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REVIEW

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# SARS-CoV-2 and its variants of concern including Omicron: A never ending pandemic

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## Abstract

The ongoing COVID-19 pandemic caused by SARS-CoV-2 is associated with high morbidity and mortality. This zoonotic virus has emerged in Wuhan of China in December 2019 from bats and pangolins probably and continuing the human-to-human transmission globally since last two years. As there is no efficient approved treatment, a number of vaccines were developed at an unprecedented speed to counter the pandemic. Moreover, vaccine hesitancy is observed that may be another possible reason for this never ending pandemic. In the meantime, several variants and mutations were identified and causing multiple waves globally. Now the safety and efficacy of these vaccines are debatable and recommended to determine whether vaccines are able to interrupt transmission of SARS-CoV-2 variant of concern (VOC). Moreover, the VOCs continue to emerge that appear more transmissible and less sensitive to virus-specific immune responses. In this overview, we have highlighted various drugs and vaccines used to counter this pandemic along with their reported side effects. Moreover, the preliminary data for the novel VOC "Omicron" are discussed with the existing animal models.

**KEYWORDS**

animal models, drugs and vaccines, SARS-CoV-2 VOCs, vaccine effectiveness, vaccine hesitancy, vaccine side effects

  

## 1 | INTRODUCTION

The unwanted COVID-19 outbreak after its possible emergence from Wuhan Seafood market of China, spread to the whole world, and has taken millions of people under its cover with successive hits (Abdalla et al., 2021; Mohapatra, Das, et al., 2020; Mohapatra et al., 2021a, 2021b; Mohapatra & Rahman, 2021). As reported, the causative virus (SARS-CoV-2) emergence from bats and pangolins. After its possible emergence on December 31, 2019, the disease is with us since last two years and putting the healthcare establishments under tremendous pressure (Mohapatra et al., 2021c; Pal et al., 2022). The virus and its variants normally affect the respiratory system with common symptoms breathing difficulties, cough, fatigue, and fever. It may also relate to neurological complications including loss of smell, taste, and also cerebrovascular disorders. However, it is still unclear that whether the neurological complications are due to the viral infections or the consequence of immune reactions (Alonso-Bellido et al., 2021). COVID-19 is causing severe complications in immunocompromised persons with diabetes, cardiovascular disorders, obesity, psychiatric disorder, or organ transplant history (Arumugam et al., 2020). As reported, it may also affect kidneys, heart, liver, gut, nervous system, and finally progresses to multiple organ damage (Dhama et al., 2020). Furthermore, the pandemic has devastated the stock and financial markets, and the global economy dramatically (Lenzen et al., 2020; Nicola et al., 2020).

The emergence of large numbers of variants and mutations of SARS-CoV-2 is not only responsible for life loss but also affect various educational, cultural, and socioeconomic activities (Mohapatra et al., 2021d, 2021e; Mohapatra, Pintilie, et al., 2020). The variants, such as Alpha (B.1.1.7), Beta (B.1.351), Delta (B.1.617.2), Gamma (P.1), Epsilon (B.1.427/B.1.1429), Eta (B.1.525), Zeta (P.2), Iota (B.1.526), Theta (P3), and Kappa (B.1.617.1), were identified previously in multiple waves of this pandemic (Choudhary et al., 2021; Mohapatra, Sarangi, et al., 2022). Now, the recent variant of concern (VOC) B.1.1.529 (Omicron) was identified from South Africa and Botswana (Choudhary et al., 2021; Mohapatra, Sarangi, et al., 2022). This new variant has large number of mutations, which are concerning. As there is no efficient approved treatment, the world is going to observe another wave of this outbreak soon if not we are wrong. The Omicron wave is observed very differently in most countries as compared to the prior waves of this pandemic (Arnaout & Arnaout, 2022). As per another recent study, initially the Omicron wave has an exponential-like growth rate and will show small resurgences in the month of April and June in Northern and Southern Hemisphere countries, respectively (Huang et al., 2022). Moreover, the safety and efficacy of the current vaccines against the VOCs of SARS-CoV-2 is debatable (Suvvari et al., 2021; Uddin et al., 2021). The COVID-19 vaccination program must be supported worldwide, especially in countries with low vaccination rate, which will be an effective strategy for preventing the virus circulation as well as the emergence of its novel VOCs (Islam et al., 2022; Mattiuzzi & Lippi, 2022). The COVID-19 case fatality rate is not fixed but it changes with population, time, and other socioeconomic factors along with the mitigatory efforts of the countries (Ghayda et al., 2022). In some regions, vaccine hesitancy is observed which may be another possible reason for this never ending pandemic. In this overview, we have highlighted various drugs and vaccines used to counter this pandemic. The vaccine safety, hesitancy, and vaccine-related side effects are also discussed herewith to make a complete understanding. Furthermore, we have also discussed the preliminary data for the novel VOC Omicron and the existing animal models for easy understanding.

## 2 | MATERIALS AND METHOD

The data were collected from authentic academic databases, such as Scopus, PubMed, Web of Science, and Google Scholar, along with some public and government health organization websites including the World Health Organization (WHO), and Centre for Disease Control and Prevention (CDC) resources. After literature search covering 2020–2022, the obtained data were carefully examined, and only the relevant studies/reports were considered for critical discussion. As per the initial search, 284 articles/data found, out of which 150 articles/data were selected for further analysis based on the specific inclusion and exclusion criteria. The most relevant and critical literature was given preference, and the obtained data were used to develop this specific area review.

## 3 | RESULTS AND DISCUSSION

### 3.1 | COVID-19 drugs

The COVID-19 pandemic is playing its game since last two years and taking millions of lives and livelihood. There is no efficient approved treatment strategy (drugs), and emergence of multiple variants along with large number of mutations is a matter of concern. A number of repurposing drugs and steroids are commonly used to treat the disease. However, some serious side effects are observed as listed in Table 1. Recently, microbiota-related coinfections were also documented in COVID-19 patients. WHO has recently recommended

**TABLE 1** Used COVID-19 drugs, their mechanism of action, side effects, and clinical trial results

| Drug name | Type of drug | Mechanism of action | Clinical trial results | Common Side effects |
|---|---|---|---|---|
| Molnupiravir | Antiviral Oral Pill (Merck and co's official release, 2021) | Molnupiravir is a ribonucleoside analogue. It inhibits the replication of nuclear matter of SARS-COV−2 variants (Merck and co's official release, 2021) | Interim analysis, Phase 3 of trail, it reduced hospitalization or death risk by around 50%. 7.3% patients receiving molnupiravir were either hospitalized or died (through Day 29) compared with 14.1% placebo-treated patients. Approved by FDA (Merck and co's official release, 2021) | Headache, Nausea, Rhinorrhea (Painter et al., 2021) |
| Fluvoxamine | Selective Serotonin Reuptake inhibitor (SSRI) | Platelets lack serotonin producing enzymes. When thrombosis occurs, platelets utilize serotonin from plasma during thrombosis and promote neutrophil recruitment. SSRIs decrease serotonin reuptake and thus decreasing neutrophil recruitment and decrease cytokine storm. Fluvoxamine also acts on mast cells and reduce histamine release, thus reducing cytokine storm in COVID patients (Sukhatme et al., 2021) | In a double-blind Placebo-controlled Clinical Trial, with total 152 patients, out of which 80 were given Fluvoxamine whereas, 72 received placebo. 1.25% of patients (1/80) that received Fluvoxamine reported serious adverse events like low oxygen saturation fever, pneumonia etc., whereas 8.32% of patients that received placebo (6/72) reported serious adverse events (U.S. National library, 2021a) | Headache, Gastroenteritis, dehydration |
| Ivermectin | Antiparasitic drug | Ivermectin is an inhibitor of nuclear transport of viral proteins. It blocks the interaction between IMPs and potential target cellular proteins (Zena et al., 2021) | In a randomized control trial with 400 patients,by day 21, 82% of ivermectin group were relieved of COVID symptoms when compared to 79% in placebo groups (López-Medina et al., 2021) | |
| Remdesivir | Antiviral drug | The active form of remdesivir is a nucleoside analog. It inhibits RNA dependent RNA polymerase activity in SARS-COV−2 (Kokic et al., 2021) | In a randomized control trail with 584 patients, 191 patients had 5-day remdesivir course, 193 of them had 10-day remdesivir course and 200 patients had standard of care treatment. There were 9 deaths,out of which 2deaths are from 5-day remdesivir group,3 from 10-day remdesivir group and 4 from SOC group (Spinner et al., 2020) | Hypokalemia, Headache, Nausea (Spinner et al., 2020) |
| Tocilizumab | Interleukin−6 receptor inhibitor | Tocilizumab can bind to both mIL−6R and sIL−6R. And inhibit classical and trans-signals. Also inhibit interleukin and thus decrease the cytokine storm (Zhang et al., 2020) | In a randomized control trail with 438 patients, 143 were given placebo, whereas 295 were given tocilizumab. Mortality after 28 days in the group that received tocilizumab was 24.41% (72/295), whereas it was 25.51% (36/143) in patients receiving placebo (U.S. National library, 2021b) | Serious skin infections, Headache, Nausea. |

(Continues)

TABLE 1 (Continued)

| Drug name | Type of drug | Mechanism of action | Clinical trial results | Common Side effects |
|---|---|---|---|---|
| Favipiravir | Antiviral drug | Favipiravir selectively inhibits RNA-dependent RNA polymerase of SARS-COV−2 virus and thus inhibiting its replication (Furuta et al., 2017) | Based on a meta-analysis on 6 different surveys, a significant clinical improvement in the favipiravir group versus the control group noticed during 7 days after hospitalization (RR = 1.24, 95% CI: 1.09–1.41; $p = 0.001$, I2 = 0.0%, $p = 0.939$) (Hassanipour et al., 2021) | Hyperuricemia, Teratogenicity, Diarrhea (Sheppard et al., 2017) |
| Dexamethasone | Corticosteroid | Dexamethasone inhibits proinflammatory genes that encode for inflammatory markers like chemokines, cytokines and cell adhesion molecules [CAM] and thus reducing the cytokine storm that occurs during COVID−19 viral invasion (Ahmed & Hassan, 2020; Burugu et al., 2020) | In a randomized control trail a total of 2104 patients with COVID−19 were assigned to receive dexamethasone, whereas 4321 were assigned to receive usual care. A total of 482 patients (22.9%) from dexamethasone group and 1,110 patients (25.7%) from the usual care group died within 28 days after randomization (The RECOVERY Collaborative Group, 2021) | Appetite, mood changes, agitation And headache (Ahmed & Hassan, 2020) |
| Methylprednisolone | Corticosteroid | Methylprednisolone interrupts the cytokine cascade, inhibits the activation of T cell, decreases extravasation of immune cells to central nervous system, and thus decreases the inflammatory effects in COVID patients (Sloka & Stefanelli, 2005) | In a randomized control trail, a total of 83 COVID patients were given methylprednisolone whereas 90 patients were not exposed to methylprednisolone. Out of them,9 patients(10.84%) from methylprednisolone group died, whereas 24 patients(26.67%) died from the non-exposed to methylprednisolone group (U.S. National library, 2021c) | Agitation, Hyperglycemia, Transaminase elevation (U.S. National library, 2021c) |
| Bamlanivimab | Monoclonal antibodies | Bamlanivimab binds to the receptor binding site of spike protein of SARS-COV2, blocking the spike protein prevents it from binding to human ACE2 receptors. (Abramowicz et al., 2021; Suvvari, 2020) | In a randomized control trail with 403 patients, the rate of 30-day hospitalization in COVID patients who received Bamlanivimab was 7.3%, whereas it was 20% in patients who did not receive Bamlanivimab (Rebecca et al., 2021) | Dizziness, Nausea, Headache, Diarrhea |
| 2-DG | Antimetabolite, Anticancer drug. | 2-DG binds to the binding site of SARS-COV2 and inactivates its binding site, thus preventing it (Mantha et al., 2021) | In a phase 3 clinical trial conducted on 220 COVID patients, 42% of patients improved symptomatically and became free from depending on oxygen supplementation, whereas 32% of patients improved symptomatically in the placebo group (Ministry of Defence, 2021) | Elevated blood glucose levels, Lethargy, Progressive weight loss. |

two new drugs to treat COVID-19 patients (WHO, 2022). An oral drug, namely, baricitinib, has been strongly recommended for the severe and critical COVID-19 patients. It is a class of JAK inhibitors and recommended to use with corticosteroids and suppress the overstimulation of immune system. The second drug sotrovimab (monoclonal antibody drug) has also recommended by WHO for moderate COVID-19 patients having high risk of hospitalization (older, immunocompromised, and unvaccinated). Vaccines and antivirals protect the people against severe COVID-19 disease manifestations and complications. In this context, the emergency use of two antivirals, namely, molnupiravir and nirmatrelvir, has been approved, which may reduce disease progression by 30% and 89%, respectively, with 5 days use (Soriano et al., 2022). The commonly used drugs, their mechanism of action, and clinical trial results are also reported in Table 1.

## 3.2 | COVID-19 vaccines

The COVID-19 caused by the novel SARS-CoV-2 has been in existence in the last two years after its discovery in December 2019, in Wuhan, China. The COVID-19 is continuing to cause severe morbidity and mortality throughout the world. The WHO has been evaluating the results of the safety and efficacy of vaccines that are currently under different stages of clinical development. More than 10 COVID-19 vaccines have been approved by the WHO for emergency use application (EUA). However, there is widespread hesitancy regarding the vaccine safety, and uncertainty on the efficacy of the available vaccines (Table 2). Moreover, the vaccines that have been currently approved have not completed the phase III clinical trials.

