IARJSET

ISSN (Online) 2393-8021
ISSN (Print) 2394-1588

International Advanced Research Journal in Science, Engineering and Technology

5th National Conference on Science, Technology and Communication Skills – NCSTCS 2K22

Narula Institute of Technology, Agarpara, Kolkata, India

Vol. 9, Special Issue 2, September 2022

Role of Covid-19 Vaccines on the Pandemic

Rajdeep Paul[1], Saurabh Kumar[2] and Subhasree Bhattacharjee[3]

Computer Application Dept., Narula Institute of Technology, Kolkata, India[1-3]

Abstract: COVID-19 is caused by the severe acute respiratory syndrome corona virus 2 (SARS-CoV-2) emerged as a global threat from 2019. Not only human life, COVID-19 causes huge impact on economy as well as on society. To mitigate the impact of COVID-19 several social restriction strategies have been adopted. Vaccination provides an emerging solution to the problem. Research on vaccine development following the discoveries on the genomics and molecular biology of the virus is carried out by the scientists. The main objective of vaccination is to impose hard immunity with reduced mortality and thus lowering the number of admitted patients. This review article focuses on the physiology on the vaccines and the immune response of humans caused by the Spike Protein. Furthermore, the overview, dosing strategies, efficiency and side effect of BioNTech/Pfiser, Moderna, AstraZeneca, Janssen, Gamaleya and SinoVac have been analysed. Moreover the development of other COVID-19 vaccines will be discussed with the sustainability of the vaccine imposed immune response. Also the impact of COVID-19 vaccinations on pregnancy is highlighted here. At last, the important variants of concern are described and the effectiveness of the applied vaccines on the variants has been illustrated.

Keywords*:* COVID-19, mortality, vaccination, variants

I. INTRODUCTION

The COVID-19diseaseis caused due to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has created a pandemic situation across the globe. As reported, 65.8 Lakh death count is on 23rd October'2022 worldwide [1]. This pandemic resulted into all time highmortality rate. This resulted into huge burden on the healthcare system and on the country's economy indirectly. This pandemic has thus pushed our global economy towards deep recession and has racked a depth of approximately 19.5 trillion USD [2].

The ideal goal of covid-19 receive is to impose a global hard immunity, but it is also important to keep in mind that this goal may never be reached. The main goal of receive is to reduce mortality and stress on health care system. Various countries have already approved COVID-19 vaccine for human use and many are expected to be licensed soon. It is important to ensure that these vaccines are safe, effective and can be deployed on a large scale.

Historically, the process of the vaccine manufacturing and clinical trials requires approximately 10 years, But due to the burden of the pandemic, scientists were under huge pressure to research and develop proper vaccine for this disease, ensuring all crucial information regarding the vaccine are collected shortly and correctly. Furthermore, there is a need to provide a compilation of accredited and appraised scientific literature for every approved vaccine, which aims to spread public health knowledge and vaccine literacy to members of the scientific and general community. In the consequent section, a dedicated part is included for covid-19 vaccine and pregnancy.

II. VARIENTS OF CONCERN

Viruses constantly evolve by mutations and therefore the detection of SARS-CoV-2 variants are not unexpected [3,4]. The B.1.617.2 (Delta) and B.1.1.7 (Alpha) variants are found to be more infectious and can lead to more community transmission. Large scale vaccine deploymentis considered an important tool against these variants [3]. The varients of concern are Alpha(B1.1.7),Delta(B.1.617.2), Beta(B.1.351) and Gama(P.1).

Alpha (B.1.1.7)

The Alpha strain is the most common variant of concern. Alpha is 50% more transmissible than earlier strains. The Alpha variant is also linked with surges in COVID-19 cases and hospitalizations among young people — although it's unclear whether those surges were due to the variant or other factors, says Dr. Gerald Evans, chair of infectious diseases at Queen's University in Kingston, Ont. [5]

Beta (B.1.351)

First documented in South Africa in May 2020, the Beta variant was linked with increases in hospitalizations and deaths during that country's second wave. Vaccines also appear to be less effective in preventing COVID-19 from the Beta variant. Recent studies suggest that mutations in the Beta variant's spike protein might allow it to escape the immune response trained by vaccines."Everybody was worried about Beta especially because there's this vaccine escape issue," says Evans. "If it was [more] transmissible like Alpha, we would have been in trouble, but it isn't. It seems to be no more transmissible [than early strains of the virus]" [5].

