The SARS-CoV-2 Pandemic: What are the Limits and Promises of Technical Mitigation Instruments Available to Humanity?

Yu-An Huang

Indooroopilly State High School, Brisbane, Australia

Abstract. The SARS-CoV-2 pandemic has brought unprecedented attention to the effectiveness and reliability of technical containment tools. Given the high mobility and frequent transcontinental travel in the modern world, we are in uncharted territory with the catastrophic effects of the COVID -19 pandemic and many more to come. Therefore, prevention, detection, and treatment tools are of utmost importance. These tools include diagnostics, drugs, and vaccines. The inequity caused by these medical tools will be briefly presented, but the main focus of the essay will be on the importance of the promise and limitations of these tools. Public health countermeasures and scientific countermeasures go hand in hand in combating the SARS-CoV-2 pandemic. To successfully combat COVID -19 and the next Disease X pandemic, the effectiveness and accuracy of technical tools to contain the virus are critical parameters.

Keywords: SARS-CoV-2, treatment tools.

1. Introduction

The COVID -19 pandemic is caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), which has infected more than 597 million people worldwide and killed at least 6.46 million (data retrieved from https://ourworldindata.org/). It has far-reaching social, economic, and political implications around the world. Although virulence varies among variants, the case fatality rate (CFR) is relatively low compared with SARS. Because of its highly infectious but not as deadly nature, an outbreak became an epidemic, which evolved into a pandemic. Some countries are now in the post-Covid 19 phases, but some are still fighting the virus (as of August 2022).

2. Diagnostics

To halt the spread of SARS-CoV-2, accurate rapid tests and access to these tools should be reliable and universal. Critical diagnostics provide information on local epidemiology and allow contact testing and tracing of confirmed cases. Due to the nature of the COVID -19 virus, asymptomatic patients may unknowingly transmit the disease to others, making tracing difficult and leading to underreporting of confirmed cases. This explicitly explains the importance of conducting extensive testing to contain the SARS-CoV-2 pandemic, regardless of the presence of symptoms.

The three predominant techniques are nucleic acid amplification tests (PCR/NAATs), antigen testing, and antibody/serological testing. Artificial nose technology, nanomaterial-based multiplex sensors, and the E-Nose Device from NASA are examples of revolutionary diagnostics that have been shown to be reliable but are not yet in widespread use and therefore will be discussed only briefly. The goal of diagnostics is to become faster, more reliable, safer, and less expensive.

The 'gold standard' for viral detection - nucleic acid amplification technology (NAAT) based on polymerase chain reaction (PCR) In the acute phase of a viral infection, viral RNA can be detected in swab samples from the nasopharynx and oropharyngeal space. Genetic material is extracted from the samples and a complementary strand is produced from the viral RNA using reverse transcriptase. Although the nucleic acid amplification test is considered the 'gold standard', false-positive and false-negative results still occur. Detection of viral RNA after recovery does not necessarily indicate an infectious state, nor does prolonged detection of viral RNA necessarily indicate viral persistence. NAATs are usually performed in large, biosafety laboratories with expensive machines and trained professionals, resulting in relatively high costs and a large amount of time. It is currently the most common diagnostic method used by hospitals worldwide to diagnose COVID -19. According to the

Centers for Disease Control and Prevention (CDC) in the United States, NAATs can detect very low levels of SARS-CoV-2 RNA in a sample, making them highly sensitive for the diagnosis of COVID -19 (Chau, et al., 2020).

The most widely used of the three dominant techniques is the antigen test. Although of limited value as an epidemiologic tool because it is often subject to inaccurate results and has lower sensitivity and specificity, it is still clinically useful because of its rapidity. Its inaccuracy is due to its rapid nature. The development of antibodies against viral antigens is often difficult and time-consuming. Quality controls are necessary to ensure specificity and sensitivity. They cannot detect all active infections, so the likelihood of false-negative results is higher than with other alternatives. At home, rapid antigen tests are now widely used and likely positive cases are not reported to authorities, so the number of confirmed cases is unreliable and therefore cannot be taken at face value. (Schildgen, et al., 2021).