Most countries have been plagued by the vaccine hesitancy problem, wherein people are hesitating to take the vaccines considering fears over both short-term and long-term safety concerns. The long-term safety of the vaccines would certainly require further extensive observational studies that could contribute to improved acceptance of the vaccines. Among the vaccines that are currently available, more than 70% efficacy was noted except for the Ad26.COV2·S vaccine developed by the Janssen pharmaceutical, USA, that revealed 66.9% efficacy as evidenced by the results of phase III clinical trials (Sadoff et al., 2021). More than 90% vaccine efficacy was noted among the Sputnik V, mRNA-1273/Moderna, and BNT162b2/Pfizer/BioNTech vaccines (Baden et al., 2021; Logunov et al., 2021; Polack et al., 2020). The vaccine adverse events (AE) were noted in all the vaccines and were mild, self-limited, and required no hospitalization. Common AE's notes were injection site pain, fatigue, myalgia, chills, and nausea. More serious AE's notes with the administration of BNT162b2/Pfizer/BioNTech vaccine included lymphadenopathy, herpes zoster, appendicitis, myocarditis, Facial palsy, among others (Barda et al., 2021).

Although more than 80% of the infections were asymptomatic, mild, and self-limiting, geriatric age patients and people with underlying chronic diseases either succumbed or needed ICU treatment and extended hospitalizations. Due to the novelty of the virus, there were no antiviral agents, and most initial therapeutic interventions were taking the help of repurposed drugs, convalescent sera, and monoclonal antibodies to manage serious cases of COVID-19. After the discovery, manufacture, approval, and availability of vaccines, people throughout the world are being vaccinated. However, the vaccination by the novel mRNA carrying the spike protein using a viral vector had caused uncertainty over the efficacy and safety of vaccination that resulted in widespread vaccine hesitancy. This is because most vaccine candidates that were approved for emergency use by the WHO, USFDA, and local regulatory authorities were still under phase III of clinical trials and not much data on the vaccine candidate's safety, efficacy, and long-term consequences were available in the public domain.

## 3.3 | COVID-19 vaccine side effects

The vaccine side effects normally play a crucial role in public confidence on vaccine and its uptake process. Riad, Pokorná, et al. (2021), have carried out a cross-sectional survey to understand the COVID-19 vaccine side effects following the Pfizer–BioNTech vaccine among the Czech Republic healthcare workers. The study reported injection site pain (89.8%) and fatigue (62.2%) along with headache (45.6%), muscle pain (37.1%), and chills (33.9%) as most common side effects. These side effects were observed among 43-year-old group people for one day (45.1%) or three days (35.8%) after vaccination. Antihistamine is the commonly used drug for side effects, and recommended for further investigation. The people having two doses of vaccine were generally associated with higher frequency of side effects.

Bangladesh started its COVID-19 vaccine administration in early 2021. Jahan et al. (2021) have evaluated the side effects shown by the Bangladeshi residents after receiving Oxford-AstraZeneca's Covishield vaccine first dose. This study was conducted on 474 vaccine recipients with both online and offline questionnaires from March to April 2021 and the data were analyzed using SPSS. Headache, fever, pain at the injection site, myalgia, and fatigue were the commonly reported symptoms. The overall side effects were found among the younger populations

**TABLE 2** COVID-19 vaccines, vaccine dosage, route of administration with efficacy, and side effects

| Name of vaccine/Strain used and the manufacturer/developer | Type of vaccine | Route of administration, dose: Single/Booster | Pre-clinical trial data |
|---|---|---|---|
| BBIBP-CorV/19nCoV-CDC-Tan-HB02 (HB02) strain (Beijing Institute of Biological Products/Sinopharm, China) | Whole cell inactivated vaccine | Intramuscular, Booster | Available |
| WIV04 strain (Wuhan Institute of Biological Products/ Sinopharm, China) | Whole cell inactivated vaccine | Intramuscular, Booster | Not available |
| CoronaVac/PiCoVac (Sinovac, China) | Whole cell inactivated vaccine | Intramuscular, Booster | Available |
| Ad5-nCoV (CanSino Biological Inc./Beijing institute of biotechnology, China) | Virus vector: a non-replicating, adenovirus type 5 (Ad5)-vector | Intramuscular, Single | Not available |
| ZF2001 (Institute of Microbiology, Chinese Academy of Sciences, and Anhui Zhifei Longcom Biopharmaceutical, China) | Recombinant tandem-repeat dimeric RBD-based protein subunit vaccine (ZF2001) | Intramuscular, booster | Not available |
| Ad26.COV2·S (Janssen pharmaceutical, USA) | Virus vector: a non-replicating, adenovirus type 26 (Ad26)-vector | Intramuscular, Single | Available |
| AZD1222/ChAdOx1nCoV−19/Covishield (Oxford University and AstraZeneca, UK/Serum Institute of India) | Virus vector: non-replicating simian adenovirus vector ChAdOx1 | Intramuscular, Single, Booster | Available |
| Sputnik V (Gamaleya research institute, Russia) | Virus vector: non-replicating viral vectors, adenovirus type 5 (rAd5) and adenovirus type 26 (rAd26) | Intramuscular, Booster | Not available |
| mRNA−1273/Moderna (Moderna/NIAID, USA) | mRNA encoding a stabilized S protein encapsulated in lipid nanoparticles | Intramuscular, Booster | Available |
| BNT162b2 (Pfizer/BioNTech/Fosun, USA) | Nucleoside-modified mRNA encapsulated in lipid nanoparticles | Intramuscular, Booster | Available |
| NVX-CoV2373 (Novavax, USA) | Trimeric SARS-CoV−2 S protein nanoparticle plus Matrix-M1 adjuvant | Intramuscular, Booster | Available |
| Covaxin/BBV152 (Bharat Biotech in collaboration with the Indian Council Medical research (ICMR), and National Institute of Virology (NIV), India) | Whole cell inactivated vaccine | Intramuscular, Booster | Available |
| CovaxinBBV154 Intranasal (vaccine candidate) (Bharat Biotech, India) | Adenovirus vector with ChAD-SARS-CoV−2-S strain | Intranasal | Available |

significantly. Moreover, a higher number of female individuals suffered post-vaccination side effects than the males. The study also concluded that the Covishield vaccine is a well-tolerated vaccine among the people of different age groups.

Menni et al. (2021) have investigated the safety and effectiveness of Pfizer-BioNTech (BNT162b2) and the Oxford-AstraZeneca (ChAdOx1 nCoV-19) COVID-19 vaccines. Systemic and local side effects were reported by individuals after both the doses of the above vaccines. The systemic side effects were found to be more common among the previous COVID-19 infected individuals than among those without known past infection. However, both the vaccines decreased the risk of COVID-19 infection

| Current status | Vaccine side effects | Vaccine efficacy/immunogenicity |
|---|---|---|
| Phase III clinical trial, WHO Emergency Use Listing | Data from phase I and II: Injection site pain, fever, headache, mild and self-limiting, no serious adverse events (Xia et al., 2020) | 100% seroconversion, 78.1% efficacy (Al Kaabi et al., 2021; Xia et al., 2020) |
| Phase III clinical trial | Injection site pain, headache (Al Kaabi et al., 2021) | 72.6% (Al Kaabi et al., 2021) |
| Phase III clinical trial, emergency use approved in China, WHO Emergency Use Listing | Injection site pain, fatigue, myalgia, chills, nausea (Tanriover et al., 2021) | 83.5% (Tanriover et al., 2021) |
| Phase III clinical trial | Fever, fatigue, headache, muscle pain (Zhu et al., 2020) | Phase III trial results have not yet been published |
| Phase II<br>Clinical trial | Fever, headache, cough, injection site pain, swelling, redness, and fatigue (Yang et al., 2021) | 83% in 2 doses and 97% after third dose (Yang et al., 2021) |
| Phase III clinical trial, WHO Emergency Use Listing | Injection site pain, fatigue, myalgia, nausea (Sadoff et al., 2021) | 66.9% (Sadoff et al., 2021) |
| Phase III clinical trial, UK, MHRA, and CDSCO, India had approved for its emergency use. WHO Emergency Use Listing | Injection site pain, and tenderness, fatigue, myalgia, joint pains, nausea (Ramasamy et al., 2020) | 70.4% (64.1% after single dose) efficacy (Polack et al., 2020; Voysey et al., 2021) |
| Phase III clinical trial, CDSCO, India had approved its emergency use | fever, pain, chills, fatigue, nausea/vomiting, headache, insomnia, lymph node enlargement, erythema, pruritus, swelling, and diarrhea (Jarynowski et al., 2021) | 91.6% (Logunov et al., 2021) |
| Phase III clinical trial, CDSCO, India approved for its emergency use, WHO Emergency Use Listing | Fatigue and headache (Baden et al., 2021) | 94.1% efficacy (Baden et al., 2021) |
| Phase III clinical trial, authorized for use under an EUA by the FDA, WHO Emergency Use Listing | mild-to-moderate pain at the injection site, fatigue, and headache, Lymphadenopathy, herpes zoster, appendicitis, myocarditis, Facial palsy (Barda et al., 2021; Polack et al., 2020) | 95% efficacy (Polack et al., 2020) |
| Phase III clinical trial | Tenderness and pain at the injection site, muscle pain, fatigue (Heath et al., 2021) | 89.7% (Heath et al., 2021) |
| Phase III clinical trial, CDSCO/ICMR, India, and the WHO had approved its emergency use | headache, pyrexia/fever, fatigue, and myalgia | 77.8% (65.2% against delta variant) (Ella et al., 2021) |
| Pre-clinical trials | NA | NA |

after 12 days. Riad, Hocková, et al. (2021) have evaluated the post-vaccination side effects of mRNA-based COVID-19 vaccines (BNT162b2) among Slovakian healthcare workers. In this nationwide cross-sectional survey of 522 participants, 77% were females and 55.7% were aged between 31 and 54 years. 91.6% participants reported at least one side effect. The side effects were mild in nature (99.6%), and most of them (90.4%) were resolved within three days. Injection site pain (85.2%) was the most common local side effect, whereas headache (34.3%), fatigue (54.2%), muscle pain (28.4%), and chills (26.4%) were the reported systemic side effects.

There is no doubt that vaccination is the ideal protocol to tackle the coronavirus disease 2019 (COVID-19)

pandemic. In quick time, a number of COVID-19 vaccines were developed and authorized. Hatmal et al. (2021) have assessed the side effects and perceptions following COVID-19 vaccination in Jordan through a cross-sectional study with total of 2213 participants. The data were statistically analyzed, and certain machine learning tools have been used to predict the severity of the side effects. As per the study, 10% severe, 39% moderate, and 21% mild side effects were reported in individuals. The post-vaccination side effects (fever, headache, fatigue, chills, joint pain, dizziness, and myalgia) were common and non-life-threatening. Saeed et al. (2021) have reported a cross-sectional survey on Sinopharm COVID-19 vaccine side effects in the United Arab Emirates. Normal injection site pain, fatigue, lethargy, and headache were more commonly reported after first vaccine dose. The post-vaccination side effects were more common in females than the males. The reported post-vaccination side effects were mild and no need to hospitalization (CDC, 2021). So the study will be helpful to reduce vaccine hesitancy among people. Elnaem et al. (2021) have investigated the attitudes, perceptions, and experiences of the COVID-19 vaccine side effects in Malaysia through a cross-sectional survey conducted between May and July 2021. A total of 428 respondents registered in this survey and 76.8% had experienced vaccine-related side effects. Nearly 40% respondents registered side effects with the second dose of Pfizer-BioNTech vaccine. Injection site pain (61.1%) and tiredness (48.8%) were the most common side effects that reported. The respondents received Sinovac vaccine was experiencing lower side effects than others with Pfizer-BioNTech and Oxford-AstraZeneca. Moreover, Xu et al. (2021) have also reported the delayed hypersensitivity reactions to Pfizer/Moderna SARS-CoV-2 mRNA vaccines with second-dose administration. The overall attitudes toward the COVID-19 vaccination drive were still positive. However, independent studies are strongly recommended to strengthen public confidence on the COVID-19 vaccine to counter the consecutive waves of this pandemic.

### 3.4 | COVID-19 vaccine hesitancy

The effectiveness of COVID-19 vaccination program depends on various factors, out of which most important is willingness to receive the COVID-19 vaccine. El-Sokkary et al. (2021) have designed a cross-sectional study to understand the attitudes of Egyptian healthcare workers toward the COVID-19 vaccines. As per the observed data, the participants were classified as follows: hesitant (41.9%), refusing (32.1%), and willing (26%). So, it is highly essential to build trust on COVID-19 vaccination programs with continuous monitoring of attitudes. Cooper et al. (2021) have reviewed the findings of various surveys on acceptance of COVID-19 vaccines conducted in South Africa. The authors have also discussed various trust-building measures to address vaccine hesitancy. The surveys were conducted by searching electronic databases and contacting experts; and the results were potentially influenced by age, education, race, politics, geographical location, and employment. Carcelen et al. (2021) have conducted a survey in Zambia in November 2020 to know the sentiments and beliefs toward COVID-19 vaccines. They have also discussed on the development of new vaccines, cold-chain storage, the logistics of mass vaccination, and vaccine hesitancy. The study showed high acceptability of COVID-19 vaccination among children, but substantial hesitancy among adults may be due to uncertainty in vaccine safety and effectiveness.

Vaccine hesitancy is the major region for the spread of COVID-19 pandemic. Qunaibi et al. (2021) have conducted an online survey among Arab-speaking subjects from January 14, 2021, to January 29, 2021. This large-scale multinational study showed significant rate of COVID-19 vaccine hesitancy (>80%) among Arabs in and outside the Arab region. The reported side effects and healthcare policies are the possible reasons for COVID-19 vaccine hesitancy. It is recommended that the health authorities have to transparently address these concerns to improve vaccine acceptance. Lucia et al. (2021) have evaluated the COVID-19 vaccine hesitancy among US medical students as they are the frontline healthcare providers and exposed more. As per this study, all the participants had positive attitudes toward COVID-19 vaccines, but only 53% agreed to participate in a vaccine trial, while 23% were unwilling to take the vaccine immediately upon FDA approval. To promote the COVID-19 vaccine drive, the study also highlighted the need of an educational curriculum with vaccine safety and effectiveness.