IARJSET

ISSN (Online) 2393-8021
ISSN (Print) 2394-1588

International Advanced Research Journal in Science, Engineering and Technology

5th National Conference on Science, Technology and Communication Skills – NCSTCS 2K22

Narula Institute of Technology, Agarpara, Kolkata, India

Vol. 9, Special Issue 2, September 2022

Gamma (P.1)

The Gamma variant, first documented in Brazil in November 2020, is estimated to be 1.7–2.4 times more transmissible than other local strains in that country. The Gamma variant has some of the same mutations in its spike protein as the Alpha and Beta strains, which allow it to attach more easily to human cells. However, "it's not anywhere near as transmissible as Alpha or Delta," says Evans.Previous infection with SARS-CoV-2 appears to provide less protection against reinfection with the Gamma variant than other strains. However, at least one preprint study showed that the Gamma variant is less resistant to antibody responses from previous illness or vaccination than the Beta variant.Evidence also suggests that the Gamma variant struggles to compete with other strains in the wild. In a pre-print study, Italian researchers tracked the concurrent spread of Alpha and Gamma variants and found that the Alpha variant became increasingly common while the Gamma variant did not [5].

Delta (B.1.617.2)

First documented in India in October last year, the highly transmissible Delta variant is on track to eclipse the Alpha variant. Studies out of the United Kingdom suggest the Delta variant is up to 60% more transmissible than the Alpha variant. Experts are urging governments to shift the focus of vaccination campaigns to deliver second doses as soon as possible. Reportes says that, deaths linked to the Delta variant, including the death of at least one person who was fully vaccinated against COVID-19[5].

III. DIFFERENT VACCINES

BioNTech/Pfizer

The BNT162b2 COVID-19 vaccine developed by BioNTech and Pfizer is a lipid nanoparticleformulated, nucleoside-modified RNA vaccine [6]. It was the first vaccine approved by the US Food and Drug Association (FDA) and now it has been approved in many other countries [7]. It requires very cold temperatures for longterm storage and shipping (−70°C) to maintain the stability of the lipid nanoparticle. In both the vaccine and placebo group, the incidence of severe adverse events did not differ significantly and no deaths occurred related to the vaccine. These studies show that the mRNA-vaccine BNT162b2 is safe and effective in protecting against COVID-19. However, further investigations are needed to confirm longterm safety and to establish safety and efficacy for populations not included in this study.

Moderna

The mRNA-1273 vaccine, developed by Moderna, relies on mRNA technology to encode prefusion stabilized SARS-CoV-2 spike protein. It is the second COVID-19 vaccine to receive emergency use approval by the US FDA. The mRNA-1273 vaccine, developed by Moderna, relies on mRNA technology to encode prefusion stabilized SARS-CoV-2 spike protein. It is the second COVID-19 vaccine to receive emergency use approval by the US FDA. In the trial, symptomatic COVID-19 illness occurred in 11 participants within the vaccine group versus 185 participants within the placebo group. Efficacy was similar across age, sex, race, and ethnicity as well as in patients with and without risk factors for severe disease (e.g. chronic lung disease, cardiac disease, and severe obesity). Regarding the side effects of the vaccine, adverse events at the injection site and systemic adverse events occurred more commonly with the mRNA-1273 group Therapeutic Advances in Vaccines and Immunotherapy compared to the placebo. The most common local reaction was mild to moderate pain at the injection site (75%). The most common systemic symptoms were fatigue, myalgia, arthralgia, and headache (50%).[8] The overall incidence of serious adverse events did not differ significantly between groups and no deaths occurred in relation to the vaccine.

AstraZeneca

The Oxford and AstraZeneca ChAdOx1 COVID19 vaccine uses a chimpanzee adenovirus vector to deliver the genetic sequence of a full-length spike protein of SARS-CoV-2 into host cells.[9] The storage for the ChAdOx1 vaccine is favorable, as it may be refrigerated at 2°C–8°C for 6 months. . Regarding safety, most of the adverse events were mild-moderate with the most frequently reported being injection site pain/tenderness, fatigue, headache, malaise, and myalgia [10]. About 175 serious adverse events were noted, only three of which were possibly linked to intervention: transverse myelitis 14 days after second dose, haemolytic anemia in a control recipient and fever >40°C in a participant still masked to group allocation.