The third predominant technique is antibody (or serological) testing. These tests detect the presence of SARS-CoV-2 antibodies produced by the body's humoral immune system. Antibody tests can also determine the different stages (in terms of time) that the patient is in by detecting the antibodies that the patient has. For example, IgA and IgM antibodies can be detected as early as 5 days after a new infection, while they appear in higher concentrations in the weeks that follow. IgG antibodies are another indicator that the patient is ill 7-14 days after infection. Recent studies have suggested that the detection of antibodies can be used as an indicator of the stage of COVID -19 progression to help guide the treatment of the disease. Limitations of antibody testing include false-positive results because they vary in specificity and sensitivity and may detect previous infections with other coronaviruses. False-negative results may also occur because antibodies may not have formed in the early stages of infection. (Robinson, et al., 2022).

3. Medication

As of February 2020, no specific antiviral treatment has been developed for coronavirus infections. Antiviral drugs developed against other viruses are being used against COVID -19, but efficacy can only be determined in randomized, controlled clinical trials. Clinical trials are essential to determine the benefits and risks of drugs against SARS-CoV-2 (Stahlmann, et al., 2020). Beyond standard supportive care, no specific agent is recommended for therapeutic use. Drugs such as chloroquine, remdesivir, hydroxychloroquine, lopinavir, arbidol, rh-ACE2, and others have been selected in clinical trials for the prevention and treatment of COVID -19 in countries such as the United Kingdom, the United States, and China. Effective pharmacotherapy can significantly reduce the mortality of COVID -19 (Stahlmann, et al., 2020).

Drugs used to prevent and treat the disease can be broadly divided into antivirals, antiviral monoclonal antibodies, anti-inflammatory drugs, and monoclonal antibodies. During the SARS-CoV-2 pandemic, the urgent goal is to alleviate the severe damage caused by the virus with antiviral and anti-inflammatory drugs or monoclonal antibodies.

Remdesivir is a drug that has been approved for the wave of COVID -19 patients due to the urgent need (Beigel, et al., 2020). It is an antiviral drug that interrupts the ability of the virus to replicate and spread in the body. Although it is recommended for patients who are hospitalized and require oxygen, it is not recommended for patients who are mechanically ventilated. Despite its approval, insufficient data were available to study the impact of remdesivir on mortality in subgroups defined by ventilatory support at baseline. In addition, the drug is in short supply worldwide, and many health care facilities have limited quantities.

Chloroquine and hydroxychloroquine are FDA-approved drugs for the treatment or prevention of malaria and other diseases. A recent study showed that they are widely available, safe, inexpensive, and effective in preclinical studies for viral infections. They have shown potential for their future use against COVID -19, but high-quality clinical data from different geographic areas are still urgently

needed. In addition, the National Institutes of Health (NIH) discourages the use of these drugs because their dangerous side effects could worsen patients' conditions.

Monupiravir is an antiviral drug with anti-RNA polymerase activity and is currently being studied for the treatment of COVID -19 patients. Based on animal studies, it has shown efficacy against COVID -19, but well-designed randomized clinical trials are needed in the future to confirm the therapeutic effect of monupiravir in COVID -19 patients.

4. Vaccines

The use of vaccines in the prevention, control, and elimination of infectious diseases is considered one of the most effective strategies. The SARS-CoV-2 pandemic has highlighted the importance of vaccination for global health. Although public health officials do not develop vaccines, they must understand the process of vaccine discovery, testing, optimization, trial, and licensure because vaccine availability, quality, efficacy, and safety are critical public health knowledge. As the following chart shows, the development of the COVID -19 vaccine has accelerated at an unprecedented pace.