Holeva et al. (2022) have reported a web based survey conducted in Greece and asking the respondents about their attitude toward the COVID-19 vaccine. The data are based on age, gender, marital status, professional status, educational level, and residential area. As per the present study, females and less educated participants were more hesitant toward COVID-19 vaccines. Hudson et al. (2021) have conducted a literature review on several factors associated with vaccine hesitancy and the public health responses toward COVID-19. The study suggested pursuing strategies to enhance public confidence on available COVID-19 vaccines. Kelekar et al. (2021) have conducted an online survey to assess vaccine hesitancy among the dental and medical students as they are exposed to COVID-19 patients. As per the survey, 45% dental and 23% medical students were hesitant to receive COVID-19 vaccines. The authors have also highlighted the need of

specific curricula design to increase the knowledge of students about the COVID-19 vaccines.

Ehde et al. (2021) have conducted a survey in the United States on early vaccine hesitancy, factors and reasons associated with it, and whether vaccine willingness changed among the participants. 90% of the undecided group wanted additional information about the vaccine before deciding. The COVID-19 vaccine hesitancy decreased during the pandemic over the time. Freeman et al. (2021) have discussed on various written information or statements about COVID-19 vaccination, efficacy, and safety to increase vaccine acceptance. In this UK-based study registered with ISRCTN, ISRCTN37254291, nearly 10% population was strongly hesitant about the vaccines. Gender and ethnicity have not affected the outcomes appreciably. Jain et al. (2021) have assessed vaccine hesitancy and the related factors among Indian medical students through an online questionnaire filled from February 2 to March 7, 2021. This study also reported vaccine hesitancy among 10.6% participants. Lack of awareness along with safety and efficacy are the major reason for COVID-19 vaccine hesitancy. Among two available vaccines, the medical students preferred Covishield.

Troiano et al. (2021) have discussed the vaccine acceptance during this COVID-19 pandemic. The percentage of COVID-19 vaccine acceptance for students (86.1%), general population (77.6%), and for influenza vaccine (69%) was recorded. Several factors influenced the vaccine hesitancy (gender, age, religiosity, ethnicity, working status, education, income, politics, etc.). The common reasons for vaccine hesitancy are concerns about safety, lack of trust, and doubts on efficiency of vaccines. Hence, efforts should be done to provide correct information to the people about vaccines. Duong et al. (2021) have examined the COVID-19 vaccine hesitancy on 387 school principals across Taiwan through an online survey. As per the survey, male principals with higher health literacy showed lower vaccine hesitancy.

COVID-19 vaccine hesitancy will pose substantial risks for the people and also making difficulty to achieve herd immunity against COVID-19. The decision-makers should be careful to develop targeted strategies to reduce vaccine hesitancy among general public as mass vaccination is the only pathway to counter this pandemic (Wiysonge et al., 2021). The attitude of healthcare professionals is crucial in creating public trust on vaccines. Keeping in mind, Riad, Abdulqader, et al. (2021) have evaluated the attitude of dental students toward COVID-19 vaccines through a cross-sectional study using an online questionnaire. Among 6639 students from 22 countries, 22.5% students were hesitant, and 13.9% students rejected COVID-19 vaccines. The participants from low- and lower-middle income economies showed greater vaccine hesitancy. Vaccine hesitancy is also an important obstacle for pediatric vaccination. Bagateli et al. (2021) have reported 2.8% vaccine hesitancy among the parents of children and adolescents living in Brazil on the basis of a validated questionnaire. As per this survey, vaccine hesitancy is very low among caregivers living in Brazil; however, they are willing to vaccinate their offspring against COVID-19. A recent study reported the willingness to receive the booster dose of COVID-19 vaccine in Poland (Rzymski et al., 2021). Women, elder individuals, people with obesity, chronic diseases, and people taken influenza vaccine previously were willing to receive a booster COVID-19 dose. This study also reported some vaccine hesitancy in the studied group.

## 3.5 | SARS-CoV-2 and its variants

Continuous changes occur in the genetic code (genetic mutations) of SARS-CoV-2 during replication of the genome. A variant is a viral genome (genetic code) and has one or more mutations which differentiate it from the other variants of the virus. However, mutation is a single change in the virus's genome (genetic code). A large number of variants of SARS-CoV-2 are documented worldwide throughout this pandemic since last two years. Moreover, a group of variants having similar genetic changes (lineage or group of lineages) is designated as VBM, VOI, VOC, and VOHC as listed below (Tables 3 and 4) and are routinely monitored (CDC, 2021c; ECDC, 2022). Vaccine inequity, hesitancy, and the presence of large number of immunocompromised persons in a particular region are the possible combined reasons for the continuous emergence of multiple SARS-CoV-2 variants (Burki, 2022; Dhawan et al., 2022).

### 3.5.1 | Omicron, the highly transmitted VOC

Omicron has become the dominant variant in many countries worldwide. The B.1.1.529 variant (Omicron, a new variant with large number of mutations) was first reported as VOC by WHO on 26 November 2021 and was identified from the specimens collected from South Africa and Botswana (GISAID, 2021b; WHO, 2021). As per preliminary evidences, this novel variant has increased risk of reinfection as compared with the other SARS-CoV-2 VOCs. It may be associated with enhanced transmissibility and reduced vaccine-induced immunity. Sore throat, body ache, fever, and weakness are the reported earliest common symptoms of Omicron. This new variant has started a fresh wave like other variants of concern (alpha, beta, and delta) across the entire world (Fontanet et al., 2021). The

**TABLE 3** Variants being monitored (VBM): (CDC, 2021c; ECDC, 2022)

| WHO label | Pango lineage | Spike mutations of interest | Country | Date |
|---|---|---|---|---|
| Alpha | B.1.1.7 and Q lineages | N501Y, P681H, D614G | UK | September 2020 |
| Beta | B.1.351 and descendent lineages | K417N, N501Y, E484K, D614G, A701V | South Africa | September 2020 |
| Gamma | P.1and descendent lineages | K417T, N501Y, E484K, D614G, H655Y | Brazil | December 2020 |
| Lambda | C.37 | L452Q, D614G, F490S | Peru | December 2020 |
| Epsilon | B.1.427<br>B.1.429 | L452R, D614G | USA | September 2020 |
| Eta | B.1.525 | E484K, Q677H, D614G | UK, Nigeria | December 2020 |
| Iota | B.1.526 | E484K, D614G, A701V | USA | December 2020 |
| Kappa | B.1.617.1 | L452R, E484Q, D614G, P681R | India | December 2020 |
| N/A | B.1.617.3 | L452R, D614G, E484Q, P681R | India | February 2021 |
| Zeta | P.2 | E484K, D614G | Brazil | January 2021 |
| Mu | B.1.621, B.1.621.1 | R346K, N501Y, E484K, D614G, P681H | Colombia | January 2021 |

**TABLE 4** The currently existing variant of concern (VOC) (CDC, 2021c; ECDC, 2022)

| WHO Label | Pango Lineage | Spike mutations of interest | Identified | Date |
|---|---|---|---|---|
| Delta | B.1.617.2 and AY lineages | L452R, D614G, T478K, P681R | India | December 2020 |
| Omicron | B.1.1.529 | A67V, Δ69-70, T95I, G142D, Δ143-145, N211I, Δ212, S373P, ins215EPE, G339D, S371L, S375F, K417N, G446S, N440K, N440K, S477N, E484A, T478K, Q493R, G496S, N501Y, Q498R, Y505H, T547K, H655Y, D614G, N679K, P681H, D796Y, N764K, N856K, Q954H, L981F, N969K | South Africa, Botswana | November 2021 |

†Currently, no SARS-CoV-2 variants are designated as VOI or VOHC.

COVID-19 cases are increasing rapidly worldwide, and the UK and the USA have reported highest cases (GISAID, 2021b; Karim & Karim, 2021; Mohapatra, Sarangi, et al., 2022). In this context, to counter the spread of Omicron several countries has announced that masks are again compulsory on public transport and in schools and shops.

The current vaccines are less effective against Omicron, but still providing some protection. Omicron contains more than 50 mutations, out of which at least 30 in its spike protein (Callaway, 2021; Torjesen, 2021). Most of the COVID-19 vaccines are based on the S-protein RBD. The Delta variant has two mutations and Beta variant has three mutations; however, Omicron has between 10 and 15 mutations in the said S-protein RBD region. The used COVID-19 vaccines were less effective against Delta and Beta variants, which may be due to the mutations that helped partially evade immune responses. However, for this new Omicron variant, many functions are still unknown. The initial laboratory data suggested that Omicron variant likely to weaken the COVID-19 vaccine protection (Callaway, 2021; Cross, 2021; Mohapatra et al., 2022b; Torjesen, 2021). As the Omicron S-protein RBD has large number of mutations, which is the primary target for the monoclonal antibody-based therapy. So, the FDA-approved monoclonal antibodies may be less effective against the B.1.1.529 (Omicron) variant (Takashita et al., 2022). Recently, Pajon et al. (2022) have reported that the neutralization of Omicron (B.1.1.529) variant has increased substantially after mRNA-1273 vaccine booster dose. Researchers are still trying to answer whether antibodies produced from vaccination can neutralize Omicron, still it is debatable as very few data's are available on it. As per the reported studies, the risk of hospitalization has been found to be lower for Omicron as compared with Delta. Moreover, the vaccine vendors have also planned to make new versions of their vaccines

to counter such emerging variants of SARS-CoV-2. In between this, the World Health Organization has suggested the individuals to take measures (maintaining physical distancing, wearing well-fitted masks, following hand hygiene, avoiding crowded spaces, receiving up-to-date vaccines, etc.) to reduce the risk of COVID-19 infection from such emerging variants. Furthermore, it is also essential to enhance the surveillance and sequencing efforts to understand circulating such VOCs.

### 3.6 | Vaccine effectiveness against SARS-CoV-2 VOCs

During the pandemic, the virus was noted to frequently undergo mutations and evolve into different variants that were named as variants of concern, variants of interest, and variants under observation depending on the type of mutations (Mohapatra, Sarangi, et al., 2022; Mohapatra et al., 2022b). The initial Wuhan strain underwent mutation (D614G), probably the first, that was identified in March 2020, and later the virus further developed into the Alpha (B.1.1.7), Beta (B.1.351), Gamma (P.1), and Delta (B.1.617.2). All of these variants along with the most recent Omicron variants (B.1.1.529) were categorized as VOCs due to the increased mutations at the spike protein, N-terminal domain (NTD), and other regions including the RBDs. Among the SARS-CoV-2 VOCs, the Delta variant and the Omicron variants showed more significant mutations, and therefore, the current vaccines and their efficacy in protecting against infection were carefully considered (Mohapatra et al., 2022c). A single dose of ChAdOx1 (Oxford/AstraZeneca) COVID-19 vaccine was not sufficient for the development of neutralizing antibodies, especially against the Delta variant. The concentrations of serum neutralizing antibodies measured after vaccination revealed that although the antibody concentrations were sufficient to neutralize the Alpha variant, there was no protection against the Delta variant. However, two-dose vaccination/complete vaccination gave 95% protection against the Alpha variant with three to fivefold lower protection against the Delta variant (Planas et al., 2021). Al-Tawfiq et al. (2022) have reported a significant reduction in neutralization rates against Delta (B.1.617.2) variants for vaccinated and convalescent patients with prior COVID-19 history. However, lower rate of infection due to Delta variant was found after the second dose of Oxford-AstraZeneca, Pfizer-BioNTech, and Moderna vaccines.

Two-dose ChAdOx1 (Oxford/AstraZeneca) vaccines and an equal number of people who were given 2 doses of BNT162b2 (Pfizer-BioNTech) vaccine were analyzed for neutralization antibody responses (Davis et al., 2021). This study noted that the 2 doses of vaccine as compared to a single dose produced higher concentrations of neutralizing antibodies. Despite effective neutralization of the original Wuhan strain, the antibody titers were reduced by 11.30-fold against the Delta variant. The BNT162b2 (Pfizer-BioNTech) vaccination elicited higher titers (mean titer = 11473) of antibodies against full vaccination with ChAdOx1 (Oxford/AstraZeneca) vaccine (mean titer = 1325.6). The serum neutralizing antibody titers were 6-fold less sensitive to the Delta variant among the convalescent patients. The serum neutralizing antibodies against Delta variant were reduced by 8-fold after complete vaccination with ChAdOx1 (Oxford/AstraZeneca), and BNT162b2 (Pfizer-BioNTech) vaccine with ChAdOx1 (serum geometric mean titer-654) being less effective (*p*-value-0.0006) as against the BNT162b2 vaccine (serum geometric mean titer-3372) (Mlcochova et al., 2021). After complete vaccination with BNT162b2 (Pfizer-BioNTech) vaccine, the concentration of neutralization antibodies was found to be reduced by more than 10-fold against the Delta variant that could have been responsible for breakthrough infections (Mlcochova et al., 2021). The neutralization antibody titers were reduced by 4-fold against the Delta variant and other VOCs after complete vaccination against most mRNA vaccines. Also, it was noted that there is a possibility of a 2- to 10-fold increase in neutralizing antibody titer after a single-dose vaccination among previously infected people (protection of 75% (95% CI 53–89) after full vaccination against 95% (CI: 85–98) protection for a previously infected person with single-dose vaccination) (Wang et al., 2021). A booster with mRNA-1273, and Coronavac (Sinovac) delivered after 6 months after the second dose demonstrated a 20-fold, and 5-fold increase in neutralization antibody titers, respectively (Cromer et al., 2022). The previous infection-related immune responses were found to wane after 6 months and only 41% protection was noted against the Delta variant. However, the levels of protection increased to about 95% after a single dose of mRNA vaccination (Cromer et al., 2022).