Janssen COVID-19 vaccine

The Janssen (Johnson & Johnson) COVID-19 vaccine, developed by Janssen Pharmaceutical in Netherlands. It is a single-dose intramuscular (IM) vaccine that contains a recombinant, replication incompetent human adenovirus (Ad26) vector encoding the spike protein of SARS-CoV-2 in the stabilized conformation [11]. It can be stored between 2°C and 8°C for up to 6 hours or at room temperature for a duration of 2 hours.Efficacy assessment was performed at day 14 and 28. The primary outcome only included moderate and severe (hospitalization and death) infection. The most common localized solitary adverse reaction was the injection site pain (48.6%). Conversely, the most common systemic adverse reactions included headache, fatigue, myalgia, and nausea [12].Overall, the data demonstrate that the Janssen vaccine has a good efficacy and side-effect profile.

IARJSET

ISSN (Online) 2393-8021
ISSN (Print) 2394-1588

International Advanced Research Journal in Science, Engineering and Technology

5th National Conference on Science, Technology and Communication Skills – NCSTCS 2K22

Narula Institute of Technology, Agarpara, Kolkata, India

Vol. 9, Special Issue 2, September 2022

Gamaleya

Sputnik V or Gam-COVID-Vac, developed by the Gamaleya Institute, is a recombinant human adenovirus-based vaccine that uses two different vectors (rAd26 and rAd5) to carry the gene encoding for the spike protein of SARS-CoV-2. It can be stored as either a liquid at −18°C, or it can be freeze-dried and stored at 2°C to 8°C [12]. The most common adverse effects in both groups were flu-like illness, injection site reactions, headaches, and asthenia, with the majority being grade 1 [12].Serious adverse events were also reported in both the vaccine group and placebo group, but they were deemed not to be associated with the vaccination.

SinoVac

CoronaVac is an inactivated vaccine developed by SinoVac Biotech containing inactivated SARSCoV-2[13].The vaccine can be stored at 2°C to 8°C for up to 3 years making it an attractive option for development. The most common adverse effect was injection site pain; others included fatigue and fever. No serious adverse events were associated with the vaccine or placebo in the ⩾60-year-old study. Doses were administered only 2 weeks apart [14]. The phase-3 SinoVac study in Chile showed the VE 14 days post second dose to prevent symptomatic COVID-19 hospital admission, intensive care unit (ICU) admission and death [15].The Phase-3 SinoVac trial in Brazil showed an overall VE against symptomatic COVID-19, moderate cases requiring hospitalization, and severe cases requiring hospitalization [16].As with any vaccine, a contraindication for CoronaVac is anaphylaxis to it or to one of its constituents.

Other prominent COVID-19 vaccines

Due to the disease burden of SARS-CoV-2, the development and manufacturing of COVID-19 vaccines has been occurring at a remarkable pace which has not been seen before. There are many emerging vaccines with different mechanisms of actions that will be briefly explored. Bharat Biotech, an Indian company, has designed the inactivated COVID-19 vaccine Covaxin (BBV152). Due to the disease burden of SARS-CoV-2, the development and manufacturing of COVID-19 vaccines has been occurring at a remarkable pace which has not been seen before. There are many emerging vaccines with different mechanisms of actions that will be briefly explored. Bharat Biotech, an Indian company, has designed the inactivated COVID-19 vaccine Covaxin (BBV152) [17, 18]. It is approved in Bahrain, U.A.E, and China. NVX-CoV2373 is another promising vaccine produced by Novavax. It is a protein subunit vaccine made by assembling SARS-CoV-2 spike proteins into nanoparticles. A phase-3 trial in the United Kingdom displayed an efficacy rate of 89.3%; however, a phase-2 trial in South Africa had an efficacy just under 50% [17]. Other emerging vaccines include CoVLP produced by Medicago which uses the plant N. *benthamiana* to create virus-like particles that mimic SARSCoV-2, CVnCoV produced by CureVac which is an mRNA vaccine, Convidecia produced by CanSino Biologics which is adenovirus based (Ad5), Ad26.COV2.S produced by Johnson & Johnson which is also adenovirus based (Ad26), and ZF2001 created by Anhui Zhifei Longcom which is a protein subunit vaccine. To meet this requirement as soon as possible, having multiple vaccines will help in maximizing the volume of doses that can be produced. In addition, there are many technical issues such as cold storage and transportation, cost, and dosing of certain vaccines that arise when trying to vaccinate remote populations.

