Chapter 32

Role of Vaccines in Controlling COVID-19 Pandemic

Zohaib Mustafa[1], Rimsha Jamil[2], Laiba Naeem[3], Farrah Deeba[4], Hamza Aziz[5], Silla Ambrose[5] and Shiv Ram Ashraf[6]

[1]Department of Medicine and Surgery, Bahria University of Health Sciences Karachi, Pakistan
[2]Department of Zoology, Faculty of Science, University of Agriculture, Faisalabad, Pakistan
[3]Department of Chemistry, Faculty of Science, University of Agriculture, Faisalabad, Pakistan
[4]Department of Clinical Medicine and Surgery, Faculty of Veterinary Science, University of Agriculture, Faisalabad, Pakistan
[5]Faculty of Veterinary Sciences, University of Agriculture, Faisalabad, Pakistan
[6]Department of Biochemistry and Biotechnology, University of Gujrat
*Corresponding author: laibanaeem401@gmail.com

ABSTRACT

This chapter thoroughly examines the critical role vaccines have played in the global effort to combat the unprecedented challenges posed by the SARS-CoV-2 virus. The chapter provides insights into the multifaceted impact of vaccination strategies on curbing transmission, reducing morbidity and mortality, and restoring societal normalcy by conducting an in-depth analysis of vaccine development, efficacy, distribution, and societal implications. It investigates the scientific underpinnings of vaccine development, encompassing diverse platforms such as mRNA, viral vector, protein subunit, and inactivated virus vaccines. It highlights the collaborative efforts of researchers, industry, and regulatory agencies to achieve accelerated timelines without compromising safety or efficacy. Furthermore, the chapter investigates the real-world effectiveness of COVID-19 vaccines in conferring immunity against symptomatic illness, severe disease, and transmission, as well as the challenges posed by emerging variants and vaccine hesitancy. It examines the complexities of vaccine distribution and deployment, emphasizing the importance of global equity, resource mobilization, and novel delivery mechanisms to ensure equitable access for all populations. Furthermore, it also investigates the broader societal implications of COVID-19 vaccination, such as ethical concerns, public health messaging, and the restoration of trust in science and public institutions. In conclusion, the chapter summarizes key insights and future perspectives, emphasizing vaccines' indispensable role as a cornerstone strategy in navigating the complexities of the ongoing pandemic and fostering global recovery and resilience.

KEYWORDS		
COVID-19, Chemical Drugs, Control, Alternatives, Vaccine, prevention	Received: 03-Jun-2024 Revised: 16-Jul-2024 Accepted: 04-Aug-2024	A Publication of Unique Scientific Publishers

Cite this Article as: Mustafa Z, Jamil R, Naeem L, Deeba F, Aziz H, Ambrose S and Ashraf SR, 2024. Role of vaccines in controlling COVID-19 pandemic. In: Alvi MA, Rashid M, Zafar MA, Mughal MAS and Toor SI (eds), Complementary and Alternative Medicine: Immunization/Vaccinology. Unique Scientific Publishers, Faisalabad, Pakistan, pp: 267-273. https://doi.org/10.47278/book.CAM/2024.280

INTRODUCTION

The COVID-19 pandemic began in late 2019 when a new coronavirus, later named Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), emerged in Wuhan, China. The disease (called coronavirus disease COVID-19), spread rapidly around the world, resulting in millions of confirmed cases and hundreds of thousands of deaths. The World Health Organization (WHO) officially declared COVID-19 a pandemic on March 11, 2020 (Baloch et al., 2020). The exact origin of SARS-CoV-2 remains unknown, with two main hypotheses: zoonotic transmission from animals to humans or a laboratory leak. The virus may have spread from bats to an intermediary species, possibly sold at Wuhan's Huanan Seafood Market, before infecting humans. SARS-CoV-2 spread quickly after being introduced into the human population, reaching more than 194 countries by mid-2022. The virus's high transmissibility and ease of person-to-person spread aided its rapid spread (Shaikh et al., 2020). SARS-CoV-2 enters cells primarily by binding to the ACE2 receptor. Once inside the cell, the virus uses the cell machinery to replicate itself, eventually killing the cell and releasing new viral particles. Symptoms range from mild to severe, with common ones being fever, cough, fatigue, shortness of breath and loss of smell or taste (Hao et al., 2022).

