Literature screening report

COVID-19 vaccines in the WHO's Emergency Use Listing (EUL) Report (12)

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Abstract

This report provides an in-depth review of the **eight**[1] World Health Organization's (WHO) Emergency Use Listing (EUL) authorized vaccines: BNT162b2/COMIRNATY (Pfizer-BioNTech, USA), Spikevax/Moderna COVID-19 Vaccine/ mRNA-1273 (Moderna, USA), Vaxzevria/ ChAdOx1 nCoV-19/ AZD1222/ Covishield (AstraZeneca/Oxford, UK, India), Janssen Covid-19 vaccine/ Ad26CoV2.S/ Johnson & Johnson (Janssen, USA), Sinopharm/ BBIBP-CorV (China), Sinovac/ CoronaVac (China), COVAXIN/ BBV152 (Bharat Biotech, India), and Novavax/ NXV-CoV2373/ COVAVAX (USA, India). The current report summarises the latest data on COVID-19 vaccine-related literature as of 28 January 2022 and presents the information in the form of a synoptic table. This report covers vaccine effectiveness, protection against variants, transmissibility, breakthrough infections, booster doses, COVID-19 vaccines for children, and further important information for each vaccine. The latest changes and additions to the synoptic table are highlighted in yellow.

[1] Since the Covishield vaccine uses the same formulation and platform as Vaxzevria (AstraZeneca's COVID-19 vaccines), we combined both vaccines into one column in the synoptic table. Henceforth, seven vaccines will be referenced as WHO EUL approved (including Covishield)

Content

Preamble

A large number of scientific publications become available on a daily basis, reflecting the rapid development of knowledge and progress of science on COVID-19 related issues. Leading authorities should base decisions or policies on this knowledge; hence they need to master the actual state of this knowledge. Due to the large number of publications shared daily, decision makers heavily depend on accurate summaries of these publications, in the different public health domains. Therefore, the authors of this report were mandated by the Swiss School of Public Health plus (SSPH+), upon request of the Federal Office of Public Health (FOPH), to inform the FOPH on recent findings from the literature.

Background

According to the current global data on vaccinations, 61% of the world populations, of which only 10% of people in low-income countries, have received at least one dose of a marketed COVID-19 vaccine as of 31 January 2022[2]. Currently, eight vaccines [namely, Comirnaty/BNT162b2 (Pfizer-BioNTech, USA), Spikevax/Moderna COVID-19 Vaccine/mRNA-1273 (Moderna, USA), Vaxzevria/ChAdOx1 nCoV-19/AZD1222/Covishield (AstraZeneca/Oxford, UK, India), Janssen Covid-19 vaccine/ Ad26CoV2.S/Johnson & Johnson (Janssen, USA), Sinopharm/BBIBP-CorV (China), Sinovac/CoronaVac (China), COVAXIN/BBV152 (Bharat Biotech, India), and Novavax/NXV-CoV2373/COVAVAX (USA, India)] were assessed and granted an authorization by WHO as of 23 December 2021[3]. **Articles regarding the latest data on vaccine effectiveness, particularly against the omicron variant, vaccine induced immune response, breakthrough infections and transmission, booster doses, and children vaccination were prioritized during the literature search and are the latest additions to the table. Data from clinical trials and observational studies for the eight EUL-accepted vaccines regarding these highlighted topics were summarized and can be found in the synoptic table below.**

[2] https://ourworldindata.org/covid-vaccinations (accessed on 31.01.2021).

[3] Status of COVID-19 vaccines within WHO EUL/ PQ evaluation process. World Health Organization. https://extranet.who.int/pqweb/sites/default/files/documents/Status_COVID_VAX_11Nov2021.pdf [Last updated 23 December 2021; Accessed 11 January 2022]

Methodology

We screened the data for the EUL-accepted vaccines and the vaccine candidate Novavax as of 28 January 2022 from PubMed, Embase, medRxiv, bioRxiv, Cochrane, and clinical trials databases such as ClinicalTrials and WHO Trial Registry. The methods used were reported previously and can be found in prior reports[4].

Results

As phase III COVID-19 vaccine trials confirmed vaccine efficacy and safety for all eight WHO EUL authorized vaccines, and as the share of fully vaccinated people begin to increase across countries, it is important to assess vaccine effectiveness in real-world conditions, especially in relation to evolving variants of concern (VOC).

The Newest Variant of Concern: Omicron (B.1.1.529)

Effectiveness and Duration of Protection

No major differences in vaccine effectiveness (VE) against the variant of concern, Omicron, were reported in recent literature. The latest preliminary studies concerning effectiveness support results summarized in the previous Synoptic Table earlier this month. For instance, a study investigating the effectiveness of mRNA-based vaccines against infection among United States veterans showed evidence that 2-dose VE against Omicron infection was **25% (95% CI, 20.0-30.0)** compared with **41% (95% CI, 37.0-44.0)** against Delta variant infection.[5] Despite lowered protection against infection, the study also showed that Omicron-related hospitalizations had a **45%**

[4] COVID-19 vaccines: efficacy and safety (Literature Review 1). *Swiss School of Public Health*. https://www.bag.admin.ch/dam/bag/de/dokumente/mt/k-und-i/aktuelle-ausbrueche-pandemien/2019-nCoV/Literaturrecherchen/literaturrecherchen_covid-19-impfstoffe_20210209.pdf.download.pdf/20210209_Literaturrecherchen_Covid-19-Impfstoffe_EN.pdf

[5] Effectiveness of mRNA COVID-19 Vaccines against Omicron among Veterans. *medRxiv.* https://www.medrxiv.org/content/10.1101/2022.01.15.22269360v1.full.pdf+html

(95% CI, 26.0-58.0) lower likelihood compared with Delta hospitalizations which is consistent with results from other studies.[6]

Alternatively, a test-negative design analysis conducted in the United States showed differences in BNT162b2 VE against Omicron-related hospital and Emergency Department (ED) admission without subsequent hospitalization. Analyses conducted on 14,137 cases from 01 December 2021 through 11 January 2022 evidenced that protection against Omicron ED admission **waned from 60% (95% CI, 43−72)** at <3 months to **41% (95% CI, 32.0−50.0)** at ≥6 months after completing primary vaccination of Pfizer-BioNTech.[7] On the other hand, VE against Omicron hospital admission was found to be **68% (95% CI, 58.0−75.0)** after 2 doses of Pfizer-BioNTech with no evidence of waning protection.[8]

While the studies described demonstrate moderate VE against Omicron infection and hospitalization, it is important to note that they are currently preprints. As early stage research articles, they have not peer-reviewed and need further examination.

Breakthrough Infections

In line with previous data on Omicron breakthrough infections, a study in the United States from 01 December 2021 to 31 December 2021 showed that post-BNT162b2 vaccination infection is **87% (95% CI, 65.0-111.0)** more likely by Omicron than the Delta variant.[9] However, with regard to COVID-associated hospitalizations, patients infected with Delta were once again found to require longer hospital stays in comparison to Omicron cases. Individuals with Omicron cases were linked with a **2-**

[6] Effectiveness of mRNA COVID-19 Vaccines against Omicron among Veterans. *medRxiv.* https://www.medrxiv.org/content/10.1101/2022.01.15.22269360v1.full.pdf+html

[7] BNT162b2 (Pfizer–Biontech) mRNA COVID-19 Vaccine Against Omicron-Related Hospital and Emergency Department Admission in a Large US Health System: A Test-Negative Design. *SSRN Preprint*. https://papers.ssrn.com/sol3/papers.cfm?abstract_id=4011905

[8] BNT162b2 (Pfizer–Biontech) mRNA COVID-19 Vaccine Against Omicron-Related Hospital and Emergency Department Admission in a Large US Health System: A Test-Negative Design. *SSRN Preprint*. https://papers.ssrn.com/sol3/papers.cfm?abstract_id=4011905

[9] Effectiveness of mRNA COVID-19 Vaccines against Omicron among Veterans. *medRxiv.* https://www.medrxiv.org/content/10.1101/2022.01.15.22269360v1.full.pdf+html

day (95% CI, 1.0-2.0) shorter hospital stay compared with Delta cases which had an average of a **6-day (95% CI, 5.0-7.0) hospital stay**.[10] Similar to patterns found in earlier studies of VE against breakthrough infections and hospitalizations, results of the United States study also demonstrate that the risk of ICU admission is **73% (95% CI, 28.0-92.0)** lower with Omicron compared with Delta. [11]

Another study also conducted in the United States corroborate results that Omicron is less severe in comparison to other VOCs such as Delta. In a cohort study assessing the risk of severe COVID-19 disease among individuals with Omicron and Delta variant infections, the authors illustrate that the adjusted Hazards Ratio for Omicron versus Delta-associated hospitalization was **0.25 (95%CI, 0.15-0.43)**.[12] Therefore, patients infected with Omicron reportedly had a **75% risk reduction of hospitalization** compared with Delta. Apart from the lower risk of hospitalization with Omicron, the authors also found that length of hospital stay was significantly shorter at **-4.0 days (95% CI, -7.2 to -0.8, p-value = 0.02)** than for Delta hospitalizations.[13] Risk of death among Omicron-infected individuals was also found to be **86% lower** compared to Delta infections, with the Odds Ratio of death at **0.14 (95% CI, 0.0011 to 1.12, p-value = 0.06)**.[14] However, the authors did not find a significant difference in mortality as evidenced by the wide confidence interval (Lower CI: 0.0011, Upper CI: 1.12) and large p-value of 0.06. [15]

With the exception of transmissibility (see below), preliminary studies have consistently shown evidence that the Omicron variant may cause less severe disease

[10] Effectiveness of mRNA COVID-19 Vaccines against Omicron among Veterans. *medRxiv.* https://www.medrxiv.org/content/10.1101/2022.01.15.22269360v1.full.pdf+html

[11] Effectiveness of mRNA COVID-19 Vaccines against Omicron among Veterans. *medRxiv.* https://www.medrxiv.org/content/10.1101/2022.01.15.22269360v1.full.pdf+html

[12] Omicron (BA.1) SARS-CoV-2 variant is associated with reduced risk of hospitalization and length of stay compared with Delta (B.1.617.2). *medRxiv.* https://www.medrxiv.org/content/10.1101/2022.01.20.22269406v1

[13] Omicron (BA.1) SARS-CoV-2 variant is associated with reduced risk of hospitalization and length of stay compared with Delta (B.1.617.2). *medRxiv.* https://www.medrxiv.org/content/10.1101/2022.01.20.22269406v1

[14] Omicron (BA.1) SARS-CoV-2 variant is associated with reduced risk of hospitalization and length of stay compared with Delta (B.1.617.2). *medRxiv.* https://www.medrxiv.org/content/10.1101/2022.01.20.22269406v1

[15] Omicron (BA.1) SARS-CoV-2 variant is associated with reduced risk of hospitalization and length of stay compared with Delta (B.1.617.2). *medRxiv.* https://www.medrxiv.org/content/10.1101/2022.01.20.22269406v1

and outcomes compared with previous VOCs. Nevertheless, the COVID-19 pandemic continuous to evolve and as subvariants of Omicron are discovered, these early studies need to be interpreted with reservations.

