation to neighboring countries could be a viable option. However, this would require the assistance of local lawmakers. In addition, it is important to have vaccines and regularly update them to cover circulating variants of interest and concern.
- Standing orders could enhance vaccination rates as patients arriving at pharmacies with medical orders for their chronic conditions could receive an invitation for the required

vaccination, leading to increased vaccination rates. Implementing a reminder call system is one possible strategy to ensure people get their required vaccines. This could be more effective than sending messages reminding individuals which vaccines they need. Although this approach may require more effort to make the calls, some countries have successfully utilized apps and reminders to automate the process. Setting an appointment through this method could also simplify the process for individuals.

- Collaborating with other countries could be beneficial in terms of vaccination. A surplus of vaccines in one place could indicate a shortage in another. An outbreak in one country could lead to new cases in neighboring countries. While travel medicine is not a new concept, with people traveling for medical evaluations or surgeries, recently, vaccine travel has become more prevalent due to a shortage of vaccines. People are traveling to other countries to get vaccinated. However, problems arise when incomplete registers exist in countries, and the vaccine is not included in their regular schedules. Collaboration would also mean that countries that produce vaccines should facilitate those who acquire them sufficiently to cover their population. In the early stages of the epidemic, there was a disparity in vaccine acquisition; for example, high-income countries could vaccinate at least 3 to 4 times more people compared to low-income countries, which only received one vaccine.
- School interventions require students to have all vaccinations before attending. However, this approach could be seen as coercive and raise ethical concerns. Instead of mandating vaccines in schools, inviting parents to vaccine education sessions could be a more effective approach to reach a larger audience. Similarly, workplaces cannot mandate vaccines, but healthcare providers can offer on-site vaccinations to employees. This strategy could help reach those unable to leave work or who have complicated schedules. However, it is important to establish alternative strategies for informal workers who may not have access to these sites.
- To encourage more people to get vaccinated, many places have introduced reward schemes. These can include tax reductions for citizens who have completed their vaccinations or bonuses for workers who have been vaccinated. However, these reward schemes can be expensive and difficult to maintain long-term and may not be applicable to low and middle-income countries. Rewards can be given in hospitals, schools, or workplaces, but it is important to remember the potential drawbacks mentioned earlier.
- Local authorities, lawmakers, and healthcare settings should be aware of the implications of vaccination to prevent discordant speeches that could cause citizens to doubt the healthcare system and increase vaccine hesitancy.

Vaccination efforts have been hindered by various internal and external factors, as discussed earlier. The emergence of new variants that cause breakthrough infections presents a challenge in constantly updating vaccine policies. While some factors cannot be changed, it is important to consider health policies. Situations such as migration and overcrowding have contributed to the difficulty of vaccine distribution. COVID-19 is not the only vaccine-preventable disease that has faced this situation, but the pandemic has highlighted the differences in healthcare systems between countries. For instance, the number of vaccines available in Latin America is significantly lower than that produced. This disparity in vaccination has created confusion about who requires a booster dose, and even if booster recommendations apply to almost all, local authorities have standardized the approach. Despite efforts to promote vaccination, conspiracy theories and myths surrounding the vaccine persist, which healthcare workers must address appropriately. Additionally, the fragile healthcare system, with shortages in personnel and resources, has dissuaded many from seeking medical attention. A disease initially preventable by vaccination and infection prevention presents an opportunity to improve vaccine strategies locally and nationally. Vaccine uptake has been low in Latin America, which could also lead to an increased risk of other vaccine-preventable diseases, such as measles. Even within a country, a low vaccination rate in a community can lead to an outbreak that spreads to neighboring communities. Therefore, a heterogeneous vaccination rate poses a risk, emphasizing the need for vaccination and strategies for high-risk groups.

Many areas of improvement have been brought to light during the COVID-19 pandemic that will continue as COVID-19 is now endemic. From shortage to hesitancy, mixed messages led individuals not to vaccinate. To increase vaccination rates, it is important to understand the challenges that lead to fewer vaccinations. Clear communication and invitations from healthcare workers to patients to keep their vaccination schedules up to date are key. Healthcare workers should also work with local hospitals to create vaccination programs, which will decrease the number of missed vaccination opportunities.

Communication with policymakers and directors is essential to develop effective vaccination campaigns. It is important to spread the message that vaccines are safe and encourage patients to take responsibility for their own health and the health of their community by getting vaccinated.

Future Directions

Researchers are working on developing newer vaccination mechanisms that will produce different immune responses to COVID-19. As the virus continues to mutate, updating the vaccine with Omicron variants, alongside the different vaccination calendars, will play a crucial role in protecting against severe COVID-19. Areas with low vaccination rates are at higher risk of the surge of new variants. Immunocompromised individuals will require further studies to ensure the vaccine's safety and efficacy. For some individuals, treatments for prevention will be necessary, including antivirals or monoclonal antibodies. Countries should share their vaccination strategies and collaborate to improve vaccine uptake.

Conclusion

The COVID-19 pandemic has highlighted the need for improvement in the healthcare crisis, particularly in vaccination. Even though vaccination has been an essential strategy for preventing infections, COVID-19 vaccines have been criticized for their rapid development and use of new technology. The global demand for vaccines has led to disparities in their acquisition and production, leaving vulnerable communities waiting for vaccines. These disparities can be seen in access to healthcare diagnosis and treatment and prevention strategies. Although no single strategy is perfect, collaboration between countries could provide a reasonable way of ensuring that more people have access to prevention measures. Migration is likely to bring challenges in the future, particularly in areas with high transmission of communicable diseases. It is important that vulnerable populations in such areas are included in local health policies. As new vaccination strategies are developed, continuous education for both the general public and healthcare workers is essential to prevent the emergence of new variants and protect vulnerable groups.

Conflict Of Interest

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