Several pneumonia cases were discovered in Wuhan, China, in November 2019. These were the first COVID-19 cases associated with the novel beta-coronavirus SARS-CoV-2. The genetic information became public on January 10, 2020, 54 days after the first case was reported. The first human vaccine doses were tested on March 13, 2020, 63 days after the SARS-CoV-2 sequence was published. By September 24, 2020, the SARS-CoV-2 vaccine landscape had 43 clinical trial candidates and over 200 candidates (Zhou et al., 2019). The virus quickly spread around the globe. Many countries acted too late to implement preventive measures, resulting in a sudden increase in cases globally (Shereen et al., 2020). The virus SARS-CoV-2 was discovered to be phylogenetically similar to other bat-derived coronaviruses such as SARS-Cov-1 and MERS-CoV, confirming that bats are the virus's primary reservoir; however, the intermediate source of origin and transmission to humans is unknown (Chavez et al., 2021).

As of February 5, 2021, the SARS-CoV-2 virus had infected more than 105 million people and killed over 2.29 million people worldwide. As of February 5, 2021, the United States had over 26.7 million cases and 456,000 deaths, followed by India, which had over 10.8 million cases and 155,000 deaths (Shadin et al., 2021). COVID-19 has hurt people's health, lifestyles, and the global economy (Garcia and Cerda 2020). An extensive search for an effective drug against SARS-CoV-2 has not yielded any promising results. Hydroxychloroquine and Remdesivir have been advocated as desperate measures based on conflicting and inconclusive studies and have failed to combat the pandemic (Zhao et al., 2020). As the number of patients with COVID-19 increases, the detection, assessment and interpretation of the immune response to SARS-CoV-2 infection becomes more critical. More vaccine candidates are being developed; however, safe and effective COVID-19 vaccines are urgently needed to combat the increasing number of cases and deaths worldwide. These candidate vaccines must be developed quickly and available to all countries and populations affected by the pandemic. Vaccines can reduce disease incidence, prevent transmission, and reduce the social and economic impact of disease (Khuroo, 2020).

The virus enters cells primarily through the angiotensin-converting enzyme 2 (ACE2) receptor, causing symptoms ranging from mild to severe (Moghadas et al., 2021). Preventive measures such as vaccination, face coverings, social distancing, hand hygiene, and quarantine have been critical in limiting the virus's spread (Hafeez et al. 2020). On March 11, 2020, the World Health Organization declared COVID-19 a pandemic, affecting more than 194 countries (Bhatia and Abraham, 2021).

Significance of Vaccination in Controlling the Spread of the Virus

Vaccination has played a very vital role in reducing the extent that COVID-19 has reached by decreasing disease burden, hospitalization, and deaths. Vaccines offer personal protection and help achieve herd immunity, which is important in breaking the chains of transmission within communities (Baba et al., 2023). Indeed, studies have shown that vaccination significantly decreased the severity of illness and adverse outcomes, especially in vulnerable populations. Even though vaccines possess partial protectiveness against infection, their effectiveness is very high in preventing severe diseases and consequences (Moghadas et al., 2020).

Vaccination plays a major role in COVID-19 outbreaks, wherein vaccines are major preventive measures aimed at preventing further outbreaks. Indeed, vaccination is a mandate for developing immunity at the population level so that the virus does not spread on large scale (Okell et al., 2020). Vaccination alone will be inadequate but must be experienced with continued adherence to the NPIs of masking, hand hygiene, testing, contact tracing, and isolation of cases for their optimal effect (Hogan and Pardi 2022). The only way for a pandemic to be effectively controlled is through vaccination coupled with following the public health measures put in place. In other words, vaccination campaigns need a strong system of distribution and public health strategy for far-reaching, equitable vaccine access. It entails public trust, good communication, and sound continuous surveillance to monitor over time the effectiveness of the vaccines and to respond quickly and efficiently to emerging matters of concerns and hesitancy (Machado et al., 2022).

COVID-19 Vaccine Development

mRNA vaccine research was initiated in the early 1990s, with the use of altered mRNA, which can escape immune responses, realized in 2005 (Wu, 2020). A wealth of data has been obtained from decades of research on coronaviruses, HIV, and other viruses, guiding vaccine design strategies and blueprinting techniques for fabrication (Szabó et al., 2022). As the COVID-19 pandemic unfolded in late 2019, governments, organizations, and the private sector made a huge investment in research and development on vaccines. Previous knowledge in the field of vaccinology, coupled with new methodologies, facilitated the fast pace in which candidate vaccine development proceeded (Kuter et al., 2021). These investments led to the approval of several COVID-19 vaccines, facilitated by effective collaborations between academic institutions, pharmaceutical companies, and governments. Prominent among them are the Pfizer-BioNTech and Moderna vaccines, made with cutting-edge mRNA technology. With more accelerated processes and increased collaboration between regulators and developers, clinical trials of the COVID-19 vaccines have been conducted in record time. The U.S. Food and Drug Administration (FDA) authorized the use of two mRNA vaccines, Moderna and Pfizer-BioNTech, for emergency use (Le *et al*., 2020).