Transmissibility

While much is still unknown about the transmissibility of the Omicron variant, rapid increases in COVID-19 cases around the world confirm that the Omicron VOC is partially able to evade vaccine-derived immunity and demonstrates higher person to person transmissibility.[16] Infection rates in South Africa, the first country to report the B.1.1.529 strain to the WHO (24 November 2021), increased substantially, faster than any previous SARS-CoV-2 waves in the country.[17] A South African lab group measured Omicron's exponential growth in the Gauteng Province from 8 November to 5 December 2021, observed that the Omicron VOC demonstrated a doubling time of **3.38 (95% CI, 3.18-3.61)** days.[18] Data collected over a four week period from early to late November 2022 revealed even shorter doubling times in Australia (**3.0 days**), New York state (**2.5 days**), Denmark (**2.0 days**), and the United Kingdom (UK; **2.4 days**).[19] By 22 December 2021, Omicron cases were doubling every **1-2 days** in the UK.[20] Omicron's increased transmissibility rate is explained by its numerous spike protein mutations; the NY501Y mutation enhanced the strain's ACE-2 binding affinity, which in combination with waning immunity, leads to greater numbers of case infections and transmissions.[21] Nevertheless, boosted individuals demonstrate reduced transmissions rates (particularly when their contacts are also boosted) compared to non-boosted individuals; for example, a Norway contact tracing

[16] Omicron variant of SARS-CoV-2: Genomics, transmissibility, and responses to current COVID-19 vaccines. *Journal of Medical Virology*. https://onlinelibrary.wiley.com/doi/10.1002/jmv.27588

[17] Omicron variant of SARS-CoV-2: Genomics, transmissibility, and responses to current COVID-19 vaccines. *Journal of Medical Virology*. https://onlinelibrary.wiley.com/doi/10.1002/jmv.27588

[18] The spread of SARS-CoV-2 variant Omicron with the doubling time of 2.0-3.3 days can be explained by immune evasion. *medRxiv*. https://dx.doi.org/10.1101/2021.12.08.21267494

[19] The spread of SARS-CoV-2 variant Omicron with the doubling time of 2.0-3.3 days can be explained by immune evasion. *medRxiv*. https://dx.doi.org/10.1101/2021.12.08.21267494

[20] Omicron daily overview: 24 December 2021. *UK Government*. https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1043866/20211224_OS_Daily_Omicron_Overview.pdf.

[21] Omicron variant of SARS-CoV-2: Genomics, transmissibility, and responses to current COVID-19 vaccines. *Journal of Medical Virology*. https://onlinelibrary.wiley.com/doi/10.1002/jmv.27588

investigation reported a **59% confirmed secondary attack rate** of Omicron cases among fully vaccinated individuals[22] while an Israeli study only reported a **2% infection rate among primary contacts** (of which 88% were triple-vaccinated and 91% wore masks).[23]

Booster Dose

The new variant of concern Omicron (B.1.1529) has raised many concerns amongst the scientific community as numerous studies demonstrated the decrease in neutralizing capacity against the variant of concern. Nevertheless, studies analyzing the effects of booster doses against the Omicron variant are showing that a third homologous or even heterologous booster dose significantly increases the neutralizing antibodies compared to the primary vaccination schedule. This increase in neutralizing antibodies can be noted in studies evaluating the third homologous dose of the BNT162b2 booster against Omicron, as well as in participants who received the third homologous dose of the BIBBP-CorV vaccine. Additionally, similar results have been seen in heterologous booster doses where the administration of a heterologous booster dose has led to an increase in neutralizing antibodies against the Omicron variant.

Booster Doses

Based on numerous studies evaluating the immunogenicity, protection, and effectiveness of booster doses, the results have demonstrated that the third homologous or heterologous dose improved the immune response and therefore the protection against SARS-CoV-2.[24] Recent studies continue to emphasize that a third

[22] Outbreak caused by the SARS-CoV-2 Omicron variant in Norway, November to December 2021. *Eurosurveillance*. https://doi.org/10.2807/1560-7917.ES.2021.26.50.2101147

[23] Low rate of transmission to triple-vaccinated contacts of an imported case of SARS-CoV-2 omicron infection: a contact study in Israel. *Journal of Travel Medicine*. https://doi.org/10.1093/jtm/taac003

[24] Effects of BNT162b2 Covid-19 Vaccine Booster in Long-Term Care Facilities in Israel. *The New England Journal of Medicine.* https://www.nejm.org/doi/full/10.1056/NEJMc2117385

homologous dose of BNT162b2[25,26,27], Ad26.COV2.S (Janssen)[28], and CoronaVac[29] provide a **higher immune response than the previous second doses**. Additionally, heterologous boosters have also shown to provide higher immune responses than the previous two doses, especially when mixing any COVID-19 vaccine platform with an mRNA vaccine[30,31].

Although booster doses have demonstrated to increase the levels of antibodies, increase the levels of neutralizing antibodies against multiple variants of concern (Alpha, Beta, Gamma, Delta, and Omicron), and provide a higher protection against infections, hospitalizations, and deaths, multiple international organizations continue to advocate for the global prioritization of the first and second doses over boosters[32]. While the debate on booster doses continues, countries such as Israel began (on 2 January 2022) vaccinating citizen aged 60 years and over and health-care workers with the fourth dose of a COVID-19 amid the rapid spread of Omicron and the increasing spike of COVID-19 infections[33].

Children Vaccination

Since 29 October 2021, The BNT162b2 vaccine has been approved in the US for usage in children as young as 5 years old. Since then, many other countries have

[25] Association of a Third Dose of BNT162b2 Vaccine with Incidence of SARS-CoV-2 Infection Among Health Care Workers in Israel. *JAMA.* https://jamanetwork.com/journals/jama/fullarticle/2788104

[26] Third Dose of BNT162b2 Vaccine Results in Very High Levels of Neutralizing Antibodies against SARS-CoV-2; Results of a Prospective Study in 150 Health Professionals in Greece. *American Journal of Hematology.* https://onlinelibrary.wiley.com/doi/10.1002/ajh.26468

[27] Serological response to COVID-19 Comirnaty booster vaccine, London, United Kingdom, September to December 2021. *Eurosurveillance.* https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2022.27.1.2101114

[28] Immunogenicity and Reactogenicity of Vaccine Booster after Ad26.COV2.S Priming. *The New England Journal of Medicine.* https://www.nejm.org/doi/full/10.1056/NEJMoa2116747

[29] Immunogenicity and safety of a third dose of CoronaVac, and immune persistence of a two-dose schedule, in health adults: interim results from two single-centre, double-blind, randomised, placebo-controlled phase 2 clinical trials. *The Lancet Infectious Diseases.* https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(21)00681-2/fulltext

[30] Immunogenicity of a third dose viral-vectored COVID-19 vaccine after receiving two-dose inactivated vaccines in health adults. *Vaccine.* https://www.sciencedirect.com/science/article/pii/S0264410X21015607?via%3Dihub

[31] The immunogenicity against variants of concern and reactogenicity of four COVID-19 booster vaccinations following CoronaVac or ChAdOx1 nCoV-19 primary series. *medRxiv.* https://www.medrxiv.org/content/10.1101/2021.11.29.21266947v2

[32] Prioritise first doses of COVID-19 vaccines over boosters, say WHO experts. *GAVI – The Vaccine Alliance.* Accessed on: 21 January 2022. https://www.gavi.org/vaccineswork/prioritise-first-doses-covid-19-vaccines-over-boosters-say-who-experts

[33] Fourth dose of COVID-19 vaccines in Israel. *The Lancet – Respiratory Medicine.* https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(22)00010-8/fulltext

moved on to this step of the vaccination scheme. Studies to assess the safety and effectiveness of vaccination in children are on-going, and many studies are pending in this area. The vaccine with the most available data so far is the BNT162b2 (Pfizer-BioNTech) vaccine. Regarding the safety of the BNT162b2 vaccine, a survey of adverse events in child vaccine recipients in the US showed that between November and December, **97.6%** of the 4,249 reports received were for nonserious events. Of the 2.4% of reports that claimed more serious events, the most common report was fever (29%).[34] Another cohort study of a large group of 12th grade students (16-18 years old) vaccinated with BN162b2 in South Korea reported similar results, with only **0.61%** of respondents reporting an adverse effect after 2 doses, and with only 0.01% of reports for serious events. Vaccine effectiveness in this study was reported to be **99.1% (95% CI, 98.5-99.5)** after two doses. It is important to note that considering the timing of this study, this figure is considered to be VE against the Delta variant.[35] During roughly this same time period (July-December 2021), an analysis of a prospective cohort of vaccinated adolescents in Arizona found an estimated adjusted vaccine effectiveness of **92% (95% CI, 98.5-92.5)**.[36]

Previous reports have mentioned the rare yet concerning adverse event of multi-system inflammatory syndrome in children (MIS-C). A French pharmacovigilance study observed that out of 4,079,324 children (12-17) who received two doses of an mRNA vaccine (most likely Pfizer as >95% of French children received this vaccine) there were 9 cases of MIS-C, corresponding to a national reporting rate of **1.1 (95% CI, 0.5-2.1)** per 1,000,000 mRNA doses. In comparison, this study also showed a higher rate of MIS-C attributable to SARS-CoV-2 infection, providing further evidence of the benefit of SARS-CoV-2 vaccination for this age group.[37] Other studies offered evidence of BNT162b2 vaccine protection against MIS-C. A report on hospitalized

[34] COVID-19 Vaccine Safety in Children Aged 5-11 Years - United States, November 3-December 19, 2021. *MMWR Morb Mortal Wkly Rep.* https://pubmed.ncbi.nlm.nih.gov/34968370