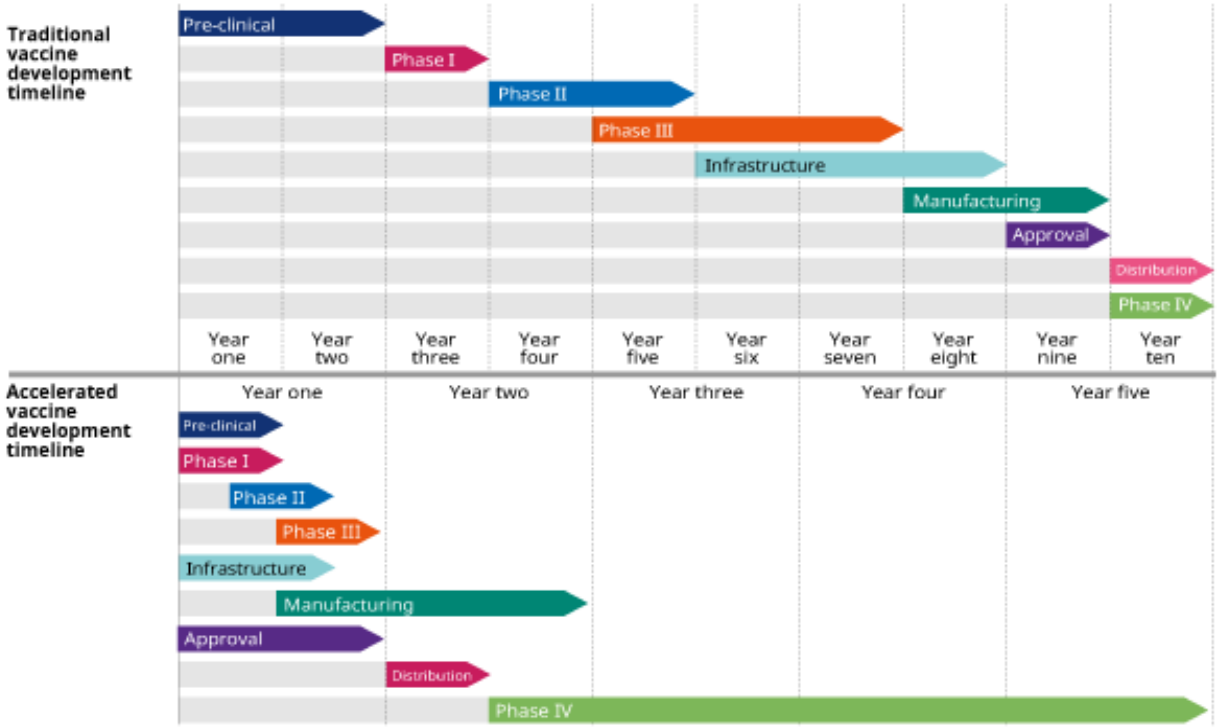

Figure 1. COVID-19 vaccine development is accelerating

There are three main approaches to developing a vaccine of any kind, and this is also true for Covid-19 vaccines. The three approaches differ in whether they use a whole virus or bacterium, just the parts of the germ that trigger the immune system, or just the genetic material that instructs the body to produce certain proteins, rather than the whole virus.

The first approach is the whole microbe approach. This includes inactivated vaccines that use the whole inactivated or attenuated virus, such as the Coronavac vaccine. This approach is also used in influenza and polio vaccines. The limitation of these vaccines is their relatively long production time, as they require specialized laboratory facilities to safely grow the virus or bacterium. Two to three doses are required for administration. The second type of the first approach, which mimics a natural infection, is the administration of specific subparts (proteins) of the germ of interest. Viral vector vaccines include ChAdOx1 nCoV-2019, Sputnik, and JNJ-78436735, which can elicit an immune response without causing disease. The safe virus, which serves as a vector to deliver the protein into the body, is provided with specific parts of the pathogen of interest. Viral vector vaccines often have

a more complicated manufacturing process. There is also a risk of genomic integration, and pre-existing immunity to the vector may dampen the immune response. Having attracted considerable attention for more than a decade in cancer and infectious diseases, mRNA-based therapeutics have now emerged as an effective prevention strategy against SARS-CoV-2 infections. The second approach is the genetic approach. Nucleic acid vaccines use a section of genetic material that contains instructions for specific proteins as DNA or RNA, rather than the entire microbe. The nucleic acid approach, particularly the development of ribonucleic acid (RNA)-based vaccines, is relatively new but is now the most promising and well-studied approach to producing safe and effective new vaccines. RNA-based vaccines first became available in response to the SARS-CoV-2 pandemic at the population level. This highlights the importance of having a safe, flexible, and scalable vaccine available for the prevention of epidemic outbreaks or, more catastrophically, pandemics. Immunogenization with mRNA has several advantages for vaccine development, such as lower cost, the absence of cell culture, and the ability to combine different targets. It is of great importance since both BNT162b2 and mRNA-1273 used this approach and showed high reliability in terms of efficacy against infections. Despite its advantages, mRNA technology still faces some critical challenges to improve its stability, delivery, and potential to generate the appropriate protein needed to elicit humoral and T cell-mediated immune responses.