Types of COVID-19 Vaccines (e.g., mRNA, Viral Vector, Protein Subunit)

Certainly! COVID-19 vaccines are broadly classified into several types based on the technology used to create them. There are three major types: mRNA vaccines, viral vector vaccines, and protein subunit vaccines.

Vaccine Efficacy and Effectiveness

Two key parameters, vaccine efficacy, and effectiveness show an understanding of how well COVID-19 vaccines work in real-world settings in the prevention of several health outcomes (Evans and Jewell 2021). The CDC conducts observational studies to assess VE related to infection (Rosenberg et al., 2022). According to recent studies, the mRNA vaccines developed against COVID-19 were found to be effective against severe illness and death during the time of the Omicron variant. At the same time, the effectiveness of the vaccines is likely to wane over time, particularly following the primary series, which therefore underlines the importance of booster doses in protection against this disease (Link-Gelles et al., 2023).

Table 1: Types of COVID-19 Vaccines with Mechanisms and Advantages

Sr. #	Vaccine type	Examples	Mechanism	Advantage	Reference
1.	Protein subunit vaccines.	Novavax (Nuvaxovid), Sanofi-GSK.	Use harmless pieces of the virus (e.g. spike protein).	Traditional technology, standard refrigeration.	(Marchese et al., 2022).
2.	mRNA vaccines	Pfizer-BioNTech (Comirnaty), Moderna (Spikevax).	mRNA is used for instructing cells to produce spike protein.	Rapid development, no live virus used, modifiable.	(Hermosilla et al., 2023).
3.	Viral vector vaccines.	Oxford-AstraZeneca, J and J's Janssen, Sputnik V.	Modified adenovirus delivers genetic material for spike protein.	1 dose option, robust immune response.	(Vanaparthy et al., 2021).

Long-term studies have shown that effectiveness against infections and hospitalization is reduced over time. This may be due to new variants emerging. Monitoring of effectiveness is important in guiding policy decisions on timing—for example, booster doses (Wu et al., 2023). Comparing COVID-19 vaccines, an mRNA vaccine from each of Pfizer-BioNTech and Moderna showed very high efficacy against symptomatic disease. The primary series, however, is inducible in protection that wanes over time, underscoring the need for updated vaccines and booster doses in order to keep up immunity against severe outcomes (Fiolet et al., 2022).

Table 2: Efficiency and Neutralization Activity of Major COVID-19 Vaccines against Variants

Sr. #	Vaccine Name	Efficiency against variants (%)	Neutralization Activity	Reference
1.	Pfizer-BioNTech	High (95%)	Effective	(Creecy *et al*., 2024).
2.	Moderna	Strong (94%)	Sustained	(Moghadas *et al*., 2020).
3.	AstraZeneca	Varied (82%)	Moderate	(Machado *et al*., 2022).
4.	Johnson and Johnson	Varies (71%)	Varies	(Livingston *et al*., 2021).

Efficacy and effectiveness of COVID-19 Vaccines

Efficiency and effectiveness are related but different concepts that describe the performance of COVID-19 vaccines (Olliaro et al., 2021). Efficacy refers to a vaccine's ability to prevent disease in controlled trial settings, with success typically measured in terms of symptomatic infection, severe disease, and mortality rates when compared to placebo groups (He et al., 2022). In contrast, effectiveness describes a vaccine's actual impact in real-world scenarios, where variables such as vaccine distribution, compliance, and emerging strains influence the outcome (Link-Gelles, 2023). Extensive analyses revealed that COVID-19 vaccines had varying levels of efficacy and effectiveness:

The overall efficacy was reported to be approximately 66.4%, 93.6%, and 79.7% against SARS-Cov-2 infection, severe COVID-19, and symptomatic COVID-19, respectively. One-dose booster immunization demonstrated 74.5% efficacy in preventing COVID-19 caused by the Delta variant (He et al., 2022). Pfizer-BioNTech and Moderna vaccines had higher efficacy rates, with 91.2% and 98.1%, respectively (Soheili et al., 2023). These findings suggest that COVID-19 vaccines are highly protective against severe diseases and mortality, even if they do not completely prevent asymptomatic infections (He et al., 2022).