[35] Safety and effectiveness of BNT162b2 mRNA Covid-19 vaccine in adolescents. *Vaccine*. doi:10.1016/j.vaccine.2021.12.044

[36] Interim Estimate of Vaccine Effectiveness of BNT162b2 (Pfizer-BioNTech) Vaccine in Preventing SARS-CoV-2 Infection Among Adolescents Aged 12-17 Years - Arizona, July-December 2021. *MMWR Morbidity and mortality weekly report*. https://pubmed.ncbi.nlm.nih.gov/34968373/

[37] Multisystemic inflammatory syndrome following COVID-19 mRNA vaccine in children: a national post-authorization pharmacovigilance study. *MedRxiv*.https://www.medrxiv.org/content/10.1101/2022.01.17.22269263v1

patients between 12-18 years old in 20 states looked at the effect of being double vaccinated in protecting against MIS-C. Findings showed that among 102 MIS-C patients and 181 controls, the estimated effectiveness of vaccination against MIS-C was **91% (95% CI, 78-97)**. Ninety-five percent of the observed MIS-C patients were unvaccinated. Conversely, all 38 patients who required life support were unvaccinated. This finding suggests the sustained value of vaccination against adverse outcomes beyond initial SARS-CoV-2 infection.[38]

The recent literature has added data on the rare potential adverse event of myocarditis, often as part of larger studies on overall vaccine safety. In the previous VAERS study from November to December 2021, there were 11 verified reports of myocarditis.[39] The South Korean cohort study of 12th graders reported myocarditis as the most common serious adverse event, with a rate of **4.3 cases per 100,000 (95%CI, 2.6-6.7)** double vaccinated people.[40] A nationwide surveillance system of vaccinated Israeli adolescents from ages 12-15 observed myocarditis outcomes. Out of 326,463 adolescents who recieved both doses of the BNT162b2 vaccine, 18 cases of myocarditis were reported. Risk estimates for myocarditis within 21 days of administration of the second dose were stated as **8.09 cases per 100,000**. All cases observed were mild, and all patients were discharged without incident.[41]

Additionally, recent literature has provided updates to estimates of vaccine effectiveness against the Omicron variant amongst children. A study investigating immunogenicity of BN162b2 vaccine in both adolescents and adults against Omicron found that in both adolescents and adults, the reduction of effectiveness against Omicron was **3-4 fold** when compared to wild-type variants. Only **3 out of 15**

[38] Effectiveness of BNT162b2 (Pfizer-BioNTech) mRNA Vaccination Against Multisystem Inflammatory Syndrome in Children Among Persons Aged 12–18 Years — United States, July–December 2021. *MMWR Morb Mortal Wkly Rep*. https://www.cdc.gov/mmwr/volumes/71/wr/mm7102e1.htm?s_cid=mm7102e1_w

[39] COVID-19 Vaccine Safety in Children Aged 5-11 Years - United States, November 3-December 19, 2021. *MMWR Morb Mortal Wkly Rep*. https://pubmed.ncbi.nlm.nih.gov/34968370

[40] Safety and effectiveness of BNT162b2 mRNA Covid-19 vaccine in adolescents. *Vaccine*. doi:10.1016/j.vaccine.2021.12.044

[41] Myocarditis after BNT162b2 Vaccination in Israeli Adolescents. *New England Journal of Medicine.* https://www.nejm.org/doi/10.1056/NEJMc2116999

adolescents showed detectable titers, showing that neutralization is mainly failing against Omicron.[42] Another study investigating the neutralization of Omicron in adolescents and children (12-17 and 6-12, respectively) vaccinated with mRNA-1273 (Moderna), showed that in adolescents, GMT was **11.8-fold** lower against Omicron than against an older variant (D614G). In children, the GMT was reduced **22.1-fold**.[43] Both studies showed a stronger immunogenic response among adolescents than adults, a finding which appears to fall in line with existing data regarding the differing immune responses against SARS-CoV-2 in different age groups.

Further (biweekly) updated data on the eight WHO EUL vaccines are synthesized in the synoptic table and new data has been highlighted in yellow.

[42] Loss of Pfizer (BNT162b2) Vaccine-Induced Antibody Responses Against the SARS-CoV-2 Omicron Variant in Adolescents and Adults. *SSRN*. https://ssrn.com/abstract=4010891

[43] mRNA-1273 Vaccine-elicited Neutralization of SARS-CoV-2 Omicron in Adolescents and Children. *medRxiv*. http://medrxiv.org/content/early/2022/01/25/2022.01.24.22269666.abstract

Synoptic Table

Synoptic table about SARS-CoV-2 vaccines accepted in the WHO's Emergency Use Listing (as of 28 January 2022)

	BNT162b2/ COMIRNATY (Pfizer-BioNTech, USA)	Spikevax/ Moderna COVID-19 Vaccine/ mRNA-1273 (Moderna, USA)	Vaxzevria/ ChAdOx1 nCoV-19/ AZD1222/ Covishield (AstraZeneca/Oxford, UK, India)	Janssen COVID-19 vaccine/Johnson & Johnson (Janssen, USA)	Covilo/ BBIBP-CorV (Sinopharm, China)	CoronaVac (Sinovac, China)	COVAXIN / BBV152 (Bharat Biotech, India)	Nuvaxovid/ NVX-CoV2373/ Covovax (Novavax, Czech Republic, India)
GENERAL VACCINE INFORMATION								
Platform	mRNA-based vaccine	mRNA-based vaccine	Non-replicating vector-based vaccine	Non-replicating vector-based vaccine	Inactivated virus (Vero cell)	Inactivated virus (Vero cell)	Whole-virion inactivated Vero cell	Recombinant protein (nanoparticle) vaccine with Matrix-M adjuvant
Dose and frequency	2 doses, 21 days apart	2 doses, 28 days apart	2 doses, 4-12 weeks apart	1 dose, once [Phase III trials currently testing 2-dose regime, 56 days apart][i]	2 doses, 21 days apart	2 doses, 14 days apart	2 doses, 28 days apart	2 doses, 21 days apart
Target population	12 years old and over	12 years old and over	18 years old and over	18 years old and over	18 years old and over	18 years old and over	18 years old and over	18 years old and over

[i] Johnson & Johnson Announces Real-World Evidence and Phase 3 Data Confirming Strong and Long-Lasting Protection of Single-Shot COVID-19 Vaccine in the U.S. *Johnson & Johnson*. https://www.jnj.com/johnson-johnson-announces-real-world-evidence-and-phase-3-data-confirming-strong-and-long-lasting-protection-of-single-shot-covid-19-vaccine-in-the-u-s

Storage conditions	2°C to 8 °C (for 1 month)	2°C to 8 °C (for 1 month)	2°C until 8 °C	2°C to 8 °C (for 3 months)	2°C until 8 °C	2°C until 8 °C	2°C until 8 °C	2°C to 8 °C
Approving authorities	FDA (11.12.20)[ii]; EMA (21.12.20); WHO EUL (31.12.20); and list of 137 countries (including Switzerland – approved on 20.12.20)	FDA (18.12.20); EMA (06.01.21); WHO EUL (30.04.21); and list of 85 countries (including Switzerland – approved 12.01.21)	FDA (awaiting on approval); EMA (29.01.21); WHO EUL (15.02.21); and list of 137 (Vaxzevria) and 47 (Covishield) countries (Switzerland awaiting on approval)	FDA (27.02.21); EMA (11.03.21), WHO EUL (12.03.21), and list of 106 countries (including Switzerland – approved 22.03.21)	WHO EUL (07.05.21); and list of 88 countries (including Argentina, Bahrain, Brazil, China, Indonesia, United Arab Emirates, Zimbabwe)	WHO EUL (01.06.21), and list of 53 countries (including Albania, Chile, Egypt, Hong Kong, Malaysia, Tunisia, Turkey, Ukraine)	WHO EUL (03.11.21) and list of 13 countries (including Guyana, Inidia, Iran, Mauritius, Mexico, Nepal, Paraguay, Philippines & Zimbabwe)	WHO EUL (17-20.12.21) and list of 32 (Nuvaxovid) and 3 countries (Covovax)
Booster shot approving authorities	EMA approved booster for those aged 18 and above, 6 months after the 2nd dose[1] FDA approved booster for those ages 16 and above, 6 months after the 2nd dose[iii]	EMA authorised booster dose for people aged 18 years and above[v] FDA approved third booster dose for individuals >65 and high-risk individuals, 6 months after the 2nd dose[vi]	-	EMA authorised	-	-	-	-

[ii] Pfizer-BioNTech's Comirnaty Vaccine received full FDA approval on 23 August 2021 for people age 16 and above, moving it beyond emergency use status. https://www.fda.gov/news-events/press-announcements/fda-approves-first-covid-19-vaccine

[iii] FDA authorizes booster dose of Pfizer-BioNTech COVID-19 vaccine for certain populations. *FDA News Release*. https://www.fda.gov/news-events/press-announcements/fda-authorizes-booster-dose-pfizer-biontech-covid-19-vaccine-certain-populations

[v] Comirnaty and Spikevax: EMA recommendations on extra doses and boosters. *European Medicines Agency*. https://www.ema.europa.eu/en/news/comirnaty-spikevax-ema-recommendations-extra-doses-boosters

[vi] F.D.A. Panel recommends booster for many Moderna vaccine recipients. *The New York Times*. https://www.nytimes.com/2021/10/14/us/politics/fda-moderna-vaccine-boosters.html