IV. RESULTS OF VACCINES ON DIFFERENT VARIENTS

Vaccine Protection against Alpha (B.1.1.7) SARS-CoV-2 Variant

Given that B.1.1.7 was the earliest variant to be designated a VOC.A total of 21 of the 35 (60%) studies reported vaccine efficacy against this variant.Several articles reported efficacies from Phase 2 and 3 clinical trials ([19,20,21]). The efficacies range from 70.4% and 85.6% against B.1.1.7 for AstraZeneca and Novavax vaccines. The Novavax Phase 3 trial was conducted between 28 September and 28 November 2020, on 16,645 adults aged between 18 and 84 years in the UK [19]. A Post hoc analysis showed that the efficacy against the Alpha (B.1.1.7) variant was lower than the non-B.1.1.7 variants.The efficacy against the Alpha variant was 86% whereas the efficacy against the non-Alpha variants were higher at 96.4%. The results from this clinical trial are further confirmed by E. Mahase [21]. A Phase 2 trial for the AstraZeneca vaccine [20] with 8534 adults aged 18 or older.A vaccine efficacy of 70.4% was reported against the Alpha variant whereas the efficacy was higher at 81.5% for non-Alpha variants.ants. From the observational studies, a wider range of efficacies are reported. The efficacy of a single dose vaccine was reported to be as low as 29.5% for BNT162b (Pfizer–BioNTech) [22] and as high as 88.1% for mRNA-1273 (Moderna) [23]. Similar variability is observed for two doses of vaccines where the lowest efficacy reported was 74.5% for two doses of ChAdOx1 nCoV-19 (AstraZeneca) vaccine [24] and the highest efficacy of 100% for mRNA-1273 (Moderna) [23]. Efficacy of 50% or greater is substantial and would offer useful herd immunity [21]. Full vaccination (two doses) offers strong protection against Alpha with 13 out of 15 studies reporting more than 84% efficacy and a single dose offers reasonable protection with 10 out of 12 studies reporting greater than 54% efficacy. Moreover, the efficacies reported by the mRNA vaccines (BNT162b and mRNA-1273) appear to be slightly higher comparatively. Furthermore, protection against B.1.1.7 is estimated to be higher than B.1.617.2 [25].

Vaccine Protection against Beta (B.1.351) and Gamma (P.1) SARS-CoV-2 Variant

Both E484K-positive mutations, B.1.351 (E484K and K417N) and P.1 (E484K and K417T) were reported together in several studies.The lowest efficacy reported is 49.4% with at least one dose of NVX-CoV2373 [26] and the highest efficacy is 100% for two doses of BNT162b2 [27].The overall vaccine efficacy was 49.4% but was slightly higher at 51.0% in HIV-negative participants.

IARJSET

ISSN (Online) 2393-8021
ISSN (Print) 2394-1588

International Advanced Research Journal in Science, Engineering and Technology

5th National Conference on Science, Technology and Communication Skills – NCSTCS 2K22

Narula Institute of Technology, Agarpara, Kolkata, India

Vol. 9, Special Issue 2, September 2022

No serious adverse effects were reported as being related to the vaccine. E. Mahase [21] reported an efficacy of 60% for the NVX-CoV2373 trial against the B.1.351 variant.The vaccine efficacy from the South Africa group was 52.0% for moderate to severe-critical COVID-19 after 14 days of administration and increased to 64.0% after 28 days. Serious adverse effects not related to COVID-19 were only reported by 83 out of 21,895 vaccine recipients constituting 0.4% of the population and 96 out of 21,888 placebo recipients constituting 0.4% of the population.Although a 91% overall efficacy was reported, the efficacy specifically for the South African group with predominantly B.1.351 variant in circulation was reported to be 100%.Moreover, for fully vaccinated individuals, 4 out of the 7 studies reported efficacies between 22 and 60%, and 3 reported efficacies between 75 and 100%. Therefore, more data are needed for convincing evidence.

The efficacies reported against Gamma (P.1) variant is all from observational studies. Three of the involved studies reported efficacies for the P.1 variant exclusively [28, 29, 30]. Protection against this variant is indicated to be lower ranging from 12.5% for a single dose of CoronaVac [29] and 61% for a single dose of mRNA vaccine (BNT162b2 and mRNA-1273) [28].P.1 For two doses of CoronaVac, the vaccine efficacy against COVID-19 infection was only at 46.8%. However, the adjusted effectiveness against COVID-19 hospital admissions and deaths was 55% and 61.2% respectively. The adjusted vaccine effectiveness was 49.6% after the first dose of CoronaVac. However, the effectiveness reported after two doses was unusually lower at 36.8%. This study was not peer-reviewed at the time of writing. Overall, the limited data available against the P.1 variant indicates lower protectiveness. The highest efficacy was only 61% with a single dose of mRNA vaccine but can be expected to be higher with full vaccination.