Variant Impact and Boosters

As new SARS-CoV-2 variants emerge, vaccine efficacy may decrease over time. For example, the Delta variant posed a problem to the existing vaccines because protection levels were down and booster shots had to be encouraged to restore the protection levels (He et al., 2022). Continued monitoring of the effectiveness of the vaccines allows public health agencies to adjust policies for the best possible protection of vulnerable populations.

Longitudinal Perspective

Longitudinal vaccine efficacy monitoring brings out the trend of protection over time. Several recent studies do point to the fact that effectiveness against infection and hospitalization may wane with time given the emergence of new variants, although the evidence is still accumulating (Evans and Jewell 2021).

Variants of Concern and Impact on Vaccine Efficacy

The discovery of new SARS-CoV-2 variants has opened up a wide avenue of concern about how they are going to impact the effectiveness and efficiency of COVID-19 vaccines. From studies, it is indicated that various variants impact vaccine performance with regard to preventing infection, symptomatic illness, or serious consequences. COVID-19 vaccines have different efficacies against different variants. For instance, it was established that the first dose vaccination attained the highest overall effectiveness against the Gamma variant; on the other hand, effectiveness against all variants stood at

96% overall after the second dose. After the first dose, the efficacy against the Alpha variant was considerably higher than in the case of the other variants studied by Szabó et al. (2022).

This, therefore, tracked the efficacy of the vaccines over time, showing us the trend in protection levels. In connection, studies are showing that against infections and hospitalization, the efficacy of the vaccines may actually wane with time. This may be due to the variants that are now coming up. The message, therefore, is that there has to be continuous evaluation; maybe booster doses should be taken for protection. Recent studies have assessed the estimated vaccine effectiveness during the BA.5 and Omicron BA.4 periods. The findings indicate that vaccine effectiveness in protecting against medically attended COVID-19 illness decreased with increasing time since the last dose; however, estimated effectiveness was higher after receiving booster doses compared to a primary series alone (Hafeez et al. 2020).

Common and Rare Adverse Reactions Associated with COVID-19 Vaccination

Common side effects from COVID-19 vaccination include pain, redness, and swelling at the injection site. Fever, fatigue, headache, muscle pain, chills, nausea and joint pain. The majority of these side effects are mild and temporary, resolving in a few days without intervention (Mohseni Afshar et al., 2022).

Rare but notable adverse reactions to COVID-19 vaccination include anaphylaxis, Thrombosis with thrombocytopenia syndrome (TTS), Myocarditis and pericarditis, Vasculitis, hearing loss and tinnitus, and Immune-mediated disorders.

Anaphylaxis which occurs in less than 0.0003% of recipients. Symptoms include difficulty breathing, hives and a fast heartbeat. The treatment requires immediate medical attention. Thrombosis with thrombocytopenia syndrome (TTS), a rare blood clotting disorder associated with the JandJ/Janssen vaccine, affects approximately 3.8 cases per million vaccinated individuals (Yaamika et al., 2023). Myocarditis and pericarditis (inflammation of the heart muscle or sac surrounding the heart) are most commonly seen in young males following mRNA vaccination. Vasculitis is the inflammation of blood vessels, which includes capillary leak syndrome, leukocytoclastic vasculitis, and cutaneous vasculitis. Hearing loss and tinnitus, are rarely reported (Beatty et al., 2021). Immune-mediated disorders include acquired haemophilia A, immune-mediated thrombocytopenia and Guillain-Barré syndrome (Singh et al., 2022).

The Safety Profile of COVID-19 Vaccines

The safety profile of COVID-19 vaccines has been extensively studied, revealing a wide safety margin with mostly minor and self-limiting side effects. According to studies, 3 authorized COVID-19 vaccines in the United States, Pfizer-BioNTech, Moderna, and Johnson and Johnson's Janssen, have a low frequency of side effects, with most patients experiencing mild systemic reactions such as headache and fever (Singh et al., 2022). Serious side effects such as anaphylaxis and death are extremely rare, with rates as low as 0.0003% and 0.002%, respectively. Despite the overall favorable safety profile of COVID-19 vaccines, ongoing monitoring and surveillance are required to investigate any unexpected serious adverse effects. According to reports, the benefits of COVID-19 vaccination far outweigh the potential risks associated with known side effects, which are typically mild and brief (Kai et al., 2021). Indeed, their safety profiles have been reassuring. Indeed, through extensive data analyses and further surveillance efforts, close monitoring by regulators of the safety and efficacy of the vaccines is assured.

