

## THE FUTURE OF COVID 19-A REVIEW

Mrs. Mangal S. Gaikwad\*<sup>1</sup>, Ms. Deshmukh Aishwarya Shahaji\*<sup>2</sup>,

Mr. Ajinkya Anna Kavitke\*<sup>3</sup>, Mr. Pranav Deepak Gawari\*<sup>4</sup>, Ms. Aliya Pinjari\*<sup>5</sup>

\*<sup>1</sup>Associate Professor Pharmacognosy Delight College Of Pharmacy, Koregaon Bhima, Pune, Maharashtra, India.

\*<sup>2,3,4,5</sup>B.Pharmacy, Delight College Of Pharmacy, Koregaon Bhima, Pune, Maharashtra, India.

### ABSTRACT

The COVID-19 pandemic has impacted individuals, families, and communities for well over a year, and has brought light to how a broad range of social, economic, and historically relevant factors take massive tolls on the health and well-being of underserved communities around the world. This literature review aims to bring light to the current landscape of vaccines, disparities that exist in COVID-19 response, the historical relevance of the ongoing pandemic, and what needs to be accomplished for a more prepared response to potential future pandemics. It will be shown that as the world continues become more interconnected, amplification of international cooperation and well-funded response organizations are imperative to provide more equitable care in future health crises. The synthesis of current research will be helpful to researchers analyzing historical trends in the COVID-19 pandemic and individuals interested in better understanding and advocating for underserved communities across the globe.

**Keywords:** COVID-19 Vaccine, Social Determinants, Health Equity.

### I. INTRODUCTION

In December 2019, the World Health Organization (WHO) China Country Office was informed of a group of cases of pneumonia of unknown etiology identified in Wuhan City, Hubei Province, China [1]. By early January 2020, Chinese authorities identified the cause of these pneumonia cases as a new coronavirus. This novel coronavirus was later named severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) and its infectious syndrome was named by the WHO, Coronavirus Disease 2019 (COVID-19). Even with significant measures taken to contain the virus, SARS-CoV-2 rapidly spread across Eastern and Southeastern Asia, and then on to every continent in the world. To date, after over a year and a half of lockdowns, strict travel restrictions, and 3.7 billion vaccines administered, SARS-CoV-2 has claimed the lives of over 4.1 million people worldwide [2]. While the exact efficacy of vaccines preventing transmission of SARS-CoV-2 is still unclear, there is strong evidence demonstrating the protective nature of the major vaccines in use against severe symptomatic COVID-19 [[3], [4], [5]]. With the potential of vaccinated individuals to asymptotically acquire COVID-19 and transmit it on to those around them, herd immunity will require close to the entire population receiving vaccines. Unfortunately, government responses and access to vaccination vary drastically country to country; this inequity opens the door to long term socioeconomic, and health disparities that could create further inequity between various communities across the world.

This literature review aims to bring light to the current landscape of vaccines, disparities that exist in COVID-19 response, the historical relevance of the global pandemic, and what needs to be accomplished for a more prepared response to potential future pandemics.

#### Vaccine protection and efficacy

Candidate vaccines primarily act against infection, disease, or transmission: a vaccine capable of reducing any of these factors would be valuable in contributing to the control of COVID-19 spread [6]. In this regard, many vaccines have demonstrated a strong case for implementation and a variety of vaccines are already in use including: Pfizer-BioNTech, Moderna, AstraZeneca-University of Oxford, Johnson & Johnson (J&J) Janssen, Russia's Sputnik, Sinovac Life Sciences, and Novavax (Table 1). However upon development of each of these vaccines, public perception heavily focused on published efficacy rates especially with the Pfizer-BioNTech mRNA vaccine leading the way with 95% efficacy in preventing COVID-19 infection. That number can be misleading to the general public, especially when compared to other vaccines such as the J&J vaccine that reported ~70% efficacy rate [7]. In calculating the Pfizer vaccine's efficacy, it is important to note that Pfizer did not test respiratory specimen of their subjects until after they demonstrated at least one of the following