For literatures reporting efficacies of both B.1.351 and P.1 variants together [31, 32, 33], the mentioned efficacies for double dose mRNA vaccines are 84%, 88%, and 77% respectively. The high efficacies against both variants combined seem to indicate slightly greater protection against B.1.351 compared to P.1. This conclusion can be drawn solely based on the efficacy results available exclusively against the two variants where the range of efficacy against the B.1.351 variant was between 22% and 100% and the range of efficacy against the P.1 variant was between 12.5% and 61%.

Vaccine Protection against Delta (B.1.617.2) SARS-CoV-2 Variant

Among the variants considered, the Delta (B.1.617.2) variant is the latest to be designated as a VOC. Consequently, only 30% of the vaccine efficacies against Delta variant is from peer-reviewed articles and no data from a clinical trial is available.Several studies have noticed a fall in protection against the Delta variant. Vaccine efficacy for Mesa County, Colorado was reported to be 78% with Delta being the dominant variant [34]. In contrast, for the same period of time, efficacy from the other Colorado counties was 89% where the Delta variant was comparatively lower. Similarly, S. Y. Tartof et al. [35] mentioned lower safety against Delta (75% efficacy) compared to other variants (91% efficacy). A sharp fall in vaccine effectiveness is found after the Delta variant became prominent with the effectiveness decreasing from 91% to 66% [36].Moreover, among the two mRNA vaccines, manyresearches indicate littlemore protection from the Moderna (mRNA-1273) vaccine compared to the Pfizer (BNT162b2) vaccine [37]. Similarly, for two doses of either, mRNA-1273 (76%) was reported to be more effective than BNT162b2 (42%) [25]. For a single dose of mRNA vaccine, more efficacy for mRNA-1273 (72%) than BNT162b2 (56%) is noticed against the Delta variant [33].

V. COVID-19 VACCINES AND PREGNANCY

It is very crucial to gain insight between COVID- 19 and pregnancy. Study showed that there was no difference in the frequency of Caesarean section, pre-eclampsia, preterm births, and abnormal fatal cardiotocography in pregnant women with and without SARS-CoV-2 infection. Further examination of the placenta revealed no abnormalities, which were initially suspected due to the cross-matching between the SARS-CoV-2 spike protein and the placental synctyin-1 protein [38]. Similarly, there was no association found between COVID-19 and first-trimester spontaneous abortions [39]. A systematic review found that COVID-19 leads to more preterm deliveries and an increase in the ICU admission rates in pregnant women [40].

Vaccination trials on pregnancy was excluded, so no data is available about it. But it can be concluded that the effect of the vaccines will be minimal and more data would be needed for confirmation [41]. Pfizer's animal studies revealed antibodies in the maternal rats, fetus, and offspring, in addition to no effects on fertility pregnancy or fatal development [42]. However, as a precaution, the National Immunization Advisory Committee (NIAC) has recommended for the two-dose schedule to not commence before 14 weeks of gestation and to be completed by week 33 of gestation. This precaution reduces any potential associations with miscarriage or pre-term birth [43].

.

VI. CONCLUSION

This review highlighted the current available vaccines and candidates being rolled out amid the ongoing prevention measures and summarized the documented findings with regards to their efficacies, side-effects, and storage requirements. An overview of the physiology of immunogenic responses against the disease provided by the more prominent vaccines were discussed, alongside questions regarding the implementation of vaccines; heterologous prime-boosting, vaccine contraindications, dosing strategies, side effects, and the presence of SARS-CoV-2 mutations and variants.At last, the important variants of concern are described and the effectiveness of the applied vaccines on the variants has been illustrated

IARJSET

ISSN (Online) 2393-8021
ISSN (Print) 2394-1588

International Advanced Research Journal in Science, Engineering and Technology

5th National Conference on Science, Technology and Communication Skills – NCSTCS 2K22

Narula Institute of Technology, Agarpara, Kolkata, India

Vol. 9, Special Issue 2, September 2022

REFERENCES

[1] COVID-19 Data Explorer (Our World in Data, accessed 23rd October 2022); https://ourworldindata.org/explorers/coronavirus-data-explorer?zoomToSelection=true&time=2020-0301.latest&country=USA~GBR~CAN~DEU~ITA~IND&region=World&pickerMetric=location&pickerSort=asc&Metric=Confrmed+cases&Interval=7-day+rolling+average&Align+outbr.

[2] McCormick LC, Benhamou M and Pogkas D. The Covid-19 pandemic has added $19.5 trillion to global debt. Bloomberg, 27 January 2021, https://www.bloomberg.com/graphics/2021-coronavirus-global-debt/#:~:text=The%20Covid%2D19%20Pandemic%20Has%20 Added%20%2419.5%20Trillion%20to%20 Global%20Debt.