BNT162b2 (Pfizer/BioNTech) vaccines who were infected with the Delta variant showed protective antibodies with considerable neutralization effect (serum antibody effective concentration (EC50) was 2152 (95% CI: 961–3596) compared with 668 (95% CI: 473–892) in controls (322% increase; $p < .001$)) (Davis et al., 2021). Both the serum IgA and IgG concentrations were noted to increase in such breakthrough infections (Serum IgA EC50 after breakthrough infection was 120 (95% CI, 44–246), compared with 24 (95% CI, 24–24) (Bates et al., 2022). The neutralization antibody concentrations against Delta, Omicron, and other VOCs were measured among people after 2 doses of vaccination with the mRNA-1273 vaccine (Spikevax, Moderna), ChAdOx1 nCoV-19; Vaxzevria, AstraZeneca), and BNT162b2 vaccine (Comirnaty, Pfizer–BioNTech).

The antibody concentrations were also measured among people who received heterologous vaccinations (alternative ChAdOx1-S and BNT162b2 vaccines), and single-dose vaccination in previously infected, convalescent, and people with breakthrough infections. The serum antibodies were able to efficiently neutralize most other VOCs except the Omicron variant. Neutralization antibodies against Omicron were noted among people who received heterologous ChAdOx1-S–BNT162b2 vaccines and homologous BNT162b2 as compared to a homologous ChAdOx1-S vaccine. Neutralization antibodies against Omicron were undetectable in persons after 6 months of receiving 2 doses of the mRNA-1273 vaccine. More effective neutralization antibodies Delta variant as compared to the Omicron were discovered in persons who received vaccination after being previously infected and vice versa (Rössler et al., 2022).

The plasma antibody concentrations at 6-month period as measured in 50% neutralization titer (NT50) among people with previous COVID-19 history revealed more than 60-fold reduction in the neutralizing antibodies against Omicron variant as against original Wuhan variant (Mean ± SD of 58 ± 51 Vs 32 ± 23). Six months after complete vaccination, a booster dose with mRNA vaccine-induced Omicron neutralizing antibodies (Schmidt et al., 2021). This suggests the potential benefit of booster vaccination against infection with the Omicron variant. Neutralization antibody titers against Delta, and Omicron variants among other VOCs after complete vaccination with mRNA-1273, BNT162b, and Ad26.COV2.S vaccines were analyzed. Omicron neutralizing antibodies were undetectable in all vaccinated people who received 2 doses. On the contrary, people who received a booster dose detectable neutralizing antibodies with 4- to 6-fold lower antibody titers against Omicron variant as against other VOCs (Garcia-Beltran et al., 2022). When CoronaVac and BNT162b2 vaccines were assessed for the presence of detectable neutralizing antibody titers against Omicron variant, people who received CoronaVac had no detectable antibodies as against BNT162b2 vaccines who developed some antibodies (35.7–39.9-fold lower antibodies against Omicron) (Lu et al., 2021). A significant reduction in the titers of neutralizing antibodies was noted among convalescent and fully vaccinated people. Nevertheless, after the third dose of the mRNA vaccine considerably improved the protection against Omicron infection (Cameroni et al., 2021). However, it is recommended that more conserved antigens be used to prepare vaccines for improved efficacy against the Omicron variant (Sievers et al., 2022).

## 3.7 | Animal models

The current COVID-19 pandemic has put enormous strain on health care system. Therefore, the development of animal models to understand the immune responses observed in patients infected with SARS-CoV-2 or its variants is urgently needed. Moreover, suitable and appropriate models are crucial to accelerate the testing of therapeutic drugs and vaccines. In this context, Bi et al. (2021) have summarized the details of transmission, pathology, and immunology induced by SARS-CoV-2 in various reported animal models. Mouse model is commonly used to understand the viral pathogenesis for different diseases due to its small size and low cost (Mohapatra et al., 2021f). Mouse (*Mus musculus*) model was widely used for other CoVs such as MERS-CoV (Cockrell et al., 2016; Li et al., 2017) and SARS-CoV (Channappanavar et al., 2016; Day et al., 2009).

As ACE2 is the principle human cellular receptor for the viral S-protein, some studies suggested that mink, ferrets, macaques, common marmosets, felines, rabbits, and hamsters are naturally susceptible to the infection (Brooke & Prischi, 2020; Chan et al., 2020; Younes et al., 2020; Zeiss et al., 2021). Due to lack of proper receptors, mice may not be naturally susceptible to SARS-CoV-2 infection. It was also confirmed by some experimental studies. SARS-CoV-2 requires human ACE2 receptor not mouse ACE2 (Hoffmann et al., 2020). Several strategies have been employed to resolve this issue, such as development of genetic modification and mouse adapted virus. Moreover, the Syrian golden hamster (Mesocricetus auratus) is small mammal and was used as a well-characterized model to study the infections of various human respiratory viruses (SARS-CoV and influenza virus) (Iwatsuki-Horimoto et al., 2018; Miao et al., 2019; Munoz-Fontela et al., 2020; Roberts et al., 2005, 2008; Rosa et al., 2021; Rosenke et al., 2020). As ACE2 domain of human closely resembles that of hamsters, hamsters may be suitable as natural model for studying the SARS-CoV-2 infection (Chan et al., 2020).

The small animals (Syrian hamsters, human ACE2 transgenic mice, wild-type mice), and large animals (ferrets,

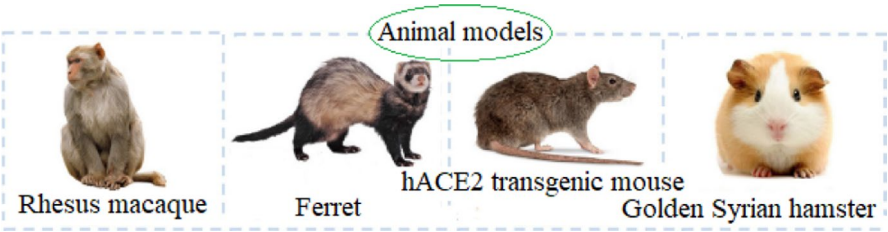


**FIGURE 1** Animal models used to understand SARS-CoV-2 transmission [Colour figure can be viewed at wileyonlinelibrary.com]

Cynomolgus macaques, Rhesus macaques) may contribute significantly as suitable animal models (Figure 1) to evaluate the vaccine efficacy and testing of therapies against SARS-CoV-2 (Takayama, 2020; Tiwari et al., 2020). The Syrian hamster (*M. auratus*) rapidly developed into a popular model. However, among other hamsters, Roborovski dwarf hamster (*P. roborovskii*) more closely mimics the disease with frequent lethal outcomes (Gruber et al., 2021). So, different hamster species should be used to study different courses of COVID-19 manifestations. Age and sex are two risk factors for COVID-19 patients. Keeping in mind, some studies confirmed age-dependent differences in SARS-CoV-2 infected Syrian hamsters. 40–80 week-old Syrian hamsters showed severe clinical signs as compared to 7- to 9-week-old hamsters (Selvaraj et al., 2021). In another study, middle-aged Syrian hamsters (32–34 weeks) showed more pronounced weight loss, delayed spread of virus in the lungs, and delayed virus clearance as compared with 6-week-old hamsters (Osterrieder et al., 2020).

A number of waves of this ongoing novel COVID-19 pandemic hit several counties since last two years and associated with high morbidity and mortality. There is no particular drug to treat this novel disease. So, to counter it vaccines were developed at an unprecedented speed and their efficacy is still debatable. Also, large number of SARS-CoV-2 variants continues to emerge and some appear more transmissible and less sensitive to virus-specific immune responses. Keeping in mind, de Vries et al. (2021) have reviewed the role of animal models in assessing therapeutic and prophylactic options to interrupt SARS-CoV-2 transmission. Jia et al. (2021) have discussed the mechanisms of SARS-CoV-2 infection, role of ACE2 in cell entry, along with immunopathology such as lymphocyte dysregulation, antibody responses, and cytokine storm. They have also highlighted the research progress of animal models for better understanding of the pathogenesis of COVID-19, which will be helpful for its treatment. Macaque infection has been the gold standard to illuminate vaccine efficacy and immune response patterns after infection by VOC (Altmann, 2021; Corbett et al., 2021; McMahan et al., 2021; Yu et al., 2020). Some recent studies suggest little differences in infectivity and virulence of emerging VOCs of SARS-CoV-2 in Syrian hamsters (Abdelnabi et al., 2021; Nunez et al., 2021; Yadav et al., 2021). However, studies are limited.

## 4 | CONCLUSION

Multiple waves of this ongoing COVID-19 pandemic hit several counties (in a more general way we can say the whole globe) since last two years after its emergence and associated with high morbidity and mortality. As there is no particular drug to treat this novel disease so, vaccines were developed at an unprecedented speed and their efficacy is still debatable. Large number of SARS-CoV-2 variants continues to emerge and some appear more transmissible and less sensitive to virus-specific immune responses. Therefore, scientists, researchers, physicians, and several agencies are in tremendous pressure to understand the way to counter it. In this mean time, we may only recommend the general public to obey the COVID-19 guideline as much as possible and stay up to date with their vaccine doses. Prior immunity from natural infection, vaccination with booster doses, compulsory mask use, and implementation of adequate prevention and control measures may contribute to less severe outcomes. Moreover, vaccinating the unvaccinated and weaker individuals and providing booster doses may prevent death and hospitalizations. Some more suitable animal models may be studied to evaluate the vaccine efficacy, and testing of therapies against SARS-CoV-2. It is also highly recommended to understand the immune response patterns after infection by VOC.

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## CONFLICT OF INTEREST

There is no potential conflict of interest.

## AUTHOR CONTRIBUTIONS

All the authors substantially contributed to the conception, design, and interpretation of data and approving the final version of the manuscript.

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## REFERENCES

Abdalla, M., Mohapatra, R. K., Sarangi, A. K., Mohapatra, P. K., Eltayb, W. A., Alam, M., El-Arabey, A. A., Azam, M., Al-Resayes, S. I., Seidel, V., & Dhama, K. (2021). In silico studies on phytochemicals to combat the emerging COVID-19 infection. *Journal of Saudi Chemical Society*, *25*, 101367. https://doi.org/10.1016/j.jscs.2021.101367

Abdelnabi, R., Boudewijns, R., Foo, C. S., Seldeslachts, L., Sanchez-Felipe, L., Zhang, X., Delang, L., Maes, P., Kaptein, S. J. F., Weynand, B., Velde, G. V., Neyts, J., & Dallmeier, K. (2021). Comparative infectivity and virulence of emerging SARS-CoV-2 variants in Syrian hamsters. *EBioMedicine*, *68*, 103403.

Abramowicz, M., Zuccotti, G., & Pflomm, J.-M. (2021). An EUA for Bamlanivimab—A monoclonal antibody for COVID-19. *JAMA*, *325*(9), 880–881. https://doi.org/10.1001/jama.2020.24415

Ahmed, M. H., & Hassan, A. (2020). Dexamethasone for the treatment of coronavirus disease (COVID-19). *SN Comprehensive Clinical Medicine*, 1–10. https://doi.org/10.1007/s42399-020-00610-8

Al Kaabi, N., Zhang, Y., Xia, S., Yang, Y., Al Qahtani, M. M., Abdulrazzaq, N., Al Nusair, M., Hassany, M., Jawad, J. S., Abdalla, J., Hussein, S. E., Al Mazrouei, S. K., Al Karam, M., Li, X., Yang, X., Wang, W., Lai, B., Chen, W., Huang, S., … Yang, X. (2021). Effect of 2 inactivated SARS-CoV-2 vaccines on symptomatic COVID-19 infection in adults: A randomized clinical trial. *JAMA*, *326*(1), 35–45. https://doi.org/10.1001/jama.2021.8565

Alonso-Bellido, I. M., Bachiller, S., Vázquez, G., Cruz-Hernández, L., Martínez, E., Ruiz-Mateos, E., Deierborg, T., Venero, J. L., Real, L. M., & Ruiz, R. (2021). The other side of SARS-CoV-2 infection: Neurological sequelae in patients. *Frontiers in Aging Neuroscience*, *13*, 632673. https://doi.org/10.3389/fnagi.2021.632673

Al-Tawfiq, J. A., Koritala, T., Alhumaid, S., Barry, M., Alshukairi, A. N., Temsah, M.-H., Al Mutair, A., Rabaan, A., Tirupathi, R., & Gautret, P. (2022). Implication of the emergence of the delta (B.1.617.2) variants on vaccine effectiveness. *Infection*, https://doi.org/10.1007/s15010-022-01759-1

Altmann, D. M. (2021). Narrating the natural history of live infection by SARS CoV-2 VOC in animal models. *EBioMedicine*, *74*, 103704. https://doi.org/10.1016/j.ebiom.2021.103704

Arnaout, R., & Arnaout, R. (2022). Visualizing Omicron: COVID-19 Deaths vs. Cases Over Time, Research Square [preprint], 2022. https://doi.org/10.21203/rs.3.rs-1257935/v2

Arumugam, V. A., Thangavelu, S., Fathah, Z., Ravindran, P., Sanjeev, A. M. A., Babu, S., Meyyazhagan, A., Yatoo, M. I., Sharun, K., Tiwari, R., Pandey, M. K., Sah, R., Chandra, R., & Dhama, K. (2020). COVID-19 and the world with co-morbidities of heart disease, hypertension and diabetes. *Journal of Pure and Applied Microbiology*, *14*(3), 1623–1638. https://doi.org/10.22207/JPAM.14.3.01