symptoms: fever, new/increased cough, new/increased shortness of breath, chills, new/increased muscle pain, loss of taste or smell, sore throat, diarrhea, or vomiting [4]. This exception is noteworthy because Pfizer's vaccine may not necessarily prevent 95% of patients from becoming infected or transmitting COVID-19: the data simply speaks to the vaccine's ability to minimize symptoms and severe cases [4]. Unlike some other vaccines, Pfizer's initial vaccine data was heavily based off of subjects living in the United States with 130 of their 152 vaccination/testing sites based in the United States [4]. These limitations suggest that other vaccines with low efficacy rates could potentially be comparably useful depending on the context. Additionally, it highlights that every vaccine manufacturer had its own process of determining vaccine efficacy. The raw efficacy scores published by different manufacturers may not all translate to real world use in the same ways. It has been well documented that the genome of SARS-COV-2 is highly susceptible to mutations that result in genetic drift and different strains seen across the world [8]. This variability means any of the vaccines in use could be highly efficacious for certain strains of SARS-CoV-2 and not for others.

Comparison of clinical endpoints between vaccinated and unvaccinated groups through randomized controlled trails would be the most efficient study design for demonstrating vaccine efficacy. Unfortunately, all the accepted vaccines in use rely on natural exposure to SARS-CoV-2 or laboratory identification of neutralizing antibodies in titer experiments for identifying vaccine efficacy: such a reliance creates an emphasis on the test subjects' demographics, and the region of the world the subjects live in. While large enough sample sizes can account for differences in age (e.g. older volunteers may pre-emptively be more carefully quarantining), profession (e.g. healthcare workers may have heavier exposures than other professions), and other demographic risk factors (e.g. comorbidities, lifestyle, etc.), the rise of regional SARS-CoV-2 variants poses a significant hurdle for the scientific community as larger variants of the spike protein could escape vaccine-induced antibodies [20]. Head-to-head comparisons of different vaccines' efficacy becomes increasingly difficult given each was developed and tested at different periods of the epidemic (different rates of infection), with different populations of experimental subjects, and are represented with efficacies that are calculated differently. Evidence is still limited regarding how efficacious the available COVID-19 vaccines will be compared to each other against different variants. Studies directly comparing the health outcomes of large but related populations of people will be required to have confirmatory comparisons between the various vaccines. In the meantime, each of the vaccines significantly reduces the rate of hospitalizations and death from COVID-19 [[3], [4], [5],7,9,10,17]. This suggests that for communities struggling to gain access to the more expensive vaccines with higher published efficacy rates, vaccines with lower published efficacy rates will provide better protection than having access to no vaccines at all. Many low- and middle-income countries (LMIC) face this dilemma and logically continue to procure vaccines that have a lower published efficacy rate.

In December 2019, the World Health Organization (WHO) China Country Office was informed of a group of cases of pneumonia of unknown etiology identified in Wuhan City, Hubei Province, China [1]. By early January 2020, Chinese authorities identified the cause of these pneumonia cases as a new coronavirus. This novel coronavirus was later named severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) and its infectious syndrome was named by the WHO, Coronavirus Disease 2019 (COVID-19). Even with significant measures taken to contain the virus, SARS-CoV-2 rapidly spread across Eastern and Southeastern Asia, and then on to every continent in the world. To date, after over a year and a half of lockdowns, strict travel restrictions, and 3.7 billion vaccines administered, SARS-CoV-2 has claimed the lives of over 4.1 million people worldwide [2]. While the exact efficacy of vaccines preventing transmission of SARS-CoV-2 is still unclear, there is strong evidence demonstrating the protective nature of the major vaccines in use against severe symptomatic COVID-19 [[3], [4], [5]]. With the potential of vaccinated individuals to asymptotically acquire COVID-19 and transmit it on to those around them, herd immunity will require close to the entire population receiving vaccines. Unfortunately, government responses and access to vaccination vary drastically country to country; this inequity opens the door to long term socioeconomic, and health disparities that could create further inequity between various communities across the world.