The third approach is the subunit approach. This type of vaccine uses only specific subunits of a bacterium or virus that the immune system must recognize. Neither the entire microbe nor vectors are needed. Novavax's COVID -19 vaccine is a protein subunit vaccine. NVX-CoV2373 (Novavax) is a SARS-CoV-2 subunit vaccine made from the full-length SARS-CoV-2 spike glycoprotein.

Studies have found that vaccination prior to global vaccination with Covid-19 vaccines could lead to a decrease in the case fatality rate (CFR) with increased testing capacity. This is because vaccinated individuals can still become infected but develop less severe symptoms than unvaccinated individuals. However, the CFR can be misleading, especially when used to assess the effectiveness of vaccines in reducing deaths or the spread of the virus.

Currently, about 16 billion vaccine doses have been administered and about 4.9 billion people (62.9% of the world's population) are fully vaccinated. However, the doses administered are not the same in all countries. The new SARS-CoV-2 pandemic is considered one of the worst pandemics in history and has divided the world into two blocks - those with vaccines and those without. The disparities, inequities, and distribution of Covid-19 vaccines show that the limitations of technical containment tools are not limited to technological and biological aspects, but there are also unequal differences between countries due to their economies and development. Approximately half of the world's population lacks access to basic health facilities, as noted in reports by WHO and the World Bank (2017). Their situation has been exacerbated by the Covid 19 pandemic. With underfunded medical facilities, shortages of doctors, paramedical staff, medical infrastructure, vaccines, and medicines, combating the virus became an even greater challenge. The COVAX program was launched by WHO when it was recognized that the COVID -19 vaccine was not accessible or affordable in developing countries. COVAX is the vaccine pillar of the Access to COVID -19 Tools (ACT) Accelerator. The original intent was to make COVID -19 vaccines available to all countries, especially the 92 low-income countries within 100 days of 2021. By December 2021, 75% of all vaccinations will be administered by 10 countries, while 130 countries will not have received even a single dose of COVID -19 vaccine. UN Foreign Minister Antonio Guterres stated that vaccine equity is the greatest moral test for the global community. As of April 2021, about 86% of doses have been administered in high- and middle-income countries, while low-income countries have been able to administer only 0.1%. This shows that the gap between rich and poor countries is widening. In addition to eradicating disease and addressing the challenges posed by new and emerging health problems, global health governance mechanisms should also address the challenges posed by new and emerging health problems. Inequities and inequities, as well as other aspects of accessibility and affordability, should also be prioritized to address health inequities in the Global South. "No one is safe until everyone is safe" is the slogan of WHO on this issue. (Upadhyay, et al., 2021).