Baden, L. R., El Sahly, H. M., Essink, B., Kotloff, K., Frey, S., Novak, R., Diemert, D., Spector, S. A., Rouphael, N., Creech, C. B., McGettigan, J., Khetan, S., Segall, N., Solis, J., Brosz, A., Fierro, C., Schwartz, H., Neuzil, K., Corey, L., … Zaks, T. (2021). COVE study Group. Efficacy and safety of the mRNA-1273 SARS-CoV-2 vaccine. *New England Journal of Medicine*, *384*(5), 403–416. https://doi.org/10.1056/NEJMoa2035389

Bagateli, L. E., Saeki, E. Y., Fadda, M., Agostoni, C., Marchisio, P., & Milani, G. P. (2021). COVID-19 vaccine hesitancy among parents of children and adolescents living in Brazil. *Vaccines*, *9*, 1115–https://doi.org/10.3390/vaccines9101115

Barda, N., Dagan, N., Ben-Shlomo, Y., Kepten, E., Waxman, J., Ohana, R., Hernán, M. A., Lipsitch, M., Kohane, I., Netzer, D., Reis, B. Y., & Balicer, R. D. (2021). Safety of the BNT162b2 mRNA Covid-19 vaccine in a nationwide setting. *New England Journal of Medicine*, *385*(12), 1078–1090. https://doi.org/10.1056/NEJMoa2110475

Bates, T. A., McBride, S. K., Winders, B., Schoen, D., Trautmann, L., Curlin, M. E., & Tafesse, F. G. (2022). Antibody response and variant cross-neutralization after SARS-CoV-2 breakthrough infection. *JAMA*, *327*(2), 179–181. https://doi.org/10.1001/jama.2021.22898

Bi, Z., Hong, W., Yang, J., Lu, S., & Peng, X. (2021). Animal models for SARS-CoV-2 infection and pathology. *MedComm*, *2*(4), 548–568. https://doi.org/10.1002/mco2.9810.1002/mco2.98

Brooke, G. N., & Prischi, F. (2020). Structural and functional modelling of SARS-CoV-2 entry in animal models. *Scientific Reports*, *10*(1), 15917.

Burki, T. (2022). The origin of SARS-CoV-2 variants of concern. *The Lancet*, *22*, 174–175. https://doi.org/10.1016/S1473-3099(22)00015-9

Burugu, H. R., Kandi, V., Kutikuppala, L. V. S., & Suvvari, T. K. (2020). Activities of serum ferritin and treatment outcomes among COVID-19 patients treated with vitamin C and dexamethasone: An uncontrolled single-center observational study. *Cureus*, *12*(11):e11442. https://doi.org/10.7759/cureus.11442

Callaway, E. (2021). Omicron likely to weaken COVID vaccine protection. *Nature*, *600*(7889), 367–368. https://doi.org/10.1038/d41586-021-03672-3

Cameroni, E., Bowen, J. E., Rosen, L. E., Saliba, C., Zepeda, S. K., Culap, K., Pinto, D., VanBlargan, L. A., De Marco, A., di Iulio, J., Zatta, F., Kaiser, H., Noack, J., Farhat, N., Czudnochowski, N., Havenar-Daughton, C., Sprouse, K. R., Dillen, J. R., Powell, A. E., … Corti, D. (2021). Broadly neutralizing antibodies overcome SARS-CoV-2 Omicron antigenic shift. *Nature*, https://doi.org/10.1038/s41586-021-04386-2

Carcelen, A. C., Prosperi, C., Mutembo, S., Chongwe, G., Mwansa, F. D., Ndubani, P., Simulundu, E., Chilumba, I., Musukwa, G., Thuma, P., Kapungu, K., Hamahuwa, M., Mutale, I., Winter, A., Moss, W. J., & Truelove, S. A. (2021). COVID-19 vaccine hesitancy in Zambia: a glimpse at the possible challenges ahead for COVID-19 vaccination rollout in sub-Saharan Africa. *Human Vaccines & Immunotherapeutics*, 1–6. https://doi.org/10.1080/21645515.2021.1948784

CDC (2021). *Possible side effects*, November 24, 2021.

CDC (2021c), SARS-CoV-2 variant classifications and definitions, Dec. 1, 2021c, https://www.CDC.gov/

Chan, J.-W., Zhang, A. J., Yuan, S., Poon, V.-M., Chan, C.-S., Lee, A.-Y., Chan, W.-M., Fan, Z., Tsoi, H.-W., Wen, L., Liang, R., Cao, J., Chen, Y., Tang, K., Luo, C., Cai, J.-P., Kok, K.-H., Chu, H., Chan, K.-H., … Yuen, K.-Y. (2020). Simulation of the clinical and pathological manifestations of Coronavirus Disease 2019 (COVID-19) in a golden Syrian hamster model: implications for disease pathogenesis and transmissibility. *Clinical Infectious Diseases*, *71*(9), 2428–2446.

Channappanavar, R., Fehr, A. R., Vijay, R., Mack, M., Zhao, J., Meyerholz, D. K., & Perlman, S. (2016). Dysregulated type I interferon and inflammatory monocyte-macrophage responses cause lethal pneumonia in SARS-CoV-infected mice. *Cell HostMicrobe*, *19*(2), 181–193.

Choudhary, O. P., Dhawan, M., & Choudhary, P. (2021). Omicron variant (B.1.1.529) of SARS-CoV-2: threat assessment and plan of action. *International Journal of Surgery*, https://doi.org/10.1016/j.ijsu.2021.106187

Cockrell, A. S., Yount, B. L., Scobey, T., Jensen, K., Douglas, M., Beall, A., Tang, X.-C., Marasco, W. A., Heise, M. T., & Baric, R. S. (2016). A mouse model for MERS coronavirus-induced acute respiratory distress syndrome. *Nature Microbiology*, *2*(2), 16226.

Cooper, S., van Rooyen, H., & Wiysonge, C. S. (2021). COVID-19 vaccine hesitancy in South Africa: how can we maximize uptake of

COVID-19 vaccines? *Expert Review of Vaccines*, *20*(8), 921–933. https://doi.org/10.1080/14760584.2021.1949291

Corbett, K. S., Gagne, M., Wagner, D. A., O' Connell, S., Narpala, S. R., Flebbe, D. R., Andrew, S. F., Davis, R. L., Flynn, B., Johnston, T. S., Stringham, C. D., Lai, L., Valentin, D., Van Ry, A., Flinchbaugh, Z., Werner, A. P., Moliva, J. I., Sriparna, M., O'Dell, S., … Seder, R. A. (2021). Protection against SARS-CoV-2 beta variant in mRNA-1273 vaccine-boosted nonhuman primates. *Science*, *374*(6573), 1343–1353. https://doi.org/10.1126/science.abl8912

Cromer, D., Steain, M., Reynaldi, A., Schlub, T. E., Wheatley, A. K., Juno, J. A., Kent, S. J., Triccas, J. A., Khoury, D. S., & Davenport, M. P. (2022). Neutralising antibody titres as predictors of protection against SARS-CoV-2 variants and the impact of boosting: A meta-analysis. *Lancet Microbe*, *3*(1), e52–e61. https://doi.org/10.1016/S2666-5247(21)00267-6

Cross, R. (2021). Omicron puts scientists on red alert. *Chemical & Engineering News*, *99*, 44. https://cen.acs.org/pharmaceuticals/vaccines/Omicron-puts-scientists-red-alert/99/i44

Davis, C., Logan, N., Tyson, G., Orton, R., Harvey, W. T., Perkins, J. S., Mollett, G., Blacow, R. M., Peacock, T. P., Barclay, W. S., Cherepanov, P., Palmarini, M., Murcia, P. R., Patel, A. H., Robertson, D. L., Haughney, J., Thomson, E. C., & Willett, B. J. (2021). Reduced neutralisation of the Delta (B.1.617.2) SARS-CoV-2 variant of concern following vaccination. *PLoS Path*, *17*(12), e1010022. https://doi.org/10.1371/journal.ppat.1010022

Day, C. W., Baric, R., Cai, S. X. et al (2009). A new mouse-adapted strain of SARS-CoV as a lethal model for evaluating antiviral agents in vitro and in vivo. *Virology*, *395*(2), 210–222.

de Vries, R. D., Rockx, B., Haagmans, B. L., Herfst, S., Koopmans, M. P. G., & de Swart, R. L. (2021). Animal models of SARS-CoV-2 transmission. *Current Opinion in Virology*, *50*, 8–16. https://doi.org/10.1016/j.coviro.2021.06.007

Dhama, K., Patel, S. K., Pathak, M., Yatoo, M. I., Tiwari, R., Malik, Y. S., Singh, R., Sah, R., Rabaan, A. A., Bonilla-Aldanag, D. K., & Rodriguez-Morales, A. J. (2020). An update on SARS-CoV-2/COVID-19 with particular reference to its clinical pathology, pathogenesis, immunopathology and mitigation strategies. *Travel Medicine and Infectious Disease*, *37*, 101755.

Dhawan, M., Priyanka Sahni, A., & Choudhary, O. P. (2022). Priyanka, Sahni A, Choudhary OP, Vaccine inequity and hesitancy: Dual factors in the emergence of novel SARS-CoV-2 variants. *Annals of Medicine and Surgery*, *73*, 103186, https://doi.org/10.1016/j.amsu.2021.103186

Duong, T. V., Lin, C.-Y., Chen, S.-C., Huang, Y.-K., Okan, O., Dadaczynski, K., & Lai, C.-F. (2021). Oxford COVID-19 vaccine hesitancy in school principals: Impacts of gender, well-being, and coronavirus-related health literacy. *Vaccines*, *9*, 985. https://doi.org/10.3390/vaccines9090985

ECDC (2022). SARS-CoV-2 variants of concern as of 13 January, 2022. https://www.ecdc.europa.eu/en/covid-19/variants-concernaccessed on: 16-01-2022

Ehde, D. M., Roberts, M. K., Humbert, A. T., Herring, T. E., & Alschuler, K. N. (2021). COVID-19 vaccine hesitancy in adults with multiple sclerosis in the United States: A follow up survey during the initial vaccine rollout in 2021. *Multiple Sclerosis and Related Disorders*, *54*, 103163. https://doi.org/10.1016/j.msard.2021.103163

Ella, R., Reddy, S., Blackwelder, W., Potdar, V., Yadav, P., Sarangi, V., Aileni, V. K., Kanungo, S., Rai, S., Reddy, P., Verma, S., Singh, C., Redkar, S., Mohapatra, S., Pandey, A., Ranganadin, P., Gumashta, R., Multani, M., Mohammad, S., … Waghmare, S. (2021). COVAXIN Study Group. Efficacy, safety, and lot-to-lot immunogenicity of an inactivated SARS-CoV-2 vaccine (BBV152): interim results of a randomised, double-blind, controlled, phase 3 trial. *Lancet*, *S0140–6736*(21), 02000–2006. https://doi.org/10.1016/S0140-6736(21)02000-6

Elnaem, M. H., MohdTaufek, N. H., AbRahman, N. S., MohdNazar, N. I., Zin, C. S., Nuffer, W., & Turner, C. J. (2021). COVID-19 vaccination attitudes, perceptions, and side effect experiences in Malaysia: Do age, gender, and vaccine type matter? *Vaccines*, *9*, 1156. https://doi.org/10.3390/vaccines9101156

El-Sokkary, R. H., El Seifi, O. S., Hassan, H. M., Mortada, E. M., Hashem, M. K., Gadelrab, M. R. M. A., & Tash, R. M. E. (2021). Predictors of COVID-19 vaccine hesitancy among Egyptian healthcare workers: a cross-sectional study. *BMC Infectious Disease*, *21*(762), 1–9. https://doi.org/10.1186/s12879-021-06392-1

Fontanet, A., Autran, B., Lina, B., & Kieny, M. P. (2021). AbdoolKarim SS, Sridhar D. SARS-CoV-2 variants and ending the COVID-19 pandemic. *Lancet*, *397*, 952–954.

Freeman, D., Loe, B. S., Yu, L.-M., Freeman, J., Chadwick, A., Vaccari, C., Shanyinde, M., Harris, V., Waite, F., Rosebrock, L., Petit, A., Vanderslott, S., Lewandowsky, S., Larkin, M., Innocenti, S., Pollard, A. J., McShane, H., & Lambe, S. (2021). Effects of different types of written vaccination information on COVID-19 vaccine hesitancy in the UK (OCEANS-III): A single-blind, parallel-group, randomised controlled trial. *Lancet Public Health*, *6*, e416–e427.