This literature review aims to bring light to the current landscape of vaccines, disparities that exist in COVID-19 response, the historical relevance of the global pandemic, and what needs to be accomplished for a more prepared response to potential future pandemics.

### **Vaccine protection and efficacy**

Candidate vaccines primarily act against infection, disease, or transmission: a vaccine capable of reducing any of these factors would be valuable in contributing to the control of COVID-19 spread [6]. In this regard, many vaccines have demonstrated a strong case for implementation and a variety of vaccines are already in use including: Pfizer-BioNTech, Moderna, AstraZeneca-University of Oxford, Johnson & Johnson (J&J) Janssen, Russia's Sputnik, Sinovac Life Sciences, and Novavax (Table 1). However upon development of each of these vaccines, public perception heavily focused on published efficacy rates especially with the Pfizer-BioNTech mRNA vaccine leading the way with 95% efficacy in preventing COVID-19 infection. That number can be misleading to the general public, especially when compared to other vaccines such as the J&J vaccine that reported ~70% efficacy rate [7]. In calculating the Pfizer vaccine's efficacy, it is important to note that Pfizer did not test respiratory specimen of their subjects until after they demonstrated at least one of the following symptoms: fever, new/increased cough, new/increased shortness of breath, chills, new/increased muscle pain, loss of taste or smell, sore throat, diarrhea, or vomiting [4]. This exception is noteworthy because Pfizer's vaccine may not necessarily prevent 95% of patients from becoming infected or transmitting COVID-19: the data simply speaks to the vaccine's ability to minimize symptoms and severe cases [4]. Unlike some other vaccines, Pfizer's initial vaccine data was heavily based off of subjects living in the United States with 130 of their 152 vaccination/testing sites based in the United States [4]. These limitations suggest that other vaccines with low efficacy rates could potentially be comparably useful depending on the context. Additionally, it highlights that every vaccine manufacturer had its own process of determining vaccine efficacy. The raw efficacy scores published by different manufacturers may not all translate to real world use in the same ways. It has been well documented that the genome of SARS-CoV-2 is highly susceptible to mutations that result in genetic drift and different strains seen across the world [8]. This variability means any of the vaccines in use could be highly efficacious for certain strains of SARS-CoV-2 and not for others.

Comparison of clinical endpoints between vaccinated and unvaccinated groups through randomized controlled trails would be the most efficient study design for demonstrating vaccine efficacy. Unfortunately, all the accepted vaccines in use rely on natural exposure to SARS-CoV-2 or laboratory identification of neutralizing antibodies in titer experiments for identifying vaccine efficacy: such a reliance creates an emphasis on the test subjects' demographics, and the region of the world the subjects live in. While large enough sample sizes can account for differences in age (e.g. older volunteers may pre-emptively be more carefully quarantining), profession (e.g. healthcare workers may have heavier exposures than other professions), and other demographic risk factors (e.g. comorbidities, lifestyle, etc.), the rise of regional SARS-CoV-2 variants poses a significant hurdle for the scientific community as larger variants of the spike protein could escape vaccine-induced antibodies [20]. Head-to-head comparisons of different vaccines' efficacy becomes increasingly difficult given each was developed and tested at different periods of the epidemic (different rates of infection), with different populations of experimental subjects, and are represented with efficacies that are calculated differently. Evidence is still limited regarding how efficacious the available COVID-19 vaccines will be compared to each other against different variants. Studies directly comparing the health outcomes of large but related populations of people will be required to have confirmatory comparisons between the various vaccines. In the meantime, each of the vaccines significantly reduces the rate of hospitalizations and death from COVID-19 [[3], [4], [5],7,9,10,17]. This suggests that for communities struggling to gain access to the more expensive vaccines with higher published efficacy rates, vaccines with lower published efficacy rates will provide better protection than having access to no vaccines at all. Many low- and middle-income countries (LMIC) face this dilemma and logically continue to procure vaccines that have a lower published efficacy rat