	Swissmedic approves booster dose for everyone aged 16 and over[iv]	Swissmedic approves booster dose for adults aged 18 and over[vii]						
	EFFECTIVENESS AGAINST ANY SARS-COV-2 INFECTION							
	BNT162b2/ COMIRNATY	**Spikevax/ Moderna COVID-19 Vaccine/ mRNA-1273**	**Vaxzevria/ ChAdOx1 nCoV-19/ AZD1222/ Covishield**	**Janssen COVID-19 vaccine/Johnson & Johnson**	**Covilo/ BBIBP-CorV**	**CoronaVac**	**COVAXIN / BBV152**	**Nuvaxovid/ NVX-CoV2373/ Covovax**
Effectiveness single dose	*Against any SARS-CoV-2 infection:* **70%**. **77.6%** (95% CI, 70.9-82.7) **36.8%** (95% CI, 33.2-40.2) [3 weeks after first dose] **57%** (95% CI, 52-61; Spain) [Apr-Aug] **72%** (pooled meta-analysis)	*Against SARS-CoV-2 infection:* **60%** (95% CI, 57-64; >2 weeks after dose).[ix] **88.9%** (95% CI, 78.7-94.2) **66%** (95% CI, 56-73; Spain) [Apr-Aug] **69%** (pooled meta-analysis) **64%** (95% CI, 59%-68%; United	*Against SARS-CoV-2 infection:* **31.4%** (95% CI, 25.7-36.7; Norway) [Jan-Sep] *Symptomatic disease:* **67%** **49%** (95% CI, 32.0-62.0; India) [Apr-Jun] **41%** (95% CI, 34-48; Spain) [Apr-Aug]	*Against SARS-CoV-2 infection:* **50.6%** (95% CI, 14.0-74.0) [<2 weeks after dose]; **76.7%** (95% CI, 30.3-95.3) [>2 weeks after dose]; **79%** (95% CI, 77-80) (when corrected for under-recording, VE was estimated to be **69%** (95% CI, 67-71).	Partial protection.[xvi]	**15.5%** for preventing COVID-19; **37.4%** for preventing hospitalization; **44.7%** for preventing admission to the ICU; and **45.7%** for preventing of COVID-19 related death. **18.6%** (95% CI, 17.6-19.6) against SARS-CoV-2	*Against symptomatic disease*: **45%** (95% CI,6.0-68.0; India) [Apr-Jun] **40%** (95% CI, -21-71; India) less than 7 days after first dose [April-May] **1%** (95% CI, -30-25); India) at least	Ongoing studies in South Africa and the United Kingdom

[iv] COVID-19 vaccine from Pfizer/BioNTech: Swissmedic approves the extension of the booster dose to everyone aged 16 years and over. *Swissmedic*. https://www.swissmedic.ch/swissmedic/en/home/news/coronavirus-covid-19/covid-19-impfstoff-pfizer-biontech-boosterdosis.html

[vii] Swissmedic approves booster dose of the Moderna COVID-19 vaccine for adults aged 18 and over. *Swissmedic*. https://www.swissmedic.ch/swissmedic/en/home/news/coronavirus-covid-19/auffrischimpfung-boosterdosis-impfstoff-moderna-ab-18-jahren.html

[ix] mRNA-aggregated data (results do not disaggregate between BNT162b2 and mRNA-1273).

[xvi] Study did not report numerical data on vaccine effectiveness. Further studies are required to validate results.

	64% (95% CI, 59%-68%; United States) [May to July 2021][2viii] **19.6%** (95% CI, 17.3-21.9; Norway) [Jan-Sep] *Against symptomatic disease*: **66%** (95% CI, 60-71; Spain) [Apr-Aug] *Individuals ≥70:* Symptomatic disease: **58%**.	States) [May to July 2021][x] **39.6%** (95% CI, 36.3-42.8; Norway) [Jan-Sep] *Against symptomatic disease*: **71%** (95% CI, 61-79; Spain) [Apr-Aug] *Individuals ≥70:* Symptomatic disease: **64%** (95% CI, 46-78; >2 weeks after dose).[xi]	**51%** (pooled meta-analysis)[3] **46%** (95% CI, 37-54; Spain) [Apr-Aug] *Individuals ≥70:* Symptomatic disease: **58%**.	**71%** (95% CI, 56-81) [11 March – 15 August]. **61%** (95% CI, 29-84) [January-June] **50.9%** (95% CI, 35.1-63.0) [June-September; Brazil] **50.0%** (95% CI, 42.0-57.0; Spain) [Apr-Aug] **73.6%** (95% CI, 65.9-79.9; US) [Feb-Jul] **82.3%** (95% CI, 75.1-87.4%; USA) [16 Dec 2020 to 30 Sep 2021][xii] Among individuals with history of infection, VE against symptomatic infection ≥ 14 days from vaccine series completion was 44.0% (95% CI, 31.5-54.2) for		infection, **28.1%** (95% CI, 26.3-29.9) against hospitalization, **28.5%** (95% CI, 25.4-31.4) against ICU admission, and **29.4%** (95% CI, 26.7.3-31.9) against death [January-April]	7 days after first dose [April-May] **-1%** (95% CI, -51-33; India) at least 21 days after first dose [April-May]	

[viii] Results do not disaggregate between mRNA vaccines, BNT162b2 and mRNA-1273.
[x] Results do not disaggregate between mRNA vaccines, BNT162b2 and mRNA-1273.
[xi] mRNA-aggregated data (results do not disaggregate between BNT162b2 and mRNA-1273).
[xii] Study does not differentiate between Pfizer, Moderna, and Janssen.

				Ad26.COV2.S. [Brazil] *Symptomatic disease*: **54%** (95% CI, 45-62; Spain) [Apr-Aug] **81%** (95% CI, 79-84) for preventing hospitalization when corrected for under-recording, VE was estimated to be **73%** (95% CI, 69-76). **75%** (95% CI, 65-82) against severe critical COVID-19 **66.1%** against moderate to severe-critical COVID-19 cases after 28 days [ENSEMBLE study; Sep 2020-Nov 2021) **85.4%** against severe COVID-19 cases after 28 days [ENSEMBLE				

				study; Sep 2020-Nov 2021) *<u>Individuals ≥50:</u>* 68% (95% CI, 50-79). VE against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection was 89.1% (95% CI 85.6–92.6%), VE against COVID-19-related hospitalization was 97.2% (95% CI 96.1–98.3%), and VE against admission to the intensive care unit 97.4% (95% CI 96.0–98.8%), and against death was 99.0% (95% CI 98.5–99.6%). [Overall average from literature review and meta-analysis][xiii]				

[xiii] Study does not differentiate between Pfizer-BioNTech, Moderna, Oxford-AstraZeneca, CoronaVac, and Janssen.

				VE against infection in the general population aged ≥16 years was 86.1% (95% CI 77.8–94.4%), for the elderly VE was 83.8% (95% CI 77.1–90.6%), and for healthcare workers VE was 95.3% (95% CI 92.0–98.6%).[Overall average from literature review and meta-analysis][xiv] Adjusted VE was 71% (95% confidence interval, 49%-83%) among fully vaccinated participants reporting contact with persons with COVID-19 versus 80% (95% CI, 72%-86%) among those without contact.[United States; February				

[xiv] Study does not differentiate between Pfizer-BioNTech, Moderna, Oxford-AstraZeneca, CoronaVac, and Janssen.

				2021 to September 2021][xv]				
Effectiveness of two doses	*SARS-Cov-2 infection:* **85%**. **94.6%**. **94.5%**. **76%** (95% CI, 69-81) [Jan-Jul]. **88.8%** (95% CI, 84.6-91.8) [Dec 2020-May] **74%** (95% CI, 72-76) [Jan-Jun] **77.5%** (95% CI, 76.4-78.6) [first month after second dose] **47%** (95% CI, 43-51) [5 months after second dose] **56%** (95% CI, 53-59) [4 months after second dose] **69%** (95% CI, 66-72; Spain) [Apr-Aug] **88%** (pooled meta-analysis) **84%** (95% CI, 40-96; Italy) [27 Dec 2020 – 24 Mar	*SARS-Cov-2 infection:* **100%**. **86%** (95% CI, 81-90.6) [January-July]. **96.3%** (95% CI, 91.3-98.4) [December-May] **85%** (95% CI, 80-90) [January-June] **71%** (95% CI, 68-74) [4 months after second dose] **63%** (95% CI, 44-76) [June-August] **82%** (95% CI, 78-86; Spain) [Apr-Aug] **80%** (pooled meta-analysis)	*Asymptomatic efficacy:* 61.9% *SARS-CoV-2 infection*: **53%** (95% CI, 12-84) [January-June] **27%** (95% CI, 17-37) [4 months after second dose] **88%** (95% CI, 79.0-94.0; India) [Apr-Jun] **54.0%** (95% CI, 48-60; Spain) [Apr-Aug] **43.4%** (95% CI, 4.4-66.5; Norway) [Jan-Sep] **80%** (95% CI; 73-86; India) [May - July 2021]	Not Applicable (one dose schedule)	Partial protection.[xli]	**65.9%** for preventing COVID-19; **87.5%** for preventing hospitalization; **90.3%** for preventing ICU admission; and **86.3%** for preventing COVID-19 related death. **52.7%** (95% CI, 52.1-53.4) against SARS-CoV-2 infection, **72.8%** (95% CI, 71.8-73.7) against hospitalization, **73.8%** (95% CI, 72.2-75.2) against ICU admission, and **73.7%** (95% CI, 72.3-75.0) against death [January-April] Among individuals with history of	*Against symptomatic disease*: **71%** (95% CI, 41-85; India) [Apr-Jun] VE against symptomatic COVID-19 (second dose administered at least 14 days before RT-PCR testing) **50%** (95%CI 33.0-62.0; India)[April 15 to May 15 2021] *Effectiveness of full vaccination:* **69%** (95% CI; 54-79; India) [May - July 2021] **50%** (95% CI, 33-62; India) 14 days after second dose [April-May]	Ongoing studies in South Africa and the United Kingdom **89.7%** protection against SARS-CoV-2 infection (95% CI, 80.2-94.6; United Kingdom)

[xv] Study does not differentiate between Pfizer, Moderna, and Janssen

[xli] Study did not report numerical data on vaccine effectiveness. Further studies are required to validate results. Death reports on fully vaccinated doctors (10 cases during June 2021 in Indonesia). It may be related to new variants [media report]. Indonesian Covid deaths add to questions over Sinovac vaccine. *The Guardian* [press release]. https://www.theguardian.com/world/2021/jun/28/indonesian-covid-deaths-add-to-questions-over-sinovac-vaccine