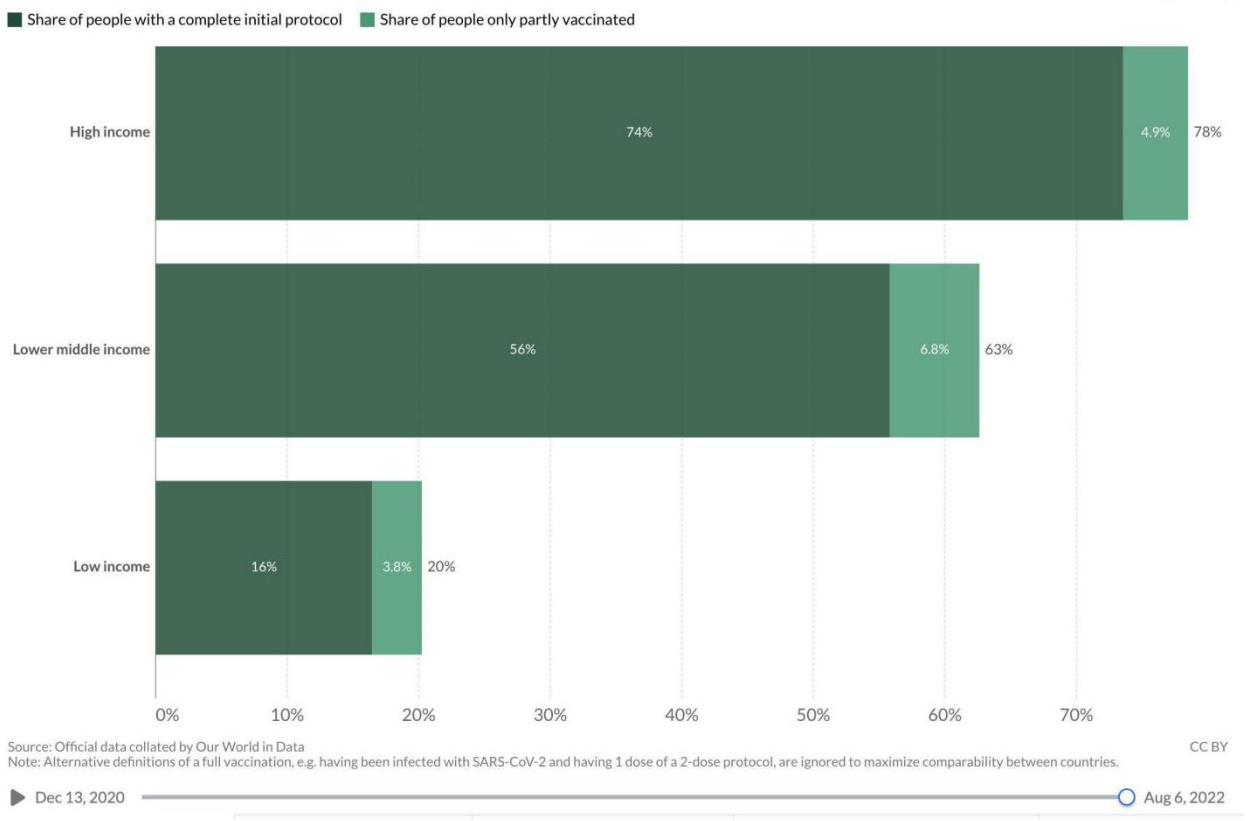

Figure 2. Share of people vaccinated against COVID-19,Aug 6,2022

5. Limitations (by emerging variants)

Viruses inherently have the ability to mutate into different variants (Caldwell, et al. 2021). The coronavirus genome consists of approximately 30,000 bases, making it the longest known plus-stranded RNA. Due to high genetic variability, new variants are constantly emerging. SARS-CoV-2 is a beta coronavirus that belongs to the Coronaviridae family. The emergence of its variants-B.1.1.7 (alpha), B.1.351 (beta), P1 (gamma), and B.1.617.2 (delta)-has further exacerbated the challenge of containing the spread of the virus. Its variants have shown increased transmissibility, morbidity, and mortality (Vasireddy, et al., 2021). They are also capable of evading detection by available diagnostic tests (as of May 2021). Their emergence underscores the need for changes in the form of diagnostic methods that are more adaptable for detecting SARS-CoV-2 infection. Variants may change the dynamics of transmission and mortality. Tests could become unreliable over time or in different locations if the tests look for viral characteristics that have been rendered obsolete by evolution. Given the alarming frequency with which variants of SARS-CoV-2 are emerging, questions arise about the efficacy of existing vaccines.

The importance of genomic surveillance is underscored by the variability of SARS-CoV-2. Genomic surveillance significantly mitigates the threat posed by mutants, as the information could allow authorities to implement new countermeasures to combat the spread of the disease more effectively. Identifying new mutants as soon as possible is a public health imperative. (Raman, et al., 2021).

6. Future Development and Goals

The speed with which the technical tools to contain SARS-CoV-2 have evolved has been extraordinary, but still needs to be improved to successfully contain the virus. This section examines the goals of each effort and the likely direction of its future development.

Diagnosis serves as the basis for rational, measured public health action. Traditional diagnostic methods such as PCR, antigen testing, and antibody testing are too costly, difficult to obtain, and insensitive. Revolutionized diagnostics such as the E-Nose Device from NASA are still in the experimental stage and not yet at the forefront. Diagnostics should become faster, more reliable, safer, and less costly.

Effective treatments suppress deaths and mitigate the severe damage done by SARS-Cov-2 with antiviral and anti-inflammatory drugs or monoclonal antibodies. There are no preventive drugs yet. A breakthrough in antiviral therapeutics could prevent catastrophic pandemics when vaccines are no longer effective, provide us with an alternative way out of the pandemic crisis, and will be critical for the management of endemic COVID -19.