[3] Fontanet, A.; Autran, B.; Lina, B.; Kieny, M.P.; Karim, S.S.A.; Sridhar, D. SARS-CoV-2 variants and ending the COVID-19 pandemic. Lancet 2021, 397, 952–954. [CrossRef]

[4] Sridhar, D.; Gurdasani, D. Herd immunity by infection is not an option. Science 2021, 371, 230–231. [CrossRef]

[5] Duong, Diana. "Alpha, Beta, Delta, Gamma: What's important to know about SARS-CoV-2 variants of concern?." CMAJ : Canadian Medical Association journal = journal de l'Associationmedicalecanadienne vol. 193,27 (2021): E1059-E1060.doi:10.1503/cmaj.1095949 Polack FP, Thomas SJ, Kitchin N, et al. Safety and efficacy of the BNT162b2 mRNA Covid-19 vaccine. N Engl J Med 2020; 383(27): 2603– 2615.

[6] Pfizer COVID-19 Vaccine EUA Letter of Authorization. Sect. Section 564(b)(1)(C) (2020).

[7] Baden LR, El Sahly HM, Essink B, et al. Efficacy and safety of the mRNA-1273 SARS-CoV-2 vaccine. N Engl J Med 2020; 384(5): 403–416.

[8] Van Doremalen N, Lambe T, Spencer A, et al. ChAdOx1 nCoV-19 vaccination prevents SARS-CoV-2 pneumonia in rhesus macaques. bioRxiv. Epub ahead of print 13 May 2020. DOI: 10.1101/2020.05.13.093195.

[9] Folegatti PM, Ewer KJ, Aley PK, et al. Safety and immunogenicity of the ChAdOx1 nCoV19 vaccine against SARS-CoV-2: a preliminary report of a phase 1/2, single-blind, randomised controlled trial. Lancet 2020; 396(10249): 467–478.

[10] Sadoff J, Gray G, Vandebosch A, et al. Safety and efficacy of single-dose Ad26.COV2.S vaccine against Covid-19. N Engl J Med 2021; 384(23): 2187–2201.

[11] Logunov DY, Dolzhikova IV, Shcheblyakov DV, et al. Safety and efficacy of an rAd26 and rAd5 vector-based heterologous prime-boost COVID19 vaccine: an interim analysis of a randomised controlled phase 3 trial in Russia. Lancet 2020; 397: 671–681.

[12] Zhang Y, Zeng G, Pan H, et al. Safety, tolerability, and immunogenicity of an inactivated SARS-CoV-2 vaccine in healthy adults aged 18–59 years: a randomised, double-blind, placebo-controlled, phase 1/2 clinical trial. Lancet Infect Dis 2021; 21(2): 181–192.

[13] Mallapaty S. China COVID vaccine reports mixed results – what does that mean for the pandemic? Nature. Epub ahead of print 15 January 2021. DOI: 10.1038/d41586-021- 00094-z.

[14] Jara A, Undurraga EA, González C, et al. Effectiveness of an inactivated SARS-CoV-2 vaccine in Chile. N Engl J Med 2021; 385: 875–884.

[15] Palacios R, Batista AP, Albuquerque CS, et al. Efficacy and safety of a COVID-19 inactivated vaccine in healthcare professionals in Brazil: the PROFISCOV study, 2021, https://europepmc. org/article/ppr/ppr341815

[16] Novavax COVID-19 vaccine demonstrates 89.3% efficacy in UK phase 3 trial. Novavax, Inc, 2021, https://ir.novavax.com/news-releases/ news-release-details/novavax-covid-19-vaccinedemonstrates-893-efficacy-uk-phase-3

[17] Al Kaabi N, Zhang Y, Xia S, et al. Effect of 2 inactivated SARS-CoV-2 vaccines on symptomatic COVID-19 infection in adults: a randomized clinical trial. JAMA 2021; 326(1): 35–45.