	2021] 14-21 days from the first dose and **95%** (95% CI, 62-99; Italy) [27 Dec 2020 – 24 Mar 2021] at least 7 days from the second dose **95%** (95% CI, 93%-96%; United States) [May to July 2021][xvii] **69.7%** (95% CI, 68.6-70.8; Norway) [Jan-Sep] **82.3%** (95% CI, 75.1-87.4%; USA) [16 Dec 2020 to 30 Sep 2021][xviii] **75%** (95% CI, 73-77; Sweden) [27 Dec 2020-2 Nov 2021] VE was 49% (95% CI 22.0%-67.0%)[England] Higher dose two VE was observed	**95%** (95% CI, 93%-96%; United States) [May to July 2021][xxvii] **78.2%** (95% CI, 76.7-79.6; Norway) [Jan-Sep] **82.3%** (95% CI, 75.1-87.4%; USA) [16 Dec 2020 to 30 Sep 2021][xxviii] **85%** (95% CI, 82-87; Sweden) [27 Dec 2020-2 Nov 2021] For those fully vaccinated the observed effectiveness of the Moderna vaccine was 98.1%. [Overall average from literature review and meta-analysis]	**60%** (95% CI, 50-67; Sweden) [27 Dec 2020-2 Nov 2021] For BNT162b2 and AZD1222, VE was higher across all age-groups from 14 days after dose two compared to one dose, but the magnitude varied with dose interval. [England] VE was approximately **96.7%** (95% CI, 87.9-99.9) 7 days after the second dose [France; December 2020 to June 2021][xxxvi] VE against severe acute respiratory syndrome			infection, VE against symptomatic infection ≥ 14 days from vaccine series completion was 39.4% (95% CI, 36.1-42.6) for CoronaVac. [Brazil] For those fully vaccinated the observed effectiveness of the CoronaVac vaccine was found to be 65.7%.[Overall average from literature review and meta-analysis] VE against infection in the general population aged ≥16 years was 86.1% (95% CI 77.8–94.4%),	**47%** (95% CI, 29-61; India) 14 days after second dose – excluding participants with previous SARS-CoV-2 infections [April-May] **46%** (95% CI, 22-62; India) 28 days after second dose [April-May] **57%** (95% CI, 21-76; India) 42 days after second dose [April-May]	

[xvii] Results do not disaggregate between mRNA vaccines, BNT162b2 and mRNA-1273.
[xviii] Study does not differentiate between Pfizer, Moderna, and Janssen.
[xxvii] Results do not disaggregate between mRNA vaccines, BNT162b2 and mRNA-1273.
[xxviii] Study does not differentiate between Pfizer, Moderna, and Janssen.
[xxxvi] Study does not differentiate between Comirnaty and Vaxrevria

	with >6 week interval between BNT162b2 doses compared to the standard schedule. Specifically, antibody levels 14–35 days after dose two are higher in BNT162b2 recipients with an extended vaccine interval (65–84 days) compared with those vaccinated with a standard (19–29 days) interval. Following the extended schedule, antibody levels were 6-fold higher at 14–35 days post dose 2 for BNT162b2 than AZD1222. [England] For BNT162b2 and AZD1222, VE was higher across	VE against symptomatic SARS-CoV-2 infection was estimated at 94% (95% CI, 86–97%) for mRNA-1273.[Based on estimations from a Rapid Review] VE greater than 26 weeks from a second dose was 65% (95% CI, 65.0-66.0) and VE against SARS-CoV-2 related hospitalizations for individuals greater than 26 weeks from a second dose was 73% (95% CI, 71.0-75.0) for Moderna.[United States] VE was 69% (95% CI, 67.0% to 70.0%) against SARS-CoV-2 infection and 86%	coronavirus 2 (SARS-CoV-2) infection was 89.1% (95% CI 85.6–92.6%), VE against COVID-19-related hospitalization was 97.2% (95% CI 96.1–98.3%), and VE against admission to the intensive care unit 97.4% (95% CI 96.0–98.8%), and against death was 99.0% (95% CI 98.5–99.6%). [Overall average from literature review and meta-analysis][xxxvii] VE against infection in the general population aged ≥16 years was 86.1% (95% CI 77.8–94.4%), for the elderly VE was 83.8% (95% CI 77.1–90.6%), and for healthcare			for the elderly VE was 83.8% (95% CI 77.1–90.6%), and for healthcare workers VE was 95.3% (95% CI 92.0–98.6%).[Overall average from literature review and meta-analysis][xlii] VE against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection was 89.1% (95% CI 85.6–92.6%), VE against COVID-19-related hospitalization was 97.2% (95% CI 96.1–98.3%), and VE against admission to the intensive care unit 97.4% (95% CI 96.0–98.8%), and against death was 99.0% (95%		

[xxxvii] Study does not differentiate between Pfizer-BioNTech, Moderna, Oxford-AstraZeneca, CoronaVac, and Janssen.
[xlii] Study does not differentiate between Pfizer-BioNTech, Moderna, Oxford-AstraZeneca, CoronaVac, and Janssen.

	all age-groups from 14 days after dose two compared to one dose, but the magnitude varied with dose interval. [England] VE greater than 26 weeks from a second dose was 45% (95% CI, 44.0-47.0) for Pfizer.[United States] For those fully vaccinated the observed effectiveness of the Pfizer-BioNTech vaccine was 91.2%. [Overall average from literature review and meta-analysis]	(95% CI, 82.0% to 89.0%) against SARS-CoV-2–related death or more days after the second vaccine dose and was similar when follow-up period was extended. VE against infection decreased with increasing age and comorbidity burden. [United States, December 2020 to March 2021][xxix] VE against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection was 89.1% (95% CI 85.6–92.6%), VE against COVID-	workers VE was 95.3% (95% CI 92.0–98.6%).[Overall average from literature review and meta-analysis][xxxviii] *Symptomatic disease*: **90%**[7]. **56%** (95% CI, 48-63; Spain) [Apr-Aug] For two doses, VE against symptomatic SARS-CoV-2 infection was 73.9% (95% CI, 26.2%–90.8%) [Portugal; December 2020 to November 2021][xxxix]			CI 98.5–99.6%). [Overall average from literature review and meta-analysis[xliii] VE was 94.3% against mild disease and 99.9% against severe infection[Colombia, 24 February 2021 to 10 August 2021][8xliv] *In pregnant women*: **41%** (95% CI, 27.1-52.2%; Brazil) against symptomatic COVID-19, **85%** (95% CI, 59.5-94.8; Brazil) against severe COVID-19, and		

[xxix] Study does not differentiate between Moderna or Pfizer-BioNTech.
[xxxviii] Study does not differentiate between Pfizer-BioNTech, Moderna, Oxford-AstraZeneca, CoronaVac, and Janssen.
[xxxix] Study does not differentiate between Pfizer and AstraZeneca.
[xliii] Study does not differentiate between Pfizer-BioNTech, Moderna, Oxford-AstraZeneca, CoronaVac, and Janssen.
[xliv] 95% CI were not reported by authors.

	VE was 69% (95% CI, 67.0% to 70.0%) against SARS-CoV-2 infection and 86% (95% CI, 82.0% to 89.0%) against SARS-CoV-2–related death or more days after the second vaccine dose and was similar when follow-up period was extended. VE against infection decreased with increasing age and comorbidity burden. [United States, December 2020 to March 2021][xix] VE was approximately **96.7%** (95% CI, 87.9-99.9) 7 days after the second dose [France;	19-related hospitalization was 97.2% (95% CI 96.1–98.3%), and VE against admission to the intensive care unit 97.4% (95% CI 96.0–98.8%), and against death was 99.0% (95% CI 98.5–99.6%). [Overall average from literature review and meta-analysis]xxx VE against infection in the general population aged ≥16 years was 86.1% (95% CI 77.8–94.4%), for the elderly VE was 83.8% (95% CI 77.1–90.6%), and for healthcare workers VE was 95.3% (95% CI 92.0–98.6%).[Overall average from	VE against symptomatic SARS-CoV-2 infection was estimated at 92% (95% CI, 78–97%) for ChAdOx.[Based on estimations from a Rapid Review] Among individuals with history of infection, VE against symptomatic infection ≥ 14 days from vaccine series completion was 56.0% (95% CI, 51.4-60.2) for ChAdOx1. [Brazil] VE was approximately 96.7% (95% CI, 87.9-99.9) 7 days after the second dose [France;			**75%** (95% CI 27.9-91.2; Brazil)		

[xix] Study does not differentiate between Moderna or Pfizer-BioNTech.
[xxx] Study does not differentiate between Pfizer-BioNTech, Moderna, Oxford-AstraZeneca, CoronaVac, and Janssen.

	December 2020 to June 2021][xx] VE against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection was 89.1% (95% CI 85.6–92.6%), VE against COVID-19-related hospitalization was 97.2% (95% CI 96.1–98.3%), and VE against admission to the intensive care unit 97.4% (95% CI 96.0–98.8%), and against death was 99.0% (95% CI 98.5–99.6%). [Overall average from literature review and meta-analysis][xxi]	literature review and meta-analysis][xxxi] Adjusted VE was 71% (95% confidence interval, 49%-83%) among fully vaccinated participants reporting contact with persons with COVID-19 versus 80% (95% CI, 72%-86%) among those without contact.[United States; February 2021 to September 2021][xxxii] *Symptomatic disease*: **91%** (95% CI, 89-93;	December 2020 to June 2021][xl]					

[xx] Study does not differentiate between Comirnaty and Vaxrevria.
[xxi] Study does not differentiate between Pfizer-BioNTech, Moderna, Oxford-AstraZeneca, CoronaVac, and Janssen.
[xxxi] Study does not differentiate between Pfizer-BioNTech, Moderna, Oxford-AstraZeneca, CoronaVac, and Janssen.
[xxxii] Study does not differentiate between Pfizer, Moderna, and Janssen.
[xl] Study does not differentiate between Comirnaty and Vaxrevria.

	VE against infection in the general population aged ≥16 years was 86.1% (95% CI 77.8–94.4%), for the elderly VE was 83.8% (95% CI 77.1–90.6%), and for healthcare workers VE was 95.3% (95% CI 92.0–98.6%).[Overall average from literature review and meta-analysis][xxii] Adjusted VE was 71% (95% confidence interval, 49%-83%) among fully vaccinated participants reporting contact with persons with COVID-19 versus	>2 weeks after dose).[xxiii] **85%** (95% CI, 80-89; Spain) [Apr-Aug] *Asymptomatic SARS-CoV-2 infection:* **90.6%**.[xxiv] **71%** (95% CI, 61-78) [January-August] *Hospitalization:* **91.6%** (95% CI, 81-97) [January-July]. **93%** (95% CI, 91-95) [11 March – 15 August). **89%** (95% CI, 87-91) for individuals ≥50 years [1 January-22 June.[xxv]							

[xxii] Study does not differentiate between Pfizer-BioNTech, Moderna, Oxford-AstraZeneca, CoronaVac, and Janssen.
[xxiii] Results do not disaggregate between BNT162b2 and mRNA-1273.
[xxiv] Results do not disaggregate between BNT162b2 and mRNA-1273
[xxv] mRNA-aggregated data (results do not disaggregate between BNT162b2 and mRNA-1273).