## **II. CONCLUSION**

With COVID-19 having affected individuals, families, and communities for well over a year and a half, we have seen the development of a broad range of social, economic, and historically relevant factors already taking massive tolls on the health and well-being of underserved communities around the world. While many questions do remain regarding the future of the COVID-19 pandemic, the current progression of world-wide infection rates and vaccination inequity raise many concerns. The wide range of vaccines available to individuals and communities world-wide have no in-depth studies comparing their real-world efficacies under a standardized metric. Wealthier nations could be receiving significantly more effective vaccines, or those same

nations may be wasting resources in prioritizing more fragile mRNA vaccines when they could instead utilize the extra funding to assist under-resourced communities beyond their borders. On the other end of the spectrum, LMIC could be on track to face dire repercussions as seen in major epidemics of the past as a result of vaccine nationalism on the part of HIC and slow global response to disease. This could be accentuated if the more readily available vaccines with lower published efficacy rates do not provide the same protection against severe disease long term as compared to the mRNA vaccines being more prominently used in HIC. Current community health safety and international leadership standards have failed to prevent continued virus transmission and death. Inequitable vaccine deployment, vaccine hesitancy, variable vaccine efficacy, and poor international cooperation all directly put LMIC at greater risk for long-term economic challenges, health disparities, and stunted growth and development.

### III. REFERENCES

- [1] World Health Organization Novel coronavirus (2019-nCoV), situation report-1 WHO, Geneva (2020) Google Scholar
- [2] World Health Organization WHO coronavirus (COVID-19) dashboard (2021) <https://covid19.who.int/> Google Scholar
- [3] L.R. Baden, H.M. el Sahly, B. Essink, K. Kotloff, S. Frey, R. Novak, et al. Efficacy and safety of the mRNA-1273 SARS-CoV-2 vaccine *N Engl J Med*, 384 (2021), 10.1056/NEJMoa2035389 View article Google Scholar
- [4] F.P. Polack, S.J. Thomas, N. Kitchin, J. Absalon, A. Gurtman, S. Lockhart, et al. Safety and efficacy of the BNT162b2 mRNA Covid-19 vaccine *N Engl J Med*, 383 (2020), 10.1056/NEJMoa2034577 View article Google Scholar
- [5] C. Liu, H.M. Ginn, W. Dejnirattisai, P. Supasa, B. Wang, A. Tuekprakhon, et al. Reduced neutralization of SARS-CoV-2 B.1.617 by vaccine and convalescent serum *Cell* (2021), 10.1016/j.cell.2021.06.020 View PDF Google Scholar
- [6] S.H. Hodgson, K. Mansatta, G. Mallett, V. Harris, K.R.W. Emary, A.J. Pollard What defines an efficacious COVID-19 vaccine? A review of the challenges assessing the clinical efficacy of vaccines against SARS-CoV-2 *Lancet Infect Dis*, 21 (2021), 10.1016/S1473-3099(20)30773-8 View PDF Google Scholar
- [7] J. Sadoff, M. Le Gars, G. Shukarev, D. Heerwegh, C. Truyers, A.M. de Groot, et al. Interim results of a phase 1–2a trial of Ad26.COV2.S Covid-19 vaccine *N Engl J Med* (2021), 10.1056/NEJMoa2034201 View article Google Scholar
- [8] T. Koyama, D. Weeraratne, J.L. Snowden, L. Parida Emergence of drift variants that may affect COVID-19 vaccine development and antibody treatment *Pathogens*, 9 (2020), 10.3390/pathogens9050324 View article Google Scholar
- [9] I. Jones, P. Roy Sputnik V COVID-19 vaccine candidate appears safe and effective *Lancet*, 397 (2021), 10.1016/S0140-6736(21)00191-4 View PDF Google Scholar
- [10] Y. Zhang, G. Zeng, H. Pan, C. Li, Y. Hu, K. Chu, et al. Safety, tolerability, and immunogenicity of an inactivated SARS-CoV-2 vaccine in healthy adults aged 18–59 years: a randomised, double-blind, placebo-controlled, phase ½ clinical trial *Lancet Infect Dis*, 21 (2021), 10.1016/S1473-3099(20)30843-4 View PDF Google Scholar
- [11] O. Dyer Covid-19: countries are learning what others paid for vaccines *BMJ* (2021), 10.1136/bmj.n281 View article Google Scholar
- [12] M. Terry Comparing COVID-19 vaccines: timelines, types and prices *BioSpace* (2021) <https://www.biospace.com/article/comparing-covid-19-vaccines-pfizer-biontech-moderna-astrazeneca-oxford-j-and-j-russia-s-sputnik-v/> Google Scholar
- [13] J.L. Bernal, N. Andrews, C. Gower, E. Gallagher, R. Simmons, S. Thelwall, et al. Effectiveness of COVID-19 vaccines against the B.1.617.2 variant *MedRxiv* (2021), 10.1101/2021.05.22.21257658 2021.05.22.21257658 View article Google Scholar
- [14] S. Ikegame, M.N.A. Siddiquey, C.-T. Hung, G. Haas, L. Brambilla, K.Y. Oguntuyo, et al. Qualitatively distinct modes of Sputnik V vaccine-neutralization escape by SARS-CoV-2 Spike variants *MedRxiv* (2021), 10.1101/2021.03.31.21254660 2021.03.31.21254660 View article Google Scholar