Furuta, Y., Komeno, T., & Nakamura, T. (2017). Favipiravir (T-705), a broad spectrum inhibitor of viral RNA polymerase. *Proceedings of the Japan Academy, Series B*, *93*(7), 449–463. https://doi.org/10.2183/pjab.93.027

Garcia-Beltran, W. F., St Denis, K. J., Hoelzemer, A., Lam, E. C., Nitido, A. D., Sheehan, M. L., Berrios, C., Ofoman, O., Chang, C. C., Hauser, B. M., Feldman, J., Roederer, A. L., Gregory, D. J., Poznansky, M. C., Schmidt, A. G., Iafrate, A. J., Naranbhai, V., & Balazs, A. B. (2022). mRNA-based COVID-19 vaccine boosters induce neutralizing immunity against SARS-CoV-2 Omicron variant. *Cell*, *S0092–8674*(21), 01496–1503. https://doi.org/10.1016/j.cell.2021.12.033

Ghayda, R. A., Lee, K. H., Han, Y. J., Ryu, S., Hong, S. H., Yoon, S., Jeong, G. H., Yang, J. W., Lee, H. J., Lee, J., Lee, J. Y., Effenberger, M., Eisenhut, M., Kronbichler, A., Solmi, M., Li, H., Jacob, L., Koyanagi, A. I., Radua, J., … Shin, J. I. (2022). Global case fatality rate of coronavirus disease 2019 (COVID-19) by continents and national income: a meta-analysis. *Journal of Medical Virology*, *31*, https://doi.org/10.1002/jmv.27610

GISAID. (2021b). Tracking of variants.2021. https://www.GISAID.org/hcov19- variants/ (accessed Nov 30, 2021)

Gruber, A. D., Firsching, T. C., Trimpert, J., & Dietert, K. (2021). Hamster models of COVID-19 pneumonia reviewed: How human can they be? *Veterinary Pathology*, https://doi.org/10.1177/03009858211057197

Hassanipour, S., Arab-Zozani, M., Amani, B., Heidarzad, F., Fathalipour, M., & Martinez-de-Hoyo, R. (2021). The efficacy and safety of Favipiravir in treatment of COVID-19: A systematic review and meta-analysis of clinical trials. *Scientific Reports*, *11*, 11022. https://doi.org/10.1038/s41598-021-90551-6

Hatmal, M. M., Al-Hatamleh, M. A. I., Olaimat, A. N., Hatmal, M., Alhaj-Qasem, D. M., Olaimat, T. M., & Mohamud, R. (2021). Side effects and perceptions following COVID-19 vaccination in Jordan: A randomized, cross-sectional study implementing machine learning for predicting severity of side effects. *Vaccines*, *9*(6), 556. https://doi.org/10.3390/vaccines9060556

Heath, P. T., Galiza, E. P., Baxter, D. N., Boffito, M., Browne, D., Burns, F., Chadwick, D. R., Clark, R., Cosgrove, C., Galloway, J., Goodman, A. L., Heer, A., Higham, A., Iyengar, S., Jamal, A., Jeanes, C., Kalra, P. A., Kyriakidou, C., McAuley, D. F., … Toback, S. (2021). Safety and Efficacy of NVX-CoV2373 Covid-19 Vaccine. *New England Journal of Medicine*, *385*(13), 1172–1183. https://doi.org/10.1056/NEJMoa2107659

Hoffmann, M., Kleine-Weber, H., Schroeder, S., Kruger, N., Herrler, T., Erichsen, S., Schiergens, T. S., Herrler, G., Wu, N.-H., Nitsche, A., Muller, M. A., Christian Drosten, C., & Pohlmann, S. (2020). SARS-CoV-2n cell entry depends on ACE2 and TMPRSS2 and is blocked by a clinically proven protease inhibitor. *Cell*, *181*(2), 271–280.

Holeva, V., Parlapani, E., Nikopoulou, V. A., Nouskas, I., & Diakogiannis, I. (2022). COVID-19 vaccine hesitancy in a sample of Greek adults. *Psychology, Health & Medicine*, 1–7. https://doi.org/10.1080/13548506.2021.1948579

Huang, J., Zhao, Y., Zhang, L., Li, X., Gao, S., & Song, X. Seasonal Prediction of Omicron Pandemic, medRxiv [preprint] 2022. https://doi.org/https://doi.org/10.1101/2022.01.13.22269198

Hudson, A., & Montelpare, W. J. (2021). Predictors of Vaccine Hesitancy: Implications for COVID-19 Public Health Messaging. *International Journal of Environmental Research and Public Health*, *18*(15), 8054. https://doi.org/10.3390/ijerph18158054

Islam, S., Islam, T., & Islam, R. (2022). New coronavirus variants are creating more challenges to global healthcare system: A brief report on the current knowledge. *Clinical Pathology*, *15*, 1–7. https://doi.org/10.1177/2632010X221075584

Iwatsuki-Horimoto, K., Nakajima, N., Ichiko, Y., Sakai-Tagawa, Y., Noda, T., Hasegawa, H., & Kawaoka, Y. (2018). Syrian hamster as an animal model for the study of human influenza virus infection. *Journal of Virology*, *92*(4), e01693–e1717.

Jahan, N., Rahman, F. I., Saha, P., Ether, S. A., Roknuzzaman, A., Sarker, R., Kalam, K. T., Haq, K., Nyeen, J., Himi, H. Z., Hossain, M. N., Chowdhury, M. H., Uddin, M. M., & Alam, N. H. (2021). Side effects following administration of the first dose of oxford-AstraZeneca's covishield vaccine in bangladesh: A cross-sectional study. *Infectious Disease Reports*, *13*, 888–901. https://doi.org/10.3390/idr13040080

Jain, J., Saurabh, S., Kumar, P., Verma, M. K., Goel, A. D., Gupta, M. K., Bhardwaj, P., & Raghav, P. R. (2021). COVID-19 vaccine hesitancy among medical students in India. *Epidemiology and Infection*, *149*, e132, 1–10. https://doi.org/10.1017/S0950268821001205

Jarynowski, A., Semenov, A., Kamiński, M., & Belik, V. (2021). Mild adverse events of sputnik V vaccine in Russia: Social media content analysis of telegram via deep learning. *Journal of Medical Internet Research*, *23*(11), e30529–https://doi.org/10.2196/30529

Jia, W., Wang, J., Sun, B., Zhou, J., Shi, Y., & Zhou, Z. (2021). The mechanisms and animal models of SARS-CoV-2 infection. *Frontiers in Cell and Developmental Biology*, *9*, 578825. https://doi.org/10.3389/fcell.2021.578825

Karim, S. S. A., & Karim, Q. A. (2021). Omicron SARS-CoV-2 variant: A new chapter in the COVID-19 pandemic. *The Lancet*, https://doi.org/10.1016/S0140-6736(21)02758-6

Kelekar, A. K., Lucia, V. C., Afonso, N. M., & Mascarenhas, A. K. (2021). COVID-19 vaccine acceptance and hesitancy among dental and medical students. *JADA*, *152*(8), 596–603. https://doi.org/10.1016/j.adaj.2021.03.006

Kokic, G., Hillen, H. S., Tegunov, D., Dienemann, C., Seitz, F., Schmitzova, J., Farnung, L., Siewert, A., Höbartner, C., & Cramer, P. (2021). Mechanism of SARS-CoV-2 polymerase stalling by remdesivir. *Nature Communications*, *12*, 279. https://doi.org/10.1038/s41467-020-20542-0

Lenzen, M., Li, M., Malik, A., Pomponi, F., Sun, Y.-Y., Wiedmann, T., Faturay, F., Fry, J., Gallego, B., Geschke, A., Gomez-Paredes, J., Kanemoto, K., Kenway, S., Nansai, K., Prokopenko, M., Wakiyama, T., Wang, Y., & Yousefzadeh, M. (2020). Global socio-economic losses and environmental gains from the Coronavirus pandemic. *PLoS One*, *15*(7), e0235654.

Li, K., Wohlford-Lenane, C. L., Channappanavar, R., Park, J.-E., Earnest, J. T., Bair, T. B., Bates, A. M., Brogden, K. A., Flaherty, H. A., Gallagher, T., Meyerholz, D. K., Perlmana, S., & McCray, P. B. Jr (2017). Mouse adapted MERS coronavirus causes lethal lung disease in human DPP4 knockin mice. *Proceedings of the National Academy of Sciences of the United States of America*, *114*(15), E3119.

Logunov, D. Y., Dolzhikova, I. V., Shcheblyakov, D. V., Tukhvatulin, A. I., Zubkova, O. V., Dzharullaeva, A. S., Kovyrshina, A. V., Lubenets, N. L., Grousova, D. M., Erokhova, A. S., Botikov, A. G., Izhaeva, F. M., Popova, O., Ozharovskaya, T. A., Esmagambetov, I. B., Favorskaya, I. A., Zrelkin, D. I., Voronina, D. V., Shcherbinin, D. N., … Gintsburg, A. L. (2021). Gam-COVID-Vac Vaccine Trial Group. Safety and efficacy of an rAd26 and rAd5 vector-based heterologous prime-boost COVID-19 vaccine: An interim analysis of a randomised controlled phase 3 trial in Russia. *Lancet*, *397*(10275):671–681.

López-Medina, E., López, P., Hurtado, I. C., Dávalos, D. M., Ramirez, O., Martínez, E., Díazgranados, J. A., Oñate, J. M., Chavarriaga, H., Herrera, S., Parra, B., Libreros, G., Jaramillo, R., Avendaño, A. C., Toro, D. F., Torres, M., Lesmes, M. C., Rios, C. A., & Caicedo, I. (2021). Effect of ivermectin on time to resolution of symptoms among adults with mild COVID-19: A randomized clinical trial. *JAMA*, *325*(14), 1426–1435. https://doi.org/10.1001/jama.2021.3071

Lu, L., Mok, B. W., Chen, L. L., Chan, J. M., Tsang, O. T., Lam, B. H., Chuang, V. W., Chu, A. W., Chan, W. M., Ip, J. D., Chan, B. P., Zhang, R., Yip, C. C., Cheng, V. C., Chan, K. H., Jin, D. Y., Hung, I. F., Yuen, K. Y., Chen, H., & To, K. K. (2021) Neutralization of SARS-CoV-2 Omicron variant by sera from BNT162b2 or Coronavac vaccine recipients. *Clinical Infectious Diseases*. 2021 Dec 16:ciab1041. https://doi.org/10.1093/cid/ciab1041

Lucia, V. C., Kelekar, A., & Afonso, N. M. (2021). COVID-19 vaccine hesitancy among medical students. *Journal of Public Health*, *43*(3), 445–449. https://doi.org/10.1093/pubmed/fdaa230

Mantha, M. K., Suvvari, T. K., & Corriero, A. C. (2021). 2-Deoxy-D-glucose as an armament against COVID-19: The key to return to normality. *Biomedical and Biotechnology Research Journal*, *5*, 347–348.

Mattiuzzi, C., & Lippi, G. (2022). COVID-19 vaccines efficacy in preventing or limiting SARS-CoV-2 infections. *Journal of Infection*, https://doi.org/10.1016/j.jinf.2022.01.033

McMahan, K., Yu, J., Mercado, N. B., Loos, C., Tostanoski, L. H., Chandrashekar, A., Liu, J., Peter, L., Atyeo, C., Zhu, A., Bondzie, E. A., Dagotto, G., Gebre, M. S., JacobDolan, C., Li, Z., Nampanya, F., Patel, S., Pessaint, L., Ry, A. V., ... Barouch, D. H. (2021). Correlates of protection against SARS-CoV-2 in rhesus macaques. *Nature*, *590*(7847), 630–634.

Menni, C., Klaser, K., May, A., Polidori, L., Capdevila, J., Louca, P., Sudre, C. H., Nguyen, L. H., Drew, D. A., Merino, J., Hu, C., Selvachandran, S., Antonelli, M., Murray, B., Canas, L. S., Molteni, E., Graham, M. S., Modat, M., Joshi, A. D., ... Spector, T. D. (2021). Vaccine side-effects and SARS-CoV-2 infection after vaccination in users of the COVID Symptom Study app in the UK: A prospective observational study. *The Lancet Infectious Diseases*, *21*, 939–949. https://doi.org/10.1016/S1473-3099(21)00224-3

Miao, J., Chard, L. S., Wang, Z., & Wang, Y. (2019). Syrian hamster as an animal model for the study on infectious diseases. *Frontiers in Immunology*, *10*, 2329.

Ministry of Defence (2021). DCGI Approves Anti-COVID Drug Developed by DRDO for Emergency use. Available from: https://pib.gov.in/PressReleasePage.aspx?PRID=1717007 (accessed on Nov14, 2021)

Mlcochova, P., Kemp, S. A., Dhar, M. S., Papa, G., Meng, B. O., Ferreira, I. A. T. M., Datir, R., Collier, D. A., Albecka, A., Singh, S., Pandey, R., Brown, J., Zhou, J., Goonawardane, N., Mishra, S., Whittaker, C., Mellan, T., Marwal, R., Datta, M., ... Gupta, R. K. (2021). SARS-CoV-2 B.1.617.2 Delta variant replication and immune evasion. *Nature*, *599*, 114–119. https://doi.org/10.1038/s41586-021-03944-y

Mohapatra, R. K., Das, P. K., & Kandi, V. (2020). Challenges in controlling COVID-19 in migrants in Odisha, India. *Diabetes & Metabolic Syndrome: Clinical Research & Reviews*, *14*, 1593–1594. https://doi.org/10.1016/j.dsx.2020.08.024

Mohapatra, R. K., Das, P. K., Pintilie, L., & Dhama, K. (2021e). Infection capability of SARS-CoV-2 on different surfaces. *Egyptian Journal of Basic and Applied Sciences*, *8*(1), 75–80. https://doi.org/10.1080/2314808X.2021.1907915

Mohapatra, R. K., Das, P. K., Sharun, K., Tiwari, R., Mohapatara, S. R., Mohapatra, P. K., Behera, A., Acharyya, T., Kandi, V., Zahan, K.-E., Natesan, S., Bilal, M., & Dhama, K. (2021c). Negative and positive environmental perspective of COVID-19: Air, water, wastewater, forest, and noise quality. *Egyptian Journal of Basic and Applied Sciences*, *8*(1), 364–384. https://doi.org/10.1080/2314808X.2021.1973182

Mohapatra, R. K., Dhama, K., El-Arabey, A. A., Sarangi, A. K., Tiwari, R., Emran, T. B., Azam, M., Al-Resayes, S. I., Raval, M. K., Seidel, V., & Abdalla, M. (2021b). Repurposing benzimidazole and benzothiazole derivatives as potential inhibitors of SARS-CoV-2: DFT, QSAR, molecular docking, molecular dynamics simulation, and *in-silico* pharmacokinetic and toxicity studies. *Journal of King Saud University*, *33*(8), 101637.