Effective vaccination neutralizes the threat and restores people to normal social and economic activity. Although the speed with which COVID -19 vaccines were developed was unprecedented, the speed with which variants emerged followed closely. The major vaccines in widespread use all have good safety, immunogenicity, and efficacy against infection with early variants of SARS-CoV-2 but have been weakened by the emergence of variants such as Omicron. Vaccines are now focusing on efficacy to protect vulnerable patients from very severe diseases. This underscores the importance of genomic surveillance and the development of a pan-coronavirus vaccine, which is the holy grail for public health because it can neutralize entire families of viruses and all their mutants and is now a major focus of research.

If therapeutic interventions ultimately become ineffective, nations unable or unwilling to avail themselves of and enforce non-therapeutic interventions could see a resurgence in morbidity and mortality due to COVID -19.

The global community should also focus on equity in the distribution of vaccines around the world. As WHO said, no one is safe until everyone is safe. Regions already lacking health care would be further burdened by the presence of SARS-CoV-2. Combating the pandemic is a global task, and no country should be left out.

7. Conclusion

The COVID-19 pandemic has taught us indelible lessons, one of which is the urgency of the development of mitigation instruments to successfully tackle the current pandemic and in preparation for the next Disease X. Prevention, detection, detection, and treatment are all important aspects to completely tackle SARS-CoV-2. It is evident that our current technical mitigation instruments have shown limitations in our current pandemic and would be unable to mitigate the next Disease-X. Thus, the development of these instruments garners the focus of ongoing research.

References

[1] Andrews, N., Stowe, J., Kirsebom, F., Toffa, S., Rickeard, T., Gallagher, E., Gower, C., Kall, M., Groves, N., O'Connell, A.-M., Simons, D., Blomquist, P. B., Zaidi, A., Nash, S., Iwani Binti Abdul Aziz, N., Thelwall, S., Dabrera, G., Myers, R., Amirthalingam, G., … Lopez Bernal, J. (2022). Covid-19 vaccine effectiveness against the Omicron (b.1.1.529) variant. *New England Journal of Medicine*, *386* (16), 1532 – 1546. https://doi.org/10.1056/nejmoa2119451.

[2] Beigel, J. H., Tomashek, K. M., Dodd, L. E., Mehta, A. K., Zingman, B. S., Kalil, A. C., Hohmann, E., Chu, H. Y., Luetkemeyer, A., Kline, S., Lopez de Castilla, D., Finberg, R. W., Dierberg, K., Tapson, V., Hsieh, L., Patterson, T. F., Paredes, R., Sweeney, D. A., Short, W. R., … Lane, H. C. (2020). Remdesivir for the treatment of covid-19 — final report. *New England Journal of Medicine*, *383* (19), 1813 – 1826. https: //doi.org/10.1056/nejmoa2007764.

[3] Binagwaho, A., Mathewos, K., & Davis, S. (2021). Time for the ethical management of covid-19 vaccines. *The Lancet Global Health*, *9* (8). https: //doi.org/10.1016/s2214-109x (21) 00180 - 7.

[4] Bollyky, T. J., Gostin, L. O., & Hamburg, M. A. (2020). The equitable distribution of Covid-19 Therapeutics and vaccines. *JAMA*, *323*(24), 2462. https: //doi.org/10.1001/jama.2020.6641.

[5] Caldwell, J. M., Le, X., McIntosh, L., Meehan, M. T., Ogunlade, S., Ragonnet, R., O'Neill, G. K., Trauer, J. M., & McBryde, E. S. (2021). Vaccines and variants: Modelling insights into emerging issues in COVID-19 epidemiology. *Paediatric Respiratory Reviews, 39*, 32–39. https://doi.org/10.1016/j.prrv.2021.07.002.

[6] Centers for Disease Control and Prevention. (n.d.). *Nucleic acid amplification tests (NAATs)*. Centers for Disease Control and Prevention. Retrieved August 24, 2022, from https://www.cdc.gov/coronavirus/2019-ncov/lab/naats.html#:~:text=Amplifying%20those%20nucleic%20acids%20enables,of%20SARS%2DCoV%2D2.