- [15] W. Dejnirattisai, D. Zhou, P. Supasa, C. Liu, A.J. Mentzer, H.M. Ginn, et al. Antibody evasion by the brazilian P.1 strain of SARS-CoV-2 *BioRxiv* (2021), 10.1101/2021.03.12.4351942021.03.12.435194 View article Google Scholar
- [16] A. Choi, M. Koch, K. Wu, G. Dixon, J. Oestreich, H. Legault, et al. Serum neutralizing activity of mRNA-1273 against SARS-CoV-2 variants *BioRxiv* (2021), 10.1101/2021.06.28.4499142021.06.28.449914 View article Google Scholar
- [17] P.T. Heath, E.P. Galiza, D.N. Baxter, M. Boffito, D. Browne, F. Burns, et al. Safety and efficacy of NVX-CoV2373 Covid-19 vaccine *N Engl J Med* (2021), 10.1056/NEJMoa2107659 View article Google Scholar
- [18] K. Katella Comparing the COVID-19 vaccines: how are they different? *Yale Medicine*, New Haven (2021) Google Scholar
- [19] G. Alter, J. Yu, J. Liu, A. Chandrashekar, E.N. Borducchi, L.H. Tostanoski, et al. Immunogenicity of Ad26.COV2.S vaccine against SARS-CoV-2 variants in humans *Nature* (2021), 10.1038/s41586-021-03681-2 View PDF Google Scholar
- [20] E. Volz, V. Hill, J.T. McCrone, A. Price, D. Jorgensen, Á. O'Toole, et al. Evaluating the effects of SARS-CoV-2 spike mutation D614G on transmissibility and pathogenicity *Cell*, 184 (2021), 10.1016/j.cell.2020.11.020 View PDF Google Scholar
- [21] S.P. Kaur, V. Gupta COVID-19 vaccine: a comprehensive status report *Virus Res*, 288 (2020), 10.1016/j.virusres.2020.198114 View article Google Scholar
- [22] S.L. Wilson, C. Wiysonge Social media and vaccine hesitancy *BMJ Glob Health*, 5 (2020), 10.1136/bmjgh-2020-004206 View article Google Scholar
- [23] R.M. Viner, S.J. Russell, H. Croker, J. Packer, J. Ward, C. Stansfield, et al. School closure and management practices during coronavirus outbreaks including COVID-19: a rapid systematic review *Lancet Child Adolesc Health*, 4 (2020), 10.1016/S2352-4642(20)30095-X View PDF Google Scholar
- [24] J.V. Lazarus, S.C. Ratzan, A. Palayew, L.O. Gostin, H.J. Larson, K. Rabin, et al. A global survey of potential acceptance of a COVID-19 vaccine *Nat Med*, 27 (2021), 10.1038/s41591-020-1124-9
- [25] World Health Organization Behavioural considerations for acceptance and uptake of COVID-19 vaccines WHO, Geneva (2020) Google Scholar
- [26] L.J. Finney Rutten, X. Zhu, A.L. Leppin, J.L. Ridgeway, M.D. Swift, J.M. Griffin, et al. Evidence-based strategies for clinical organizations to address COVID-19 vaccine hesitancy *Mayo Clin Proc*, 96 (2021), 10.1016/j.mayocp.2020.12.024 View article Google Scholar
- [27] A. Clark, M. Jit, C. Warren-Gash, B. Guthrie, H.H.X. Wang, S.W. Mercer, et al. Global, regional, and national estimates of the population at increased risk of severe COVID-19 due to underlying health conditions in 2020: a modelling study *Lancet Glob Health*, 8 (2020), 10.1016/S2214-109X(20)30264-3 View PDF Google Scholar
- [28] D.P. Fidler Negotiating equitable access to influenza vaccines: global health diplomacy and the controversies surrounding avian influenza H5N1 and pandemic influenza H1N1 *PLoS Med*, 7 (2010), 10.1371/journal.pmed.1000247 View article Google Scholar
- [29] J.H. Kim, P. Hotez, C. Batista, O. Ergonul, J.P. Figueroa, S. Gilbert, et al. Operation Warp speed: implications for global vaccine security *Lancet Glob Health* (2021), 10.1016/S2214-109X(21)00140-6 View PDF Google Scholar
- [30] J. Guzman, T. Hafner, L.A. Maiga, U. Giedion COVID-19 vaccines pricing policy options for low-income and middle-income countries *BMJ Glob Health*, 6 (2021), 10.1136/bmjgh-2021-005347 View article Google Scholar
- [31] T. McCoy, H. Traiano One disease. Two Brazils *Washington Post* (2020) Google Scholar
- [32] J. Hopkins, J. Córdoba de Pfizer identifies fake Covid-19 shots abroad as criminals exploit vaccine demand *Wall Street J* (2021) Google Scholar
- [33] O. Sharma, A.A. Sultan, H. Ding, C.R. Triggles A review of the progress and challenges of developing a vaccine for COVID-19 *Front Immunol*, 11 (2020), 10.3389/fimmu.2020.585354 View article Google Scholar