Challenges in Vaccine Distribution and Equitable Access

The difficult issues in the settings of COVID-19 vaccine distribution and access have been outstanding. Of many challenges, the low supply and heterogeneity in the vaccine distribution process can be said to be the most important, wherein high-income countries receive a disproportionately high number of vaccine doses in comparison with the struggling LMICs to get the required amount (Bae et al., 2020). Another challenge is the lack of domestic manufacturing capacity in LMICs, which favors reliance on imported vaccines at the cost of autonomy and flexibility in the distribution. The challenges in cold chain management are specifically in the cases of delivery of such vaccines which need special conditions for handling and storage (Ye et al., 2022).

Socioeconomic factors result in vaccine hesitancy and access problems, mostly in underserved populations. Persistent misconceptions about the safety and efficacy of vaccines continue to fan the embers of vaccination resistance, which have severely vexed herd immunity efforts globally. To design cost-effective public vaccination regimes, careful consideration needs to be given to timelines for vaccine efficacy and immunity. Global and local governance is in serious need of reform to drive accountability on equitable access and vaccination. These challenges underline the pressing need for coordinated efforts to enhance vaccine distribution and equity, more so in LMICs. Such initiatives, like COVAX or regional vaccine technology and manufacturing hubs, can help to solve these problems and turn the concept of more equal sharing of vaccines globally into reality (Privor-Dumm et al., 2023).

Role of Booster Doses and Ongoing Vaccination Efforts

Booster doses and continued COVID-19 vaccination efforts are very critical in the augmentation of immunity against the pandemic. Booster doses have, therefore, become necessary in boosting immunity due to the adaptation of viruses. Updated boosters of COVID-19 show improved immunogenicity over prior vaccines, underscoring the need for heightened vigilance with tailored strategies to improve booster vaccination coverage among adults. Booster uptake varies across demographic subgroups; targeted interventions are required to improve vaccination equity. The recommendation that all adults, regardless of history of previous infection, be vaccinated with a booster dose underlined boosters' role in conferring maximum protection against COVID-19 (Lu et al., 2023).

Vaccination campaigns will reduce cases of COVID-19, hospitalization, and mortality. Indeed, they have been at the core of reducing disease severity and preventing infectivity, particularly in vulnerable populations with comorbidities. That notwithstanding, achieving wide-scale immunity through vaccination is important in the control of this pandemic; however, it requires persistent compliance with NPIs alongside vaccination efforts. At the same time, the speed of vaccine development and dissemination is unprecedented, reflecting global resolve in fighting COVID-19 through vaccination campaigns. The scale of mobilization entailed by public health resources and the application of thought-through vaccination strategies is thus, in particular, crucial to lessening disease burden and societal impact. Key among these findings is the contribution of booster doses and additional vaccination efforts toward slowing COVID-19 spread and mitigating public health repercussions. By paying attention to disparities in vaccine uptake, public health officials at all levels can help raise immunity levels toward a more effective pandemic response by implementing tailored strategies that increase coverage and underscore the role of vaccines in reducing disease severity (Moghadas et al., 2020).

Potential Impact of Vaccination on Future Control of the Pandemic

The COVID-19 vaccination campaign is a hefty potential for change both in the pandemic and protection of global public health. Vaccines are very outstanding tools in slowing down the infection and reducing its alarming consequences during nations' continuous battle with the crisis. Here is how COVID-19 vaccination might affect the control efforts of future pandemics:

First and foremost, vaccination opens the pathway to achieving herd immunity, which is defined as the point at which enough people have developed immunity to the virus, either by vaccination or previous infection, to disrupt its transmission cycle (Kassianos et al., 2022). As much as the achievement of herd immunity is quite elusive due to the complexities involved in human behavior and new viral variants cropping up, vaccination stands as a very decisive approach toward its realization. Second, vaccination reduces morbidity and mortality since cases of severe illness and deaths due to COVID-19 are significantly reduced. The strengthening of individual immunity, vaccines reduce loads on healthcare systems and thereby enable societies to return to pre-pandemic norms. Other than that, vaccination also reduces long-term complications from severe COVID-19, supporting the case for universal vaccination.

Thirdly, vaccination breaks transmission chains, slowing the virus's spread and providing room for gradual relaxation of NPIs. With increasing vaccination rates, NPIs will need modification in accordance with local epidemiology, releasing economies from a standstill and easily returning daily routines. Vaccination provides a platform for the development of novel COVID-19 therapies, particularly during the fourth phase. The study of the host-virus interaction has been very instrumental in developing anti-viral drugs and monoclonal antibodies that have the prowess to neutralize the virus and treat infected people. Globally, vaccination promotes global solidarity and cooperation; hence, people will display a united front against the pandemic. International organizations, like the WHO, work tirelessly to ensure that vaccines are rolled out and distributed equally between countries so that none is left behind in the war on COVID-19.