[7] Chau, C. H., Strope, J. D., & Figg, W. D. (2020). Covid-19 clinical diagnostics and testing technology. *Pharmacotherapy: The Journal of Human Pharmacology and Drug Therapy*, *40*(8), 857–868. https://doi.org/10.1002/phar.2439.

[8] di Lego, V., Sánchez-Romero, M., & Prskawetz, A. (2022). The impact of covid-19 vaccines on the case fatality rate: The importance of monitoring breakthrough infections. *International Journal of Infectious Diseases*, *119*, 178–183. https://doi.org/10.1016/j.ijid.2022.03.059.

[9] Huang, Y., Yang, C., Xu, X.-feng, Xu, W., & Liu, S.-wen. (2020). Structural and functional properties of SARS-COV-2 spike protein: Potential antivirus drug development for covid-19. *Acta Pharmacologica Sinica*, *41*(9), 1141–1149. https: //doi.org/10.1038/s41401 - 020 - 0485 - 4.

[10] Hu, E. COVID-19 Testing: Challenges, Limitations, and Suggestions for Improvement. Preprints 2020, 2020040155 (doi: 10.20944/preprints202004. 0155.v1).

[11] Jayk Bernal, A., Gomes da Silva, M. M., Musungaie, D. B., Kovalchuk, E., Gonzalez, A., Delos Reyes, V., Martín-Quirós, A., Caraco, Y., Williams-Diaz, A., Brown, M. L., Du, J., Pedley, A., Assaid, C., Strizki, J., Grobler, J. A., Shamsuddin, H. H., Tipping, R., Wan, H., Paschke, A., … De Anda, C. (2022). Molnupiravir for oral treatment of covid-19 in non-hospitalized patients. *New England Journal of Medicine*, *386* (6), 509 – 520. https://doi.org/10.1056/nejmoa2116044.

[12] Liu, G., & Rusling, J. F. (2021). Covid-19 antibody tests and their limitations. *ACS Sensors*, *6*(3), 593–612. https://doi.org/10.1021/acssensors.0c02621.

[13] Machado BAS; Hodel KVS; Fonseca LMDS; Mascarenhas LAB; Andrade LPCDS; Rocha VPC; Soares MBP; Berglund P; Duthie MS; Reed SG; Badaró R; (n.d.). *The importance of RNA-based vaccines in the fight against COVID-19: An overview*. Vaccines. From https://pubmed.ncbi.nlm.nih.gov/34835276/.

[14] McCarthy, N., & Richter, F. (2021, February 2). *Infographic: How effective are the COVID-19 vaccines?* Statista Infographics. Retrieved August 24, 2022, from https://www.statista.com/chart/23510/estimated-effectiveness-of-covid-19-vaccine-candidates/.

[15] Qasem, A., Shaw, A. M., Elkamel, E., & Naser, S. A. (2021). Coronavirus disease 2019 (COVID-19) diagnostic tools: A focus on detection technologies and limitations. *Current Issues in Molecular Biology*, *43*(2), 728–748. https://doi.org/10.3390/cimb43020053.

[16] Raman, R., Patel, K. J., & Ranjan, K. (2021). Covid-19: Unmasking emerging SARS-COV-2 variants, vaccines, and therapeutic strategies. *Biomolecules*, *11* (7), 993. https://doi.org/10.3390/biom11070993.

[17] Stahlmann, R., & Lode, H. (2020). Medication for COVID-19—an overview of approaches currently under study. *Deutsches Ärzteblatt International*. https://doi.org/10.3238/arztebl.2020.0213.

[18] Upadhyay, P., Mehmood, Q., Jabbar, A., Ullah, I., Siddiqi, A. R., & Tahir, M. J. (2021). Disproportionate coronavirus disease 2019 (COVID-19) vaccine distribution—a great threat to low- and middle-income countries. *Infection Control & Hospital Epidemiology*, 1–2. https://doi.org/10.1017/ice.2021.320.

[19] Vasireddy, D., Vanaparthy, R., Mohan, G., Malayala, S. V., & Atluri, P. (2021). Review of covid-19 variants and COVID-19 vaccine efficacy: What the clinician should know? *Journal of Clinical Medicine Research*, *13*(6), 317–325. https://doi.org/10.14740/jocmr4518.

[20] World Health Organization. (n.d.). *The different types of covid-19 vaccines*. World Health Organization.