[18] Heath, P.T.; Galiza, E.P.; Baxter, D.N.; Boffito, M.; Browne, D.; Burns, F.; Chadwick, D.R.; Clark, R.; Cosgrove, C.; Galloway, J.; et al. Safety and Efficacy of NVX-CoV2373 COVID-19 Vaccine. New Engl. J. Med. 2021, 385, 1172–1183. [CrossRef] [PubMed] 17 of 18

[19] Emary, K.R.W.; Golubchik, T.; Aley, P.K.; Ariani, C.V.; Angus, B.; Bibi, S.; Blane, B.; Bonsall, D.; Cicconi, P.; Charlton, S.; et al. Efficacy of ChAdOx1 nCoV-19 (AZD1222) vaccine against SARS-CoV-2 variant of concern 202012/01 (B.1.1.7): An exploratory analysis of a randomised controlled trial. Lancet 2021, 397, 1351–1362. [CrossRef]

[20] Mahase, E. COVID-19: Novavax vaccine efficacy is 86% against UK variant and 60% against South African variant. BMJ 2021, 372, n296. [CrossRef]

[21] Abu-Raddad, L.J.; Chemaitelly, H.; Butt, A.A. Effectiveness of the BNT162b2 COVID-19 Vaccine against the B.1.1.7 and B.1.351 Variants. N. Engl. J. Med. 2021, 385, 187–189. [CrossRef]

[22] Chemaitelly, H.; Yassine, H.M.; Benslimane, F.M.; Al Khatib, H.A.; Tang, P.; Hasan, M.R.; Malek, J.A.; Coyle, P.; Ayoub, H.H.; Al Kanaani, Z.; et al. mRNA-1273 COVID-19 vaccine effectiveness against the B.1.1.7 and B.1.351 variants and severe COVID-19 disease in Qatar. Nat. Med. 2021, 27, 1614–1621. [CrossRef]

[23] Bernal, J.L.; Andrews, N.; Gower, C.; Gallagher, E.; Simmons, R.; Thelwall, S.; Stowe, J.; Tessier, E.; Groves, N.; Dabrera, G.; et al. Effectiveness of COVID-19 Vaccines against the B.1.617.2 (Delta) Variant. N. Engl. J. Med. 2021, 385, 585–594. [CrossRef]

[24] Puranik, A.; Lenehan, P.J.; Silvert, E.; Niesen, M.J.M.; Corchado-Garcia, J.; O'Horo, J.C.; Virk, A.; Swift, M.D.; Halamka, J.; Badley, A.D.; et al. Comparison of two highly-effective mRNA vaccines for COVID-19 during periods of Alpha and Delta variant prevalence. medRxiv 2021. [CrossRef]

[25] Shinde, V.; Bhikha, S.; Hoosain, Z.; Archary, M.; Bhorat, Q.; Fairlie, L.; Lalloo, U.; Masilela, M.S.; Moodley, D.; Hanley, S.; et al. Efficacy of NVX-CoV2373 COVID-19 Vaccine against the B.1.351 Variant. N. Engl. J. Med. 2021, 384, 1899–1909. [CrossRef] [PubMed]

[26] Thomas, S.J.; Moreira, E.D., Jr.; Kitchin, N.; Absalon, J.; Gurtman, A.; Lockhart, S.; Perez, J.L.; Perez, G.M.; Polack, F.P.; Zerbini, C.; et al. Six Month Safety and Efficacy of the BNT162b2 mRNA COVID-19 Vaccine. medRxiv 2021. [CrossRef]

[27] Skowronski, D.M.; Setayeshgar, S.; Zou, M.; Prystajecky, N.; Tyson, J.R.; Galanis, E.; Naus, M.; Patrick, D.M.; Sbihi, H.; El Adam, S.; et al. Single-dose mRNA Vaccine Effectiveness Against Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), Including Alpha and Gamma Variants: A Test-negative Design in Adults 70 Years and Older in British Columbia, Canada. Clin. Infect. Dis. 2021, ciab616. [CrossRef]

[28] Ranzani, O.T.; Hitchings, M.D.T.; Dorion, M.; D'Agostini, T.L.; de Paula, R.C.; de Paula, O.F.P.; Villela, E.F.D.M.; Torres, M.S.S.; de Oliveira, S.B.; Schulz, W.; et al. Effectiveness of the CoronaVac vaccine in older adults during a gamma variant associated epidemic of COVID-19 in Brazil: Test negative case-control study. BMJ 2021, 374, 2015. [CrossRef]

[29] Hitchings, M.D.T.; Ranzani, O.T.; Torres, M.S.S.; de Oliveira, S.B.; Almiron, M.; Said, R.; Borg, R.; Schulz, W.L.; de Oliveira, R.D.; da Silva, P.V.; et al. Effectiveness of CoronaVac among healthcare workers in the setting of high SARS-CoV-2 Gamma variant transmission in Manaus, Brazil: A test-negative case-control study. medRxiv 2021. [CrossRef]