COVID-19 vaccination is one of the most powerful weapons in the fight against the pandemic. The vaccines have the potential to be a game-changer in the pandemic, shifting into a post-COVID period that is much safer and healthier: protection against severe diseases, reduction in transmission, and empowering the researchers to develop novel therapies (Harshani et al., 2022).

Conclusion:

It is propagated in this chapter that vaccination can play a very important role in every diversified strategy for the fight against SARS-CoV-2. Four key conclusions draw from an in-depth analysis of vaccine development, efficacy, distribution, and societal dimensions: both remarkable achievements and ongoing challenges in using vaccines to mitigate the pandemic's impact. The rapid development and deployment of the COVID-19 vaccines are an unprecedented scientific achievement, realized by a degree of collaboration, innovation, and regulatory agility to match. Real-world evidence shows vaccines reduce the burden of disease, hospitalizations, and deaths, pointing out hope where chanced uncertainty and despair had taken over the world amidst the pandemic. Therefore, it places major constraints on global vaccination disparities, second-generation variants, vaccine hesitancy, and calls for international cooperation, resource mobilization, and community engagement. Otherwise, the social dimensions of vaccination against COVID-19 stretch beyond the public health measures for responding to ethical concerns and public trust in society's road to recovery and resilience. As we come near the critical stage in pandemic responses, lessons learned from vaccines on board serve as a guiding framework for traversing these complex terrains that lie ahead. It highlights that it is not possible to forge a healthier and more resilient future without there being a continued commitment to vaccination efforts along with complementary public health measures.

REFERENCES

Baba, I. A., Humphries, U. W., and Rihan, F. A. (2023). Role of vaccines in controlling the spread of COVID-19: A fractional-order model. *Vaccines*, *11*(1), 145.

Bae, J., Gandhi, D., Kothari, J., Shankar, S., Bae, J., Patwa, P., and Raskar, R. (2020). Challenges in equitable COVID-19 vaccine distribution: A roadmap for digital technology solutions. *arXiv Preprint arXiv:2012.12263*.

Baloch, S., Baloch, M. A., Zheng, T., and Pei, X. (2020). The coronavirus disease 2019 (COVID-19) pandemic. *The Tohoku Journal of Experimental Medicine*, *250*(4), 271-278.

Beatty, A. L., Peyser, N. D., Butcher, X. E., Cocohoba, J. M., Lin, F., Olgin, J. E., and Marcus, G. M. (2021). Analysis of COVID-19 vaccine type and adverse effects following vaccination. *JAMA Network Open*, *4*(12), e2140364-e2140364.

Bhatia, R., and Abraham, P. (2021). COVID-19 vaccines and pandemic. *The Indian Journal of Medical Research*, *153*(5-6), 517.

Centers for Disease Control and Prevention. (2021). Selected adverse events reported after COVID-19 vaccination. *Google Scholar*.

Chavez, S., Long, B., Koyfman, A., and Liang, S. Y. (2021). Coronavirus Disease (COVID-19): A primer for emergency physicians. *The American Journal of Emergency Medicine*, *44*, 220-229.

Creecy, A., Awosanya, O. D., Harris, A., Qiao, X., Ozanne, M., Toepp, A. J., and McCune, T. (2024). COVID-19 and bone loss: a review of risk factors, mechanisms, and future directions. *Current Osteoporosis Reports*, 1-13.

Evans, S. J., and Jewell, N. P. (2021). Vaccine effectiveness studies in the field. *New England Journal of Medicine*, *385*(7), 650-651.

Fiolet, T., Kherabi, Y., MacDonald, C. J., Ghosn, J., and Peiffer-Smadja, N. (2022). Comparing COVID-19 vaccines for their characteristics, efficacy and effectiveness against SARS-CoV-2 and variants of concern: a narrative review. *Clinical Microbiology and Infection*, *28*(2), 202-221.

Garcia, L.Y., and Cerda, A.A. (2020). Contingent assessment of the COVID-19 vaccine. *Vaccine*, 38:5424–9.

Hafeez, A., Ahmad, S., Siddqui, S. A., Ahmad, M., and Mishra, S. (2020). A review of COVID-19 (Coronavirus Disease-2019) diagnosis, treatments and prevention. *Ejmo*, *4*(2), 116-125.

Hao, Y. J., Wang, Y. L., Wang, M. Y., Zhou, L., Shi, J. Y., Cao, J. M., and Wang, D. P. (2022). The origins of COVID-19 pandemic: A brief overview. *Transboundary and Emerging Diseases*, *69*(6), 3181-3197.