Mohapatra, R. K., Dhama, K., Mishra, S., Sarangi, A. K., Kandi, V., Tiwari, R., & Pintilie, L. (2021f). The microbiota-related coinfections in COVID-19 patients: a real challenge. *Beni-Suef University Journal of Basic and Applied Sciences*, *10*, 47. https://doi.org/10.1186/s43088-021-00134-7

Mohapatra, R. K., Mishra, S., Azam, M., & Dhama, K. (2021d). COVID-19, WHO guidelines, pedagogy, and respite. *Open Medicine*, *16*, 491–493. https://doi.org/10.1515/med-2021-0266

Mohapatra, R. K., Perekhoda, L., Azam, M., Suleiman, M., Sarangi, A. K., Semenets, A., Pintilie, L., & Al-Resayes, S. I. (2021a). Computational investigations of three main drugs and their comparison with synthesized compounds as potent inhibitors of SARS-CoV-2 main protease (Mpro): DFT, QSAR, molecular docking, and in silico toxicity analysis. *Journal of King Saud University - Science*, *33*, 101315. https://doi.org/10.1016/j.jksus.2020.101315

Mohapatra, R. K., Pintilie, L., Kandi, V., Sarangi, A. K., Das, D., Sahu, R., & Perekhoda, L. (2020). The recent challenges of highly contagious COVID-19; causing respiratory infections: symptoms, diagnosis, transmission, possible vaccines, animal models and immunotherapy. *Chemical Biology & Drug Design*, *96*(5), 1187–1208. https://doi.org/10.1111/cbdd.13761

Mohapatra, R. K., & Rahman, M. (2021). Is it possible to control the outbreak of COVID-19 in Dharavi, Asia's largest slum situated in Mumbai? *Anti-Infect Agents*, *19*(4), 1–2. https://doi.org/10.2174/2211352518999200831142851

Mohapatra, R. K., Sarangi, A. K., Kandi, V., Azam, M., Tiwari, R., & Dhama, K. (2022). Omicron (B.1.1.529 variant of SARS-CoV-2); an emerging threat: Current global scenario. *Journal of Medical Virology*, https://doi.org/10.1002/jmv.27561

Mohapatra, R. K., Tiwari, R., Sarangi, A. K., Islam, R., Chakraborty, C., & Dhama, K. (2022c). Omicron (B.1.1.529) variant of SARS-CoV-2– Concerns, challenges and recent updates. *Journal of Medical Virology*, https://doi.org/10.1002/jmv.27561

Mohapatra, R. K., Tiwari, R., Sarangi, A. K., Sharma, S. K., Khandia, R., Saikumar, G., & Dhama, K. (2022b). Twin combination of Omicron and Delta variant triggering a Tsunami wave of ever high surges in COVID-19 cases: A challenging global threat with a special focus on Indian sub-continent. *Journal of Medical Virology*, https://doi.org/10.1002/jmv.27585

Moody, M., Ryan, P., Dannenbaum, P., Kruper, R., & Carvalho, C. Merck and co's official release on Molnupiravir. Available from https://www.merck.com/news/merck-and-ridgebacks-investigational-oral-antiviral-molnupiravir-reduced-the-risk-of-hospitalization-or-death-by-approximately-50-percent-compared-to-placebo-for-patients-with-mild-or-moderat/ [last accessed on 2021,Nov 7]

Munoz-Fontela, C., Dowling, W. E., Funnell, S. G. P., Gsell, P. S., Balta, X. R., Albrecht, R. A., Andersen, H., Baric, R. S., Carroll, M. W., Qin, C., Crozier, I., Dallmeier, K., de Waal, L., de Wit, E., Delang, L., Dohm, E., Duprex, W. P., Falzarano, D., Finch, C., ... Barouch, D. H. (2020). Animal models for COVID-19. *Nature*, *586*(7830), 509–515.

Nicola, M., Alsafi, Z., Sohrabi, C., Kerwand, A., Al-Jabird, A., Iosifidisc, C., Aghae, M. & Agha, R. (2020). The socio-economic implications of the Coronavirus pandemic (COVID-19): A review. *International Journal of Surgery*, *78*, 185–193.

Nunez, I. A., Lien, C. Z., Selvaraj, P., Stauft, C. B., Liu, S., Starost, M. F., & Wang, T. T. (2021). *SARS-CoV-2 B.1.1.7 infection of Syrian hamster does not cause more severe disease and is protected by naturally acquired immunity*. bioRxiv. Preprint, https://doi.org/10.1101/2021.04.02.438186

Osterrieder, N., Bertzbach, L. D., Dietert, K., Abdelgawad, A., Vladimirova, D., Kunec, D., Hoffmann, D., Beer, M., Gruber, A. D., & Trimpert, J. (2020). Age-dependent progression of SARS-CoV-2 infection in Syrian hamsters. *Viruses*, *12*(7), 779. https://doi.org/10.3390/v12070779

Painter, W. P., Holman, W., Bush, J. A., Almazedi, F., Malik, H., Eraut, N. C. J. E., Morin, M. J., Szewczyk, L. J., & Painter, G. R. (2021). Human safety, tolerability, and pharmacokinetics

of Molnupiravir, a novel broad-spectrum oral antiviral agent with activity against SARS-CoV-2. *Antimicrobial Agents and Chemotherapy*. 1;*65*(5):e02428-20.

Pajon, R., Doria-Rose, N. A., Shen, X., Schmidt, S. D., O'Dell, S., McDanal, C., Feng, W., Tong, J., Eaton, A., Maglinao, M., Tang, H., Manning, K. E., Edara, V. V., Lai, L., Ellis, M., Moore, K. M., Floyd, K., Foster, S. L., Posavad, C. M., ... Montefiori, D. C. (2022). SARS-CoV-2 omicron variant neutralization after mRNA-1273 Booster vaccination. *New England Journal of Medicine*, https://doi.org/10.1056/NEJMc2119912

Pal, M., Tiwari, R., Dhama, K., Parija, S., Jena, O. P., & Mohapatra, R. K. (2022). Machine learning algorithms and COVID-19; A step for predicting future pandemics with a systematic overview, Chapter-18, 203–218. https://doi.org/10.1201/9781003226147-11

Planas, D., Veyer, D., Baidaliuk, A., Staropoli, I., Guivel-Benhassine, F., Rajah, M. M., Planchais, C., Porrot, F., Robillard, N., Puech, J., Prot, M., Gallais, F., Gantner, P., Velay, A., Le Guen, J., Kassis-Chikhani, N., Edriss, D., Belec, L., Seve, A., ... Schwartz, O. (2021). Reduced sensitivity of SARS-CoV-2 variant Delta to antibody neutralization. *Nature*, *596*, 276–280. https://doi.org/10.1038/s41586-021-03777-9

Polack, F. P., Thomas, S. J., Kitchin, N., Absalon, J., Gurtman, A., Lockhart, S., Perez, J. L., Pérez Marc, G., Moreira, E. D., Zerbini, C., Bailey, R., Swanson, K. A., Roychoudhury, S., Koury, K., Li, P., Kalina, W. V., Cooper, D., Frenck, R. W., Hammitt, L. L., ... Gruber, W. C. (2020). C4591001 Clinical Trial Group. Safety and efficacy of the BNT162b2 mRNA COVID-19 vaccine. *New England Journal of Medicine*, *383*(27), 2603–2615. https://doi.org/10.1056/NEJMoa2034577

Qunaibi, E. A., Helmy, M., Basheti, I., & Sultan, I. (2021). A high rate of COVID-19 vaccine hesitancy in a large-scale survey on Arabs. *eLife*, *10*, e68038.

Ramasamy, M. N., Minassian, A. M., Ewer, K. J., Flaxman, A. L., Folegatti, P. M., Owens, D. R., Voysey, M., Aley, P. K., Angus, B., Babbage, G., Belij-Rammerstorfer, S., Berry, L., Bibi, S., Bittaye, M., Cathie, K., Chappell, H., Charlton, S., Cicconi, P., Clutterbuck, E. A., & Pollard, A. J. ... the Oxford COVID Vaccine Trial Group (2020). Safety and immunogenicity of ChAdOx1 nCoV-19 vaccine administered in a prime-boost regimen in young and old adults (COV002): A single-blind, randomised, controlled, phase 2/3 trial. *The Lancet*, *396*(10267), 1979–1993. https://doi.org/10.1016/S0140-6736(20)32466-1

Rebecca, N. K., En-Ling, W. U., Valentina, S., Moore, W. J., Achenbach, C., Ison, M. G., & Angarone, M. P. (2021). M. P. real-world experience of bamlanivimab for coronavirus disease 2019 (COVID-19): A case-control study. *Clinical Infectious Diseases*, *74*(1), 24–31. https://doi.org/10.1093/cid/ciab305

Riad, A., Abdulqader, H., Morgado, M., Domnori, S., Koščík, M., Mendes, J. J., Klugar, M., & Kateeb, E. (2021). On behalf of IADS-SCORE. Global Prevalence and Drivers of Dental Students' COVID-19 Vaccine Hesitancy. *Vaccines*, *9*(6), 566–https://doi.org/10.3390/vaccines9060566

Riad, A., Hocková, B., Kantorová, L., Slávik, R., Spurná, L., Stebel, A., Havriľak, M., & Klugar, M. (2021). Side effects of mRNA-Based COVID-19 vaccine: Nationwide Phase IV Study among Healthcare Workers in Slovakia. *Pharmaceuticals*, *14*, 873. https://doi.org/10.3390/ph14090873

Riad, A., Pokorná, A., Attia, S., Klugarová, J., Koščík, M., & Klugar, M. (2021). Prevalence of COVID-19 vaccine side effects among healthcare workers in the Czech Republic. *Journal of Clinical Medicine*, *10*, 1428. https://doi.org/10.3390/jcm10071428

Roberts, A., Lamirande, E. W., Vogel, L., Jackson, J. P., Paddock, C. D., Guarner, J., Zaki, S. R., Sheahan, T., Baric, R., & Subbarao, K. (2008). Animal models and vaccines for SARS-CoV infection. *Virus Research*, *133*(1), 20–32.

Roberts, A., Vogel, L., Guarner, J., Hayes, N., Murphy, B., Zaki, S., & Subbarao, K. (2005). Severe acute respiratory syndrome coronavirus infection of golden Syrian hamsters. *Journal of Virology*, *79*(1), 503–511.

Rosa, R. B., Dantas, W. M., do Nascimento, J. C. F., da Silva, M. V., de Oliveira, R. N., & Pena, L. J. (2021). In vitro and in vivo models for studying SARS-CoV-2, the etiological agent responsible for COVID-19 pandemic. *Viruses*, *13*(3), 379.

Rosenke, K., Meade-White, K., Letko, M., Clancy, C., Hansen, F., Liu, Y., Okumura, A., Tang-Huau, T.-L., Li, R., Saturday, G., Feldmann, F., Scott, D., Wang, Z., Munster, V., Jarvisa, M. A., & Feldmann, H. (2020). Defining the Syrian hamster as a highly susceptible preclinical model for SARS-CoV-2 infection. *Emerging Microbes & Infections*, *9*(1), 2673–2684.

Rössler, A., Riepler, L., Bante, D., von Laer, D., & Kimpel, J. (2022). SARS-CoV-2 omicron variant neutralization in serum from vaccinated and convalescent persons. *New England Journal of Medicine*, *386*(7), 698–700. https://doi.org/10.1056/NEJMc2119236

Rzymski, P., Poniedziałek, B., & Fal, A. (2021). willingness to receive the booster COVID-19 vaccine dose in Poland. *Vaccines*, *9*, 1286. https://doi.org/10.3390/vaccines9111286

Sadoff, J., Gray, G., Vandebosch, A. N., Cárdenas, V., Shukarev, G., Grinsztejn, B., Goepfert, P. A., Truyers, C., Fennema, H., Spiessens, B., Offergeld, K., Scheper, G., Taylor, K. L., Robb, M. L., Treanor, J., Barouch, D. H., Stoddard, J., Ryser, M. F., Marovich, M. A., ... Douoguih, M. (2021). ENSEMBLE Study Group. Safety and efficacy of single-dose Ad26.COV2.S vaccine against Covid-19. *New England Journal of Medicine*, *384*(23), 2187–2201. https://doi.org/10.1056/NEJMoa2101544

Saeed, B. Q., Al-Shahrabi, R., Alhaj, S. S., Alkokhardi, Z. M., & Adrees, A. O. (2021). Side effects and perceptions following Sinopharm COVID-19 vaccination. *International Journal of Infectious Diseases*, *111*, 219–226. https://doi.org/10.1016/j.ijid.2021.08.013

Schmidt, F., Muecksch, F., Weisblum, Y., Da Silva, J., Bednarski, E., Cho, A., Wang, Z., Gaebler, C., Caskey, M., Nussenzweig, M. C., Hatziioannou, T., & Bieniasz, P. D. (2021). Plasma neutralization of the SARS-CoV-2 omicron variant. *New England Journal of Medicine*, *386*(6), 599–601. https://doi.org/10.1056/NEJMc2119641

Selvaraj, P., Lien, C. Z., Liu, S., Stauft, C. B., Nunez, I. A., Hernandez, M., Nimako, E., Ortega, M. A., Starost, M. F., Dennis, J. U., & Wang, T. T. (2021). SARS-CoV-2 infection induces protective immunity and limits transmission in Syrian hamsters. *Life Science Alliance*, *4*(4), e202000886.