	80% (95% CI, 72%-86%) among those without contact.[United States; February 2021 to September 2021][xxiii] Adjusted VE against infection was **93·0%** (CI:92·6–93·4%) [Israel][4] VE against infection among older population was **34.5%** (95% CI, 18.5-47.3)[France][5] VE against any infection during predominance of alpha variant was **94.5%** (95% CI, 82.6%-98.2%)[Israel][6] VE against severe disease among older population								

[xxiii] Study does not differentiate between Pfizer, Moderna, and Janssen.

	was **58.6%** (95% CI, 43.8-69.6). [France][5] *Symptomatic disease*: **72%** (95% CI, 69-75; Spain) [Apr-Aug] Adjusted VE was 59% (95% CI 23.0%-78.0%)[England] VE against symptomatic SARS-CoV-2 infection was estimated at 89–97% BNT162b2.[Based on estimations from a Rapid Review] Among individuals with history of infection, VE against symptomatic infection ≥ 14 days from vaccine series completion was 64.8% (95% CI, 54.9-72.4) for								

	BNT162b2. [Brazil] For two doses, VE against symptomatic SARS-CoV-2 infection was 73.9% (95% CI, 26.2%–90.8%) [Portugal; December 2020 to November 2021][xxiv] *<u>Asymptomatic SARS-CoV-2 infection:</u>* **90.6%**.[xxv] **73.1** (95% CI, 70.3-75.5) *<u>Hospitalization:</u>* **85%** (95% CI, 73-93) [January-July]. **88%** (95% CI, 85-91) [11 March – 15 August]. **89%** (95% CI, 87-91) for individuals ≥50 years [1								

[xxiv] Study does not differentiate between Pfizer and AstraZeneca
[xxv] Results do not disaggregate between BNT162b2 and mRNA-1273

	January-22 June.[xxvi] **90%** (95% CI, 89-92) [Dec 2020 – Aug 2021] VE against SARS-CoV-2 related hospitalizations for individuals greater than 26 weeks from a second dose was 67% (95% CI, 65.0-69.0) for Pfizer.[United States] VE against hospitalization or death ≥ 14 days from vaccine series completion was 89.7% (95% CI, 54.3-97.7) for BNT162b2. [Brazil] VE against hospitalization 14–119 days following second Pfizer-BioNTech dose was 86.0% (95%								

[xxvi] mRNA-aggregated data (results do not disaggregate between BNT162b2 and mRNA-1273).

	CI = 77.6%–91.3%); at ≥120 days VE was 75.1% (95% CI = 64.6%–82.4%).[United States; February 2021 to September 2021] *Individuals ≥65:* **61%** (95% CI, 57-65) against SARS-CoV-2 infection and **86%** (95% CI, 82-88) against hospitalizations *Individuals ≥ 80:* VE of **68.3%** (95% CI, 65.5-70.9) for infections, **73.2%** (95% CI, 65.3-79.3) for hospitalization, **85.1%** (95% CI, 80.0-89.0) for mortality [Germany, 09 Jan – 11 Apr 2021]									

EFFECTIVENESS AGAINST VARIANTS[xlv]

[xlv] Effectiveness data against the latest variant of interest (Mu) will be included in upcoming reports based on data availability.

	BNT162b2/ COMIRNATY	Spikevax/ Moderna COVID-19 Vaccine/ mRNA-1273	Vaxzevria/ ChAdOx1 nCoV-19/ AZD1222/ Covishield	Janssen COVID-19 vaccine/Johnson & Johnson	Covilo/ BBIBP-CorV	CoronaVac	COVAXIN / BBV152	Nuvaxovid/ NVX-CoV2373/ Covovax
Alpha (B.1.1.7)	*Single dose:* **48.7%** (95% CI, 45.5 to 51.7) **66%** (95% CI,64-68). **54.5%** (95 CI, 50.4-58.3) *Two doses:* **93.7%** (95% CI, 91.6 to 95.3) **92%** (95% CI, 90-93). **89%** (95% CI, 86-91). **78%** (95% CI, 68-84) **84.4%** (95 CI, 81.8-86.5)	*Single dose:* **88.1%** (95% CI, 83.7 to 91.5) **83%** (95% CI, 80-86). *Two doses:* **100%** (95% CI, 91.8 to 100) **92%** (95% CI, 86-96). **98.4%** (95% CI, 96.9-99.1)	*Single dose:* **48.7%** (95% CI 45.5 to 51.7) 6**4%** (95% CI, 60-68). *Two doses:* **74.5%** (95% CI, 68.4 to 79.4) **73%** (95% CI, 66-78). 79% (95% CI, 56-90).	-	No published data	*Two doses:* Equally effective **(~76%)** in neutralizing D614G, B.1.1.7 and B.1.429 as the wild-type strain.	No available data	Ongoing studies in South Africa and the United Kingdom Post hoc analysis showed efficacy of **86.3%** (95% CI, 71.3-93.5; United Kingdom) **against B.1.1.7 variants** and **96.4%** (95% CI, 73.8-99.5; United Kingdom) **against non-B.1.1.7 variants.**
Beta (1.351)	*Against SARS-CoV-2 infection:* *Single dose:* **60%** (95% CI, 52-67). *Two doses:* **84%** (95% CI, 69-92)	*Single dose:* **61.3%** (95% CI, 56.5 to 65.5) **77%** (95% CI, 69-92). *Two doses:* **96.4%** (95% CI, 91.9 to 98.7)[9]	*Single dose:* **48%** (95% CI, 28-63).	-	No published data	Neutralization capacity was decreased by factor **5.27**.	No available data	No available data

	72% (95% CI, -5-97; Israel) [Dec 2020-Mar 2021] *<u>Against symptomatic infection:</u>* **100%** (95% CI, 19-100; Israel) [Dec 2020-Mar 2021]							
Gamma (P.1)	Neutralization activity reduced by **3.3-fold**.	No available data	No available data	No available data	No published data	Demonstrated **42%** vaccine effectiveness in a setting with high P.1 transmission, in individuals aged 70 and above. **50.2%** against P.1 (>14 days after 2nd dose). Neutralization was decreased by factor **3.92**. *<u>Against symptomatic COVID-19:</u>* **80.5%** (95% CI, 75.1-84.7)[10]	No available data	No available data

Delta (1.617.2)	*Single dose:* **30.7%** (95% CI, 25.2 to 35.7); **57%** (95% CI, 50-63) **22.5%** (95 CI, 17.0-27.4) **22%** (95% CI, 10-32; France) [May-August 2021] *Two doses:* **88.0%** (95% CI, 85.3 to 90.1); **80%** (95% CI, 77-83) **79%** (95% CI,75-82). **80%** (95% CI, 77-83) **40.5%** (95% CI, 8.7-61.2). **42%** (95% CI, 13-62). **89.8%** (95% CI, 89.6-90.0) [2-9 weeks after second dose]. **69.7%** (95% CI, 68.7-70.5) [≥20 weeks after second dose]. **64.6%** (95 CI, 60.6-68.2)	*Single dose:* **72%** effective against symptomatic SARS-Cov-2 infection. *≥14 days after second dose:* **76%** (95% CI, 58-87). **94.5%** (95% CI, 94.1-95) [2-9 weeks after second dose]. **50.6%** (95% CI, 45.0-55.7) [among nursing home residents]. **86.7%** (95% CI, 84.3-88.7) **56.6%** (95% CI, 42.0-67.5) *against infection* **84.2%** (95% CI, 56.4-94.3) *against symptomatic infection* **64%** (95% CI, 62-66) [August; elderly Veteran population] **76.5%** (95% CI, 40.9-90.6; USA)	*Single dose:* **30.7%** (95% CI 25.2 to 35.7) **73%** (95% CI, 64-80; India) [May – July 2021] *Two doses:* **67.0%** (95% CI, 61.3 to 71.8) **67%** (95% CI, 62-71). **60%** (95% CI, 53-66). **66.7%** (95% CI, 45-49.6) [2-9 weeks after second dose]. **47.3%** (95% CI, 66.3-67.0) [≥20 weeks after second dose]. **81%** (95% CI, 71-88; India) [May – July 2021] Odds ratio of **5.45** (95% CI, 1.39-21.4) to become infected with B.1.167.2 compared to non-B.1.167.2.	**78%** (95% CI, 73-82) against SARS-CoV-2 infection. **3%** (95% CI, -7-12) [August] **76.5%** (95% CI, 40.9-90.6; USA) [01 Jul 2021 to 30 Sep 2021][lx] Prior to the predominance of the delta variant (delta comprising 1.8% of circulating variants), median VE against infection was **86.6%** (95% CI, 77.8 to 89.7) for Ad26.COV2.S and **continuously declined in all cohorts** (BNT162b2, mRNA-1273, Ad26.COV2.S) from a median of **93.4%** (95% CI, 77.8- 98.0) when the prevalence of delta was at 1.8% to **73.5%** (95% CI,	No available data	*Single dose:* **13.8%** (95% CI, -60.2-54.8). *Two doses:* **59%** (95% CI, 16-81.6) against SARS-CoV-2 infection and **70.2%** (95% CI, 29.6-89.3) against moderate COVID-19 infection.	*Single dose*: **44%** (95% CI, 0-71; India) [May – July 2021] *Two doses:* **64%** (95% CI, 40-79; India) [May – July 2021] VE was **44%** (95% CI, 37.0-51.0) against symptomatic infection and **61%** (95% CI, 37.0-76.0) against hospitalization or death 2 weeks after second dose during the delta dominant period. [India][16]	No available data

[lx] Study does not differentiate between Pfizer, Moderna, and Janssen.