- 
- [34] C. Çakmaklı, S. Demiralp, Kalemli-Özcan Şebnem, S. Yeşiltaş, M. Yıldırım The economic case for global vaccinations: an epidemiological model with international production networks National Bureau of Economic Research, Cambridge, MA (2021) Google Scholar
- [35] I. Ferreira, R. Datir, S. Kemp, G. Papa, P. Rakshit SARS-CoV-2 B.1.617 emergence and sensitivity to vaccine-elicited antibodies bioRxiv, Cambridge (2021) Google Scholar
- [36] Gavi The Vaccine Alliance COVID-19 vaccine global access (COVAX) facility (2020) Google Scholar
- [37] D. McAdams, K.K. McDade, O. Ogbuaji, M. Johnson, S. Dixit, G. Yamey Incentivising wealthy nations to participate in the COVID-19 Vaccine Global Access Facility (COVAX): a game theory perspective BMJ Glob Health, 5 (2020), 10.1136/bmjgh-2020-003627 View article Google Scholar
- [38] Y. Yang, F. Peng, R. Wang, K. Guan, T. Jiang, G. Xu, et al. The deadly coronaviruses: the 2003 SARS pandemic and the 2020 novel coronavirus epidemic in China J Autoimmun, 109 (2020), 10.1016/j.jaut.2020.102434 View PDF Google Scholar
- [39] J.K. Taubenberger, D.M. Morens 1918 Influenza: the mother of all pandemics Emerg Infect Dis, 12 (2006), 10.3201/eid1201.050979 View article Google Scholar
- [40] H.D. Gayle, G.L. Hill Global impact of human immunodeficiency virus and AIDS Clin Microbiol Rev, 14 (2001), 10.1128/CMR.14.2.327-335.2001