Harshani, Y., Patel, M. A., Gupta, V., Toram, B., Shubekshya, U., Nour, S., and Rohit, J. (2022). COVID-19 Vaccine Challenges in Developing and Developed Countries. *Cureus*, *14*(4).

He, X., Su, J., Ma, Y. N., Zhang, W., and Tang, S. (2022). A comprehensive analysis of the efficacy and effectiveness of COVID-19 vaccines. *Frontiers in Immunology*, *13*, 945930.

Hermosilla, J., Alonso-García, A., Salmerón-García, A., Cabeza-Barrera, J., Medina-Castillo, A. L., Pérez-Robles, R., and Navas, N. (2023). Analysing the In-Use Stability of mRNA-LNP COVID-19 Vaccines Comirnaty™ (Pfizer) and Spikevax™(Moderna): A Comparative Study of the Particulate. *Vaccines*, *11*(11), 1635.

Hogan, M. J., and Pardi, N. (2022). mRNA Vaccines in the COVID-19 Pandemic and Beyond. *Annual review of medicine*, *73*, 17-39.

Kai, X. I. N. G., Xiao-Yan, T. U., Miao, L. I. U., Liang, Z. W., Jiang-Nan, C. H. E. N., Jiao-Jiao, L. I., and Jiang, Y. (2021). Efficacy and safety of COVID-19 vaccines: a systematic review. *Chinese Journal of Contemporary Pediatrics*, *23*(3), 221.

Kassianos, G., Puig-Barberà, J., Dinse, H., Teufel, M., Türeci, Ö., and Pather, S. (2022). Addressing COVID-19 vaccine hesitancy. *Drugs in Context*, *11*.

Khuroo, M.S. (2020). Chloroquine and hydroxychloroquine in coronavirus disease 2019 (COVID-19). Facts, fiction and the hype: a critical appraisal. *International Journal Antimicrobiology Agents*, 56:10610

Kuter, B. J., Offit, P. A., and Poland, G. A. (2021). The development of COVID-19 vaccines in the United States: Why and how so fast?. *Vaccine*, *39*(18), 2491.

Le, T. T., Andreadakis, Z., Kumar, A., Román, R. G., Tollefsen, S., Saville, M., and Mayhew, S. (2020). The COVID-19 vaccine development landscape. *National Review Drug Discovery*, *19*(5), 305-306.

Link-Gelles, R. L. (2023). COVID-19 vaccine effectiveness updates.

Link-Gelles, R., Levy, M. E., Natarajan, K., Reese, S. E., Naleway, A. L., Grannis, S. J., and Tenforde, M. W. (2023). Estimation of COVID-19 mRNA vaccine effectiveness and COVID-19 illness and severity by vaccination status during Omicron BA. 4 and BA. 5 sublineage periods. *JAMA Network Open*, *6*(3), e232598-e232598.

Livingston, E. H., Malani, P. N., and Creech, C. B. (2021). The Johnson and Johnson Vaccine for COVID-19. *Jama*, *325*(15), 1575-1575.

Lu, P. J., Srivastav, A., Vashist, K., Black, C. L., Kriss, J. L., Hung, M. C., and Singleton, J. A. (2023). COVID-19 Booster Dose Vaccination Coverage and Factors Associated with Booster Vaccination among Adults, United States, March 2022. *Emerging Infectious Diseases*, *29*(1), 133.

Machado, B. A. S., Hodel, K. V. S., Fonseca, L. M. D. S., Pires, V. C., Mascarenhas, L. A. B., da Silva Andrade, L. P. C., and Badaró, R. (2022). The importance of vaccination in the context of the COVID-19 pandemic: a brief update regarding the use of vaccines. *Vaccines*, *10*(4), 591.

Marchese, A. M., Beyhaghi, H., and Orenstein, W. A. (2022). With established safe and effective use, protein vaccines offer another choice against COVID-19. *Vaccine*.

Moghadas, S. M., Vilches, T. N., Zhang, K., Wells, C. R., Shoukat, A., Singer, B. H., and Galvani, A. P. (2021). The impact of vaccination on coronavirus disease 2019 (COVID-19) outbreaks in the United States. *Clinical Infectious Diseases*, *73*(12), 2257-2264.

Moghadas, S. M., Vilches, T. N., Zhang, K., Wells, C. R., Shoukat, A., Singer, B. H., and Galvani, A. P. (2020). The impact of vaccination on COVID-19 outbreaks in the United States (preprint).