[30] Charmet, T.; Schaeffer, L.; Grant, R.; Galmiche, S.; Chény, O.; Von Platen, C.; Maurizot, A.; Rogoff, A.; Omar, F.; David, C.; et al. Impact of original, B.1.1.7, and B.1.351/P.1 SARS-CoV-2 lineages on vaccine effectiveness of two doses of COVID-19 mRNA vaccines: Results from a nationwide case-control study in France. Lancet Reg. Health Eur. 2021, 8, 100171. [CrossRef]

[31] Chung, H.; He, S.; Nasreen, S.; Sundaram, M.E.; Buchan, S.A.; Wilson, S.E.; Chen, B.; Calzavara, A.; Fell, D.B.; Austin, P.C.; et al. Effectiveness of BNT162b2 and mRNA-1273 COVID-19 vaccines against symptomatic SARS-CoV-2 infection and severe COVID-19 outcomes in Ontario, Canada: Test negative design study. BMJ 2021, 374, 1943. [CrossRef]

[32] Nasreen, S.; Chung, H.; He, S.; Brown, K.A.; Gubbay, J.B.; Buchan, S.A.; Fell, D.B.; Austin, P.C.; Schwartz, K.L.; Sundaram, M.E.; et al. Effectiveness of COVID-19 vaccines against variants of concern in Ontario, Canada. medRxiv 2021. [CrossRef]

[33] Herlihy, R.; Bamberg, W.; Burakoff, A.; Alden, N.; Severson, R.; Bush, E.; Kawasaki, B.; Berger, B.; Austin, E.; Shea, M.; et al. Rapid Increase in Circulation of the SARS-CoV-2 B.1.617.2 (Delta) Variant–Mesa County, Colorado, April–June 2021. MMWR Morb. Mortal. Wkly. Rep. 2021, 70, 1084–1087. [CrossRef]

[34] Tartof, S.Y.; Slezak, J.M.; Fischer, H.; Hong, V.; Ackerson, B.K.; Ranasinghe, O.N.; Frankland, T.B.; Ogun, O.A.; Zamparo, J.M.; Gray, S.; et al. Six-Month Effectiveness of BNT162B2 mRNA COVID-19 Vaccine in a Large US Integrated Health System: A Retrospective Cohort Study; SSRN Scholarly Paper ID 3909743; Social Science Research Network: Rochester, NY, USA, 2021. [CrossRef]

[35] Fowlkes, A.; Gaglani, M.; Groover, K.; Thiese, M.S.; Tyner, H.; Ellingson, K.; Cohorts, H.-R. Effectiveness of COVID-19 Vaccines in Preventing SARS-CoV-2 Infection Among Frontline Workers Before and During B.1.617.2 (Delta) Variant Predominance—Eight US Locations, December 2020–August 2021. MMWR Morb. Mortal. Wkly. Rep. 2021, 70, 1167–1169. [CrossRef] [PubMed]

[36] Tang, P.; Hasan, M.R.; Chemaitelly, H.; Yassine, H.M.; Benslimane, F.M.; Al Khatib, H.A.; AlMukdad, S.; Coyle, P.; Ayoub, H.H.; Al Kanaani, Z.; et al. [r. Nat. Med. 2021. [CrossRef] [PubMed]

[37] Adhikari EH, Moreno W, Zofkie AC, et al. Pregnancy outcomes among women with and without severe acute respiratory syndrome coronavirus 2 infection. JAMA Netw Open 2020; 3(11): e2029256.

[38] Cosma S, Carosso AR, Cusato J, et al. Coronavirus disease 2019 and first-trimester spontaneous abortion: a case-control study of 225 pregnant patients. Am J Obstet Gynecol 2021; 224(4): 391.e1–391.e7.

[39] Allotey J, Stallings E, Bonet M, et al. Clinical manifestations, risk factors, and maternal and perinatal outcomes of coronavirus disease 2019 in pregnancy: living systematic review and metaanalysis. BMJ 2020; 370: m3320.

[40] Quach THT, Mallis NA and Cordero JF. Influenza vaccine efficacy and effectiveness in pregnant women: systematic review and metaanalysis. Matern Child Health J 2020; 24(2): 229–240.

[41] Clean COVID-19 Vaccine SmPC-PL (ed European Medicines Agency). European Medicines Agency, 2020, https://ec.europa.eu/health/documents/ community-register/2020/20201221150522/ anx_150522_en.pdf

[42] Clinical guidance for COVID-19 vaccination. Health Service Executive Ireland, 2021, https:// www.hse.ie/eng/health/immunisation/hcpinfo/ covid19vaccineinfo4hps/clinicalguidance.pdf