	52.4% (95% CI, 48.0-56.4) [among nursing home residents]. **53%** (95% CI, 39-65) [4 months after second dose] **50%** (95% CI, 47-52) [August; elderly Veteran population] **76.5%** (95% CI, 40.9-90.6; USA) [01 Jul 2021 to 30 Sep 2021][xlvi] **67%** (95% CI, 63-71; France) [May-August 2021] VE against Delta variant-related symptomatic infection was 88% (95% CI, 85.3–90.1%) by BNT162b2 after full vaccination. [Based on estimations from a Rapid Review]	[01 Jul 2021 to 30 Sep 2021][lii] *<u>10-14 weeks after second dose:</u>* **90.3%** (95% CI, 67.2-97.1). VE against Delta variant-related symptomatic infection was 67.0% (95% CI, 61.3–71.8%) ChAdOx1 after full vaccination.[Based on estimations from a Rapid Review] Among early recipients of mRNA-1273, VE decreased an estimated 10 percentage when the Delta variant became dominant. Among individuals who received 2	Among individuals who received 2 doses of vaccines (with at least 1mRNA vaccine) VE against Delta declined steadily over time from 84% (95%CI, 81-86%) 7-59 days after the second dose to 71% (95%CI, 66-75%) ≥240 days after the second dose, but recovered to 93% (95%CI, 92-94%) ≥7 days after receiving an mRNA vaccine for the third dose.[Canada; November 2021 to December 2021] [lviii] VE against severe COVID-19 was **86%** (95% CI,	13.8-90.0) when delta prevalence was **85.3%,** and 74.2% (95% CI, 63.4-86.8) when the prevalence of delta was 99.6%.[United States][15] VE against severe COVID-19 was **86%** (95% CI, 79.0–90.0) for ages 18-49, **89%** (95% CI, 85.0–91.0) for 50-64, **77%** (95% CI, 74.0–81.0) for ≥ 65 year-olds. Among ≥ 65 year-olds fully vaccinated with mRNA vaccines, **VE decreased from 93%** (95% CI: 88–96) in those vaccinated ≤ 3 months ago to **43%** (95% CI: 30–				

[xlvi] Study does not differentiate between Pfizer, Moderna, and Janssen.
[lii] Study does not differentiate between Pfizer, Moderna, and Janssen.
[lviii] Study does not differentiate between Pfizer, Moderna, or AstraZeneca.

	VE against hospitalization was 93% (95% CI, 90.0-94.0); South Africa)[September 2021 to October 2021] Among early recipients of BNT162b2, VE decreased an estimated 15 percentage when the Delta variant became dominant. Among individuals who received 2 doses of vaccines (with at least 1mRNA vaccine) VE against Delta declined steadily over time from 84% (95%CI, 81-86%) 7-59 days after the second dose to 71% (95%CI, 66-75%) ≥240 days after	doses of vaccines (with at least 1mRNA vaccine) VE against Delta declined steadily over time from 84% (95%CI, 81-86%) 7-59 days after the second dose to 71% (95%CI, 66-75%) ≥240 days after the second dose, but recovered to 93% (95%CI, 92-94%) ≥7 days after receiving an mRNA vaccine for the third dose.[Canada; November 2021 to December 2021] [liii] VE was 62.0% (95% CI, 45.6-73.5) in the first month after complete vaccination and decreased to 57.8% (95%CI, 52.5-62.5) by	79.0–90.0) for ages 18-49, **89%** (95% CI, 85.0–91.0) for 50-64, **77%** (95% CI, 74.0–81.0) for ≥ 65 year-olds. Among ≥ 65 year-olds fully vaccinated with mRNA vaccines, **VE decreased from 93%** (95% CI: 88–96) in those vaccinated ≤ 3 months ago to **43%** (95% CI: 30–54) in those vaccinated ≥ 6 months ago. [Slovenia][13lix]	54) in those vaccinated ≥ 6 months ago. [Slovenia][13lxi] *Individuals ≥50:* **83% (**95% CI, 81-85)				

[liii] Study does not differentiate between Pfizer, Moderna, or AstraZeneca.
[lix] Study does not differentiate between Pfizer, Moderna, Oxford-AstraZeneca, or Janssen.
[lxi] Study does not differentiate between Pfizer, Moderna, Oxford-AstraZeneca, or Janssen.

	the second dose, but recovered to 93% (95%CI, 92-94%) ≥7 days after receiving an mRNA vaccine for the third dose.[Canada; November 2021 to December 2021][xlvii] VE was 62.0% (95% CI, 45.6-73.5) in the first month after complete vaccination and decreased to 57.8% (95%CI, 52.5-62.5) by month 3, similar to to results from pre-Delta period.[xlviii] Prior to the predominance of the delta variant (delta comprising 1.8% of circulating	month 3, similar to to results from pre-Delta period.[liv] One dose VE was 77.0% (95% CI, 60.7-86.5%). Two dose VE was 86.7% (95% CI 84.3%-88.7%). VE against hospitalization was 97.5% (95% CI 92.7%-99.2%). VE against infection declined from 94.1% (95% CI 90.5%-96.3%) 14-60 days after vaccination to 80.0%(95% CI, 70.2-86.6%) 151-180 days after. VE against infection was lower for ≥ 65 years at 75.2%							

[xlvii] Study does not differentiate between Pfizer, Moderna, or AstraZeneca.
[xlviii] Study does not differentiate between mRNA vaccines, Pfizer and Moderna.
[liv] Study does not differentiate between mRNA vaccines, Pfizer and Moderna.

	variants), median VE against infection was **91.3%** (95% CI, 84.1-97.0) for BNT162b2, and **continuously declined in all cohorts** (BNT162b2, mRNA-1273, Ad26.COV2.S) from a median of **93.4% (**95% CI, 77.8- 98.0) when the prevalence of delta was at 1.8% to **73.5%** (95% CI, 13.8-90.0) when delta prevalence was 85.3%, and **74.2%** (95% CI, 63.4-86.8) when the prevalence of delta was 99.6%.[United States] For those who have received 2 doses of mRNA vaccines, VE is 41% (95% CI, 37.0-44.0) against Delta.[United States; 01	(95% CI 59.6%-84.8) than those 18-64 years at 87.9%(95% CI, 85.5%-89.9%). Prior to the predominance of the delta variant (delta comprising 1.8% of circulating variants), median VE against infection was **96.9%** (95% CI, 93.7-98.0) for mRNA-1273 and **continuously declined in all cohorts** (BNT162b2, mRNA-1273, Ad26.COV2.S) from a median of **93.4%** (95% CI, 77.8- 98.0) when the prevalence of delta was at 1.8% to **73.5%** (95% CI, 13.8-90.0) when delta prevalence was 85.3%, and **74.2%** (95% CI, 63.4-86.8) when the prevalence of delta was						

	December 2021 to 31 December 2021][11xlix] VE against symptomatic infection was **88.7%** (95% CI], 78.8-93.9) among patients aged 16 to 64 and **90.3%** (95% CI, 73.6-96.4) among patients aged ≥65.[Japan, 01 July to 30 September 2021][12l] *Against severe COVID-19:* **91.4%** (95% CI, 82.5-95.7). **86%** (95% CI, 79.0–90.0) for ages 18-49, **89%** (95% CI, 85.0–91.0) for 50-64, **77%** (95% CI, 74.0–81.0) for ≥ 65 year-olds.	99.6%.[United States] For those who have received 2 doses of mRNA vaccines, VE is 41% (95% CI, 37.0-44.0) against Delta.[United States; 01 December 2021 to 31 December 2021][11lv] VE against severe COVID-19 was **86%** (95% CI, 79.0–90.0) for ages 18-49, **89%** (95% CI, 85.0–91.0) for 50-64, **77%** (95% CI, 74.0–81.0) for ≥ 65 year-olds. Among ≥ 65 year-olds fully vaccinated with mRNA vaccines, **VE decreased from 93%** (95%							

[xlix] Study does not differentiate between mRNA vaccines.
[l] Study does not differentiate between BNT162b2 or mRNA-1273.
[lv] Study does not differentiate between mRNA vaccines.

	Among ≥ 65 year-olds fully vaccinated with mRNA vaccines, **VE decreased from 93%** (95% CI: 88–96) in those vaccinated ≤ 3 months ago to **43%** (95% CI: 30–54) in those vaccinated ≥ 6 months ago. [Slovenia][13li]	CI: 88–96) in those vaccinated ≤ 3 months ago to **43%** (95% CI: 30–54) in those vaccinated ≥ 6 months ago. [Slovenia][13lvi] VE against symptomatic infection was **88.7%** (95% CI], 78.8-93.9) among patients aged 16 to 64 and **90.3%** (95% CI, 73.6-96.4) among patients aged ≥65.[Japan, 01 July to 30 September 2021][12lvii] Pooled VE was **66%** (95% CI, 65.0-67.0) ≥ 21 days after the first dose and **91%** (95% CI, 84.0-						

[li] Study does not differentiate between Pfizer, Moderna, Oxford-AstraZeneca, or Janssen.
[lvi] Study does not differentiate between Pfizer, Moderna, Oxford-AstraZeneca, or Janssen.
[lvii] Study does not differentiate between BNT162b2 or mRNA-1273.

		95.0) ≥14 days after the second dose.[14]						
Mu (B.1.621)	Mu variant is 9.1 times more resistant than the wild type strain when vaccinated with BNT162b2	*Two doses:* **90.4%** (95% CI, 73.9-96.5) (demonstrated similar protective measures as against the Alpha variant)	No available data	No available data	No available data	No available data	No available data	No available data
Omicron (B.1.1.529)	**88.0%** (95% CI, 65.9-95.8) after 2-9 weeks following second dose, **48.5%** (95% CI, 24.3-65.0) after 10-14 weeks following second dose, **34-37%** from 15 weeks after second dose[17] If assuming a 25-fold decrease in pseudovirus neutralization **66%** (95% CI, 42-86)[18] VE against the Omicron variant	2-dose VE against omicron infection was 30.4% (95% CI, 5.0%-49.0%) at 14-90 days after vaccination and declined quickly thereafter. [United States; December 6 2021 to December 23 2021][21] VE against the Omicron variant was 36.7% (95% CI: -69.9 to 76.4%) for mRNA-1273 in the first month after primary vaccination.	No protective effect of vaccination against symptomatic disease with Omicron from 15 weeks after the second dose[17] 2 doses of COVID-19 vaccines was not protective against Omicron infection at any point in time, and VE was –38% (95%CI, –61%, –18%) 120-179 days and –42% (95%CI, –69%, –19%) 180-					

	was 55.2% (95% CI, 23.5 to 73.7%) for BNT162b2 in the first month after primary vaccination. However, the VE is significantly lower than that against Delta infection and declines rapidly over just a few months. [Denmark, November 2021 to December 2021][19] 2 doses of COVID-19 vaccines was not protective against Omicron infection at any point in time, and VE was –38% (95%CI, –61%, –18%) 120-179 days and –42% (95%CI, –69%, –19%) 180-239 days after the second dose. VE	[Denmark, November 2021 to December 2021][19] 2 doses of COVID-19 vaccines was not protective against Omicron infection at any point in time, and VE was –38% (95%CI, –61%, –18%) 120-179 days and –42% (95%CI, –69%, –19%) 180-239 days after the second dose. VE against Omicron was 37% (95%CI, 19-50%) ≥7 days after receiving an mRNA vaccine for the third dose.[Canada; November 2021 to December 2021] [20] [lxiv] VE was **30.4% (95% CI, 5.0%-49.0%)** 14-90	239 days after the second dose. VE against Omicron was 37% (95%CI, 19-50%) ≥7 days after receiving an mRNA vaccine for the third dose.[Canada; November 2021 to December 2021] [20] [lxvi]						

[lxiv] Study does not differentiate between Pfizer, Moderna, or AstraZeneca.
[lxvi] Study does not differentiate between Pfizer, Moderna, or AstraZeneca.

	against Omicron was 37% (95%CI, 19-50%) ≥7 days after receiving an mRNA vaccine for the third dose.[Canada; November 2021 to December 2021] [20] [lxii] VE was 25% (95% CI, 20.0-30.0) against Omicron infection. [United States; 01 December 2021 to 31 December 2021] [11] [lxiii]	days after vaccination and declined thereafter.[21] VE was 25% (95% CI, 20.0-30.0) against Omicron infection. [United States; 01 December 2021 to 31 December 2021] [11][lxv]						
	EFFECTIVENESS AGAINST HOSPITALIZATION							
	BNT162b2/ COMIRNATY	**Spikevax/ Moderna COVID-**	**Vaxzevria/ ChAdOx1 nCoV-**	**Janssen COVID-19**	**Covilo/ BBIBP-CorV**	**CoronaVac**	**COVAXIN / BBV152**	**Nuvaxovid/ NVX-CoV2373/ Covovax**

[lxii] Study does not differentiate between Pfizer, Moderna, or AstraZeneca.

[lxiii] Study does not differentiate between mRNA vaccines.

[lxv] Study does not differentiate between mRNA vaccines.

		19 Vaccine/ mRNA-1273	19/ AZD1222/ Covishield	vaccine/Johnson & Johnson				
Any SARS-CoV-2 infection	*Single dose:* **85%** (pooled meta-analysis) Hospitalization risk reduced by 35-**45%**. Risk of death reduced by **54%**. *Individuals ≥50:* ≥14 days after first dose: **54%** (95% CI, 47-61) [1 Jan-22 Jun. [lxvii] *Two doses:* **91%** (pooled meta-analysis)[3] **91%** (95% CI, 93%-96%; United States) [May to July 2021][lxviii] **89%** (95% CI, 84-93; Sweden) [27	*Single dose:* **73%** (pooled meta-analysis) *Individuals ≥50:* ≥14 days after first dose: **54%** (95% CI, 47-61) [1 Jan-22 Jun.[lxxiii] *Two doses:* **88%** (pooled meta-analysis)[3] **91%** (95% CI, 93%-96%; United States) [May to July 2021][lxxiv] **79%** (95% CI, 60-89; Sweden) [27 Dec 2020-2 Nov 2021] Adjusted Hazard Ratio for COVID-19 hospitalization from day 7 after the second dose	*Single dose:* **56%** (pooled meta-analysis) Hospitalization risk reduced by **35-45%**. *Two doses:* **91%** (pooled meta-analysis) **92%** (95% CI, 80-97; Sweden) [27 Dec 2020-2 Nov 2021] VE against hospitalization or death ≥ 14 days from vaccine series completion was 89.9% (95% CI, 83.5-93.8) for ChAdOx1. [Brazil]	VE against hospitalization or death ≥ 14 days from vaccine series completion was 57.7% (95% CI, −2.6-82.5) for Ad26.COV2.S. [Brazil]	*Two doses:* VE against hospitalization was **71.9%** [95% CI: 70.7-73.1%] for those who received the full vaccination schedule of BBIBP-CorV.[Iran] [30]	*Against hospitalization:* **71.2%** (95%CI, 70.0-72.4)[Brazil, 18 January 2021 to July 2021] [29] *Against ICU admission*: **72.0%** (95% CI, 69.9-73.9; Malaysia) [Apr-Sep 2021] **72.2%** (95%CI, 70.2-74.0)[Brazil, 18 January 2021 to July 2021][29] *Against death:* **82.4%** (95% CI, 81.0-83.7; Malaysia) [Apr-Sep 2021] VE against hospitalization or	No available data	No available data

[lxvii] mRNA-aggregated data (results do not disaggregate between BNT162b2 and mRNA-1273).

[lxviii] Results do not disaggregate between mRNA vaccines, BNT162b2 and mRNA-1273.

[lxxiii] mRNA-aggregated data (results do not disaggregate between BNT162b2 and mRNA-1273).

[lxxiv] Results do not disaggregate between mRNA vaccines, BNT162b2 and mRNA-1273.

	Dec 2020-2 Nov 2021] *Against ICU admission*: **90.3%** (95% CI, 88.8-91.6; Malaysia) [Apr-Sep 2021] *Against death:* **92.7%** (95% CI, 91.7-93.6; Malaysia) [Apr-Sep 2021][22] Adjusted Hazard Ratio for COVID-19 hospitalization from day 7 after the second dose was estimated at 0.14 (95% CI, 0.11–0.17), for an estimated 86% (95% CI, 83.0%-88.0%) risk reduction in people aged 75 and older [France] [lxix]	was estimated at 0.14 (95% CI, 0.11–0.17), for an estimated 86% (95% CI, 83.0%-88.0%) risk reduction in people aged 75 and older [France] [27] [lxxv] Fully vaccinated patients had a shorter overall length of stay in hospitals (aHR for discharge: 1.61, 95%CI: 1.24–2.08), shorter LoS without ICU (aHR: 1.27, 95%CI: 1.07–1.52), and lower risk of ICU admission (aHR: 0.50, 95%CI: 0.37–0.69) compared to unvaccinated patients. We observed no difference in the LoS in ICU, nor	VE against hospitalization, **91.4%** (95%C, 90.1-92.5). [29] VE against hospitalization was **81.5%** [95% CI: 79.5-83.4%] for those who received the full vaccination schedule of ChAdOx1-S/nCoV-19. [Iran][30] *Against ICU admission*: **95.6%** (95% CI, 88.3-98.4; Malaysia) [Apr-Sep 2021] **91.1%** (95%CI, 88·9-92.9). [29] *Against death:* **95.3%** (95% CI, 91.3-97.4;			death ≥ 14 days from vaccine series completion was 81.3% (95% CI, 75.3-85.8) for CoronaVac. [Brazil] Adjusted odds ratios of COVID hospitalisation or death were significantly increased from 98 days since series completion, compared to individuals vaccinated 14-41 days previously: 1.40 (95% CI, 1.09 to 1.79) from 98-125 days, 1.55 (1.16 to 2.07) from 126-153 days, 1.56 (1.12 to 2.18) from 154-181 days, and 2.12 (1.39-3.22) from 182 days. [Brazil; January 2021 to		

[lxix] Study does not differentiate between Pfizer/BioNTech and Moderna.
[lxxv] Study does not differentiate between Pfizer/BioNTech and Moderna.

	Fully vaccinated patients had a shorter overall length of stay in hospitals (aHR for discharge: 1.61, 95%CI: 1.24–2.08), shorter LoS without ICU (aHR: 1.27, 95%CI: 1.07–1.52), and lower risk of ICU admission (aHR: 0.50, 95%CI: 0.37–0.69) compared to unvaccinated patients. We observed no difference in the LoS in ICU, nor risk of in-hospital death between fully vaccinated and unvaccinated patients. [Norway, February 2021 to November 2021] 23[lxx]	risk of in-hospital death between fully vaccinated and unvaccinated patients. [Norway, February 2021 to November 2021] 23 [lxxvi] VE was observed to increase after the first dose of mRNA vaccines with week 6 effectiveness approximating 84% (95% CI 72.0-91.0) for COVID-19 infection and 86% (95% CI, 69.0-95.0) for COVID-19-associated hospitalization.[United States] 24 [lxxvii] VE against hospitalization 14–119 days following second Moderna	Malaysia) [Apr-Sep 2021][22] **92.3%** (95%CI, 90.5-93.7)[Brazil, 18 January 2021 to July 2021] 29 <60 years VE against death was **96.5%** (95%CI, 82.1–99.3) versus **68·5%** (95%CI, 40.0–83.4) in those ≥90 years.[Brazil, 18 January 2021 to July 2021][29]			September 2021] 31 **73.7%** (95%CI, 72.1–75.2)[Brazil, 18 January 2021 to July 2021] 29 **84.8%** (95%CI:77.1–89.9) in those <60 years compared to **63.5** (95%CI 58.7–67.7) for those aged 80–89 years and **48.6%**; (95%CI:35.0–59.3) for individuals aged ≥90 years. [Brazil, 18 January 2021 to July 2021][29]		

[lxx] Study does not differentiate between mRNA vaccines Pfizer and Moderna.

[lxxvi] Study does not differentiate between mRNA vaccines Pfizer and Moderna.

[lxxvii] Study does not differentiate between Pfizer and Moderna.

	VE was observed to increase after the first dose of mRNA vaccines with week 6 effectiveness approximating 84% (95% CI 72.0-91.0) for COVID-19 infection and 86% (95% CI, 69.0-95.0) for COVID-19-associated hospitalization.[United States] 24 [lxxi] Adjusted VE against hospitalization was 93·4% (CI:91·9–94·7%) and 91·1% (CI:86·5–94·1%) against death.[Israel][4] Adjusted Hazard Ratio was 0.14% (95% CI, 0.11-	vaccine dose was 89.6% (95% CI = 80.1%–94.5%) at ≥120 days VE was 86.1% (95% CI = 77.7%–91.3%).[United States; February 2021 to September 2021][28] Adjusted Hazard Ratio was 0.14% (95% CI, 0.11-0.17) against hospitalization 7 days after second dose among people aged 75 and older; which is an **estimated 86% risk reduction**. [France