Mohseni Afshar, Z., Tavakoli Pirzaman, A., Liang, J. J., Sharma, A., Pirzadeh, M., Babazadeh, A., and Ebrahimpour, S. (2022). Do we miss rare adverse events induced by COVID-19 vaccination?. *Frontiers in Medicine*, *9*, 933914.

Okell, L. C., Verity, R., Watson, O. J., Mishra, S., Walker, P., Whittaker, C., and Bhatt, S. (2020). Have deaths from COVID-19 in Europe plateaued due to herd immunity?. *The Lancet*, *395*(10241), e110-e111.

Olliaro, P., Torreele, E., and Vaillant, M. (2021). COVID-19 vaccine efficacy and effectiveness—the elephant (not) in the room. *The Lancet Microbe*, *2*(7), e279-e280.

Privor-Dumm, L., Excler, J. L., Gilbert, S., Karim, S. S. A., Hotez, P. J., Thompson, D., and Kim, J. H. (2023). Vaccine access, equity and justice: COVID-19 vaccines and vaccination. *BMJ Global Health*, *8*(6), e011881.

Rosenberg, E. S., Dorabawila, V., Easton, D., Bauer, U. E., Kumar, J., Hoen, R., and Zucker, H. A. (2022). Covid-19 vaccine effectiveness in New York state. *New England Journal of Medicine*, *386*(2), 116-127.

Shadin, N. S., Sanjana, S., and Farzana, M. (2021, September). Automated detection of COVID-19 pneumonia and non COVID-19 pneumonia from chest X-ray images using convolutional neural network (CNN). In *2021 2nd International Conference on Innovative and Creative Information Technology (ICITech)* (pp. 57-63). IEEE.

Shaikh, S. S., Jose, A. P., Nerkar, D. A., Vijaykumar Kv, M., and Shaikh, S. K. (2020). COVID-19 pandemic crisis—a complete outline of SARS-CoV-2. *Future Journal of Pharmaceutical Sciences*, *6*, 1-20.

Shereen, M. A., Khan, S., Kazmi, A., Bashir, N., and Siddique, R. (2020). COVID-19 infection: Emergence, transmission, and characteristics of human coronaviruses. *Journal of Advanced Research*, *24*, 91-98.

Singh, A., Khillan, R., Mishra, Y., and Khurana, S. (2022). The safety profile of COVID-19 vaccinations in the United States. *American journal of infection control*, *50*(1), 15-19.

Soheili, M., Khateri, S., Moradpour, F., Mohammadzedeh, P., Zareie, M., Mortazavi, S. M. M., and Moradi, Y. (2023). The efficacy and effectiveness of COVID-19 vaccines around the world: a mini-review and meta-analysis. *Annals of Clinical Microbiology and Antimicrobials*, *22*(1), 1-14.

Szabó, G. T., Mahiny, A. J., and Vlatkovic, I. (2022). COVID-19 mRNA vaccines: Platforms and current developments. *Molecular Therapy*.

Vanaparthy, R., Mohan, G., Vasireddy, D., and Atluri, P. (2021). Review of COVID-19 viral vector-based vaccines and COVID-19 variants. *Le Infezioni in Medicina*, *29*(3), 328.

Wu, N., Joyal-Desmarais, K., Ribeiro, P. A., Vieira, A. M., Stojanovic, J., Sanuade, C., and Bacon, S. L. (2023). Long-term effectiveness of COVID-19 vaccines against infections, hospitalisations, and mortality in adults: findings from a rapid living systematic evidence synthesis and meta-analysis up to December, 2022. *The Lancet Respiratory Medicine*, *11*(5), 439-452.

Wu, S. C. (2020). Progress and concept for COVID-19 vaccine development. *Biotechnology Journal*, *15*(6).

Yaamika, H., Muralidas, D., and Elumalai, K. (2023). Review of adverse events associated with COVID-19 vaccines, highlighting their frequencies and reported cases. *Journal of Taibah University Medical Sciences*.

Ye, Y., Zhang, Q., Wei, X., Cao, Z., Yuan, H. Y., and Zeng, D. D. (2022). Equitable access to COVID-19 vaccines makes a life-saving difference to all countries. *Nature Human Behaviour*, *6*(2), 207-216.

Zhao, J., Zhao, S., Ou, J., Zhang, J., Lan, W., Guan, W., and Zhang, Q. (2020). COVID-19: coronavirus vaccine development updates. *Frontiers in immunology*, *11*, 602256.

Zhu, N., Zhang, D., Wang, W., Li, X., Yang, B., Song, J andTan, W. (2020). A novel coronavirus from patients with pneumonia in China, 2019. *New England journal of medicine*, *382*(8), 727-733.