Sheppard, M., Laskou, F., Stapleton, P. P., Hadavi, S., & Dasgupta, B. (2017). Tocilizumab (Actemra). *Hum VaccinImmunother*, *13*(9), 1972–1988. https://doi.org/10.1080/21645515.2017.1316909

Sievers, B. L., Chakraborty, S., Xue, Y., Gelbart, T., Gonzalez, J. C., Cassidy, A. G., Golan, Y., Prahl, M., Gaw, S. L., Arunachalam, P. S., Blish, C. A., Boyd, S. D., Davis, M. M., Jagannathan, P., Nadeau, K. C., Pulendran, B., Singh, U., Scheuermann, R. H., Frieman, M. B., ... Tan, G. S. (2022). Antibodies elicited by

SARS-CoV-2 infection or mRNA vaccines have reduced neutralizing activity against Beta and Omicron pseudoviruses. *Science Translational Medicine*, https://doi.org/10.1126/scitranslmed.abn7842

Sloka, J. S., & Stefanelli, M. (2005). The mechanism of action of methylprednisolone in the treatment of multiple sclerosis. *MultScler*, *11*(4), 425–432. https://doi.org/10.1191/1352458505ms1190oa

Soriano, V., de-Mendoza, C., Edagwa, B., Treviño, A., Barreiro, P., Fernandez-Montero, J. V., Gendelman, H. E. (2022). Oral antivirals for the prevention and treatment of SARS-CoV-2 infection. *Aids Reviews*, https://doi.org/10.24875/AIDSRev.22000001

Spinner, C. D., Gottlieb, R. L., Criner, G. J., Arribas López, J. R., Cattelan, A. M., Soriano Viladomiu, A., Ogbuagu, O., Malhotra, P., Mullane, K. M., Castagna, A., Chai, L. Y. A., Roestenberg, M., Tsang, O. T. Y., Bernasconi, E., Le Turnier, P., Chang, S.-C., SenGupta, D., Hyland, R. H., Osinusi, A. O., … Marty, F. M. (2020). Effect of remdesivir vs standard care on clinical status at 11 days in patients with moderate COVID-19: A randomized clinical trial. *JAMA*, *324*(11), 1048–1057. https://doi.org/10.1001/jama.2020.16349

Sukhatme, V. P., Reiersen, A. M., Vayttaden, S. J., & Sukhatme, V. V. (2021). Fluvoxamine: A review of its mechanism of action and its role in COVID-19. *Frontiers in Pharmacology*, *12*, 652688. https://doi.org/10.3389/fphar.2021.652688

Suvvari, T. K. (2020). Therapeutic uses of monoclonal antibodies for COVID-19. *Biomed Research International*, *7*, 60–61.

Suvvari, T. K., Kuppili, P. C., Kandi, S., Kutikuppala, K. V. L. V. S., Mishra, V. D. K., Sarangi, A. K., Mohapatra, R. K., Dhama, K. (2021). Consecutive hits of COVID-19 in India: The mystery of plummeting cases and current scenario. *Archives of Razi Institute*, *76*(5), 1165–1174.

Takashita, E., Kinoshita, N., Yamayoshi, S., Sakai-Tagawa, Y., Fujisaki, S., Ito, M., Iwatsuki-Horimoto, K., Chiba, S., Halfmann, P., Nagai, H., Saito, M., Adachi, E., Sullivan, D., Pekosz, A., Watanabe, S., Maeda, K., Imai, M., Yotsuyanagi, H., Mitsuya, H., … Kawaoka, Y. (2022). Efficacy of antibodies and antiviral drugs against Covid-19 omicron variant. *New England Journal of Medicine*, https://doi.org/10.1056/NEJMc2119407

Takayama, K. (2020). In vitro and animal models for SARS-CoV-2 research. *Trends in Pharmacological Sciences*, *41*(8), 513–517. https://doi.org/10.1016/j.tips.2020.05.005

Tanriover, M. D., Doğanay, H. L., Akova, M., Güner, H. R., Azap, A., Akhan, S., Köse, Ş., Erdinç, F. Ş., Akalın, E. H., Tabak, Ö. F., Pullukçu, H., Batum, Ö., Şimşek Yavuz, S., Turhan, Ö., Yıldırmak, M. T., Köksal, İ., Taşova, Y., Korten, V., Yılmaz, G., … Aksu, K. (2021). Efficacy and safety of an inactivated whole-virion SARS-CoV-2 vaccine (CoronaVac): interim results of a double-blind, randomised, placebo-controlled, phase 3 trial in Turkey. *Lancet*, *398*(10296), 213–222. https://doi.org/10.1016/S0140-6736(21)01429-X

The RECOVERY Collaborative Group (2021). Dexamethasone in hospitalized patients with Covid-19. *The New England Journal of Medicine*. *384*, 693–704. https://doi.org/10.1056/NEJMoa2021436

Tiwari, R., Dhama, K., Sharun, K., Iqbal Yatoo, M., Malik, Y. S., Singh, R., Michalak, I., Sah, R., Bonilla-Aldana, D. K., & Rodriguez-Morales, A. J. (2020). COVID-19: Animals, veterinary and zoonotic links. *The Veterinary Quarterly*, *40*(1), 169–182. https://doi.org/10.1080/01652176.2020.1766725

Torjesen, I. (2021). Covid-19: Omicron may be more transmissible than other variants and partly resistant to existing vaccines, scientists fear. *BMJ*, *2021*(375), n2943. https://doi.org/10.1136/bmj.n2943

Troiano, G., & Nardi, A. (2021). Vaccine hesitancy in the era of COVID-19. *Public Health*, *194*, 245–251. https://doi.org/10.1016/j.puhe.2021.02.025

U.S. National library of medicine clinical trails.gov (2021a) A Double-blind, Placebo-controlled Clinical Trial of Fluvoxamine for Symptomatic Individuals With COVID-19 Infection (STOP COVID), ClinicalTrials.gov Identifier: NCT04342663. Available from https://clinicaltrials.gov/ct2/show/results/NCT04342663 [last accessed on Nov 9, 2021]

U.S. National library of medicine clinical trails.gov (2021b) A Study to Evaluate the Safety and Efficacy of Tocilizumab in Patients With Severe COVID-19 Pneumonia (COVACTA), ClinicalTrials.gov Identifier: NCT04320615. Available from https://clinicaltrials.gov/ct2/show/results/NCT04320615 [last accessed on Nov10, 2021]

U.S. National library of medicine clinical trails.gov (2021c) Methylprednisolone for Patients With COVID-19 Severe Acute Respiratory Syndrome (MP-C19), ClinicalTrials.gov Identifier: NCT04323592. Available from https://clinicaltrials.gov/ct2/show/results/NCT04323592 [last accessed on Nov14, 2021]

Uddin, E., Islam, R., Ashrafuzzaman, N., Bitu, A., Hossain, M. S., Islam, A. B. M. N., Asraf, A., Hossen, F., Mohapatra, R. K., & E-Zahan, M. (2021). Potential drugs for the treatment of COVID-19: Synthesis, brief history and application. *Current Drug Research Reviews*, *13*(3). https://doi.org/10.2174/2589977513666210611155426

Voysey, M., Clemens, S. A. C., Madhi, S. A., Weckx, L. Y., Folegatti, P. M., Aley, P. K., Angus, B., Baillie, V. L., Barnabas, S. L., Bhorat, Q. E., Bibi, S., Briner, C., Cicconi, P., Collins, A. M., Colin-Jones, R., Cutland, C. L., Darton, T. C., Dheda, K., Duncan, C. J. A., … Zuidewind, P. (2021). Oxford COVID Vaccine Trial Group. Safety and efficacy of the ChAdOx1 nCoV-19 vaccine (AZD1222) against SARS-CoV-2: An interim analysis of four randomised controlled trials in Brazil, South Africa, and the UK. *Lancet*, *397*(10269), 99–111. https://doi.org/10.1016/S0140-6736(20)32661-1

Wang, B., Goh, Y. S., Fong, S. W., Young, B. E., Ngoh, E. Z. X., Chavatte, J. M., Salleh, S. N. M., Yeo, N. K., Amrun, S. N., Hor, P. X., Loh, C. Y., Lee, C. Y., Chan, Y. H., Chang, Z. W., Tay, M. Z., Rouers, A., Torres-Ruesta, A., Carissimo, G., Soh, M. K., … Wang, C. I. (2021). Resistance of SARS-CoV-2 Delta variant to neutralization by BNT162b2-elicited antibodies in Asians. *The Lancet Regional Health - Western Pacific*, *15*, 100276. https://doi.org/10.1016/j.lanwpc.2021.100276

WHO (2021), Classification of Omicron (B.1.1.529): SARS-CoV-2 Variant of Concern, 26 November 2021. https://www.WHO.int/news/item/26-11-2021-classification-of-omicron-(b.1.1.529)-sars-cov-2-variant-of-concern

WHO (2022). WHO recommends two new drugs to treat COVID-19, 14 January 2022. https://www.who.int/news/item/14-01-2022-who-recommends-two-new-drugs-to-treat-covid-19accessed on: 06-02-2022

Wiysonge, C. S., Ndwandwe, D., Ryan, J., Jaca, A., Batouré, O., Anya, B.-P.-M., & Cooper, S. (2021). Vaccine hesitancy in the era of COVID-19: Could lessons from the past help in divining the future? *Human Vaccines & Immunotherapeutics*, *9*, 1–3. https://doi.org/10.1080/21645515.2021.1893062

Xia, S., Duan, K., Zhang, Y., Zhao, D., Zhang, H., Xie, Z., Li, X., Peng, C., Zhang, Y., Zhang, W., Yang, Y., Chen, W., Gao, X., You, W., Wang, X., Wang, Z., Shi, Z., Wang, Y., Yang, X., … Yang, X. (2020). Effect of an inactivated vaccine against SARS-CoV-2 on safety and immunogenicity outcomes: interim analysis of 2 randomized clinical trials. *JAMA*, *324*(10), 951–960. https://doi.org/10.1001/jama.2020.15543

Xu, J., Vanijcharoenkarn, K., Sexton, M. E., Martin, L., Lee, F.-E.-H., & Kuruvilla, M. E. (2021). Delayed hypersensitivity reactions following first dose of the SARS-CoV2 mRNA vaccines. *Journal of General Internal Medicine*, *36*(10), 3298–3300. https://doi.org/10.1007/s11606-021-07015-w

Yadav, P. D., Mohandas, S., Shete, A. M., Nyayanit, D. A., Gupta, N., Patil, D. Y., Sapkal, G. N., Potdar, V., Kadam, M., Kumar, A., Kumar, S., Suryavanshi, D., Mote, C. S., Abraham, P., Panda, S., & Bhargava, B. (2021). *SARS CoV-2 variant B.1.617.1 is highly pathogenic in hamsters than B.1 variant*. bioRxiv. Preprint, https://doi.org/10.1101/2021.05.05.442760

Yang, S., Li, Y., Dai, L., Wang, J., He, P., Li, C., Fang, X., Wang, C., Zhao, X., Huang, E., Wu, C., Zhong, Z., Wang, F., Duan, X., Tian, S., Wu, L., Liu, Y., Luo, Y. I., Chen, Z., … Gao, G. F. (2021). Safety and immunogenicity of a recombinant tandem-repeat dimeric RBD-based protein subunit vaccine (ZF2001) against COVID-19 in adults: two randomised, double-blind, placebo-controlled, phase 1 and 2 trials. *The Lancet Infectious Diseases*, *21*(8), 1107–1119. https://doi.org/10.1016/S1473-3099(21)00127-4

Younes, S., Younes, N., Shurrab, F., & Nasrallah, G. K. (2020). Severe acute respiratory syndrome coronavirus-2 natural animal reservoirs and experimental models: Systematic review. *Reviews in Medical Virology*, *31*(4), e2196.

Yu, J., Tostanoski, L. H., Peter, L., Mercado, N. B., McMahan, K., Mahrokhian, S. H., Nkolola, J. P., Liu, J., Li, Z., Chandrashekar, A., Martinez, D. R., Loos, C., Atyeo, C., Fischinger, S., Burke, J. S., Slein, M. D., Chen, Y., Zuiani, A., Lelis, F. J. N., … Barouch, D. H. (2020). DNA vaccine protection against SARS-CoV-2 in rhesus macaques. *Science*, *369*(6505), 806–811.

Zeiss, C. J., Compton, S., & Veenhuis, R. T. (2021). Animal models of COVID-19. I. Comparative virology and disease pathogenesis. *ILAR Journal*, https://doi.org/10.1093/ilar/ilab007

Zena, W., Wehbe, M., Rabah, I., Gianfranco, P., Hassan, Z., Yassine, H. M., & Eid, A. H. (2021). Repurposing ivermectin for COVID-19: Molecular aspects and therapeutic possibilities. *Frontiers in Immunology*, *12*, 1040. https://doi.org/10.3389/fimmu.2021.663586

Zhang, S., Li, L., Shen, A., Chen, Y., & Qi, Z. (2020). Rational use of tocilizumab in the treatment of novel coronavirus Pneumonia. *Clinical Drug Investigation*, *40*(6), 511–518. https://doi.org/10.1007/s40261-020-00917-3

Zhu, F.-C., Li, Y.-H., Guan, X.-H., Hou, L.-H., Wang, W.-J., Li, J.-X., Wu, S.-P., Wang, B.-S., Wang, Z., Wang, L., Jia, S.-Y., Jiang, H.-D., Wang, L., Jiang, T., Hu, Y. I., Gou, J.-B., Xu, S.-B., Xu, J.-J., Wang, X.-W., … Chen, W. (2020). Safety, tolerability, and immunogenicity of a recombinant adenovirus type-5 vectored COVID-19 vaccine: A dose-escalation, open-label, non-randomised, first-in-human trial. *Lancet*, *395*(10240), 1845–1854. https://doi.org/10.1016/S0140-6736(20)31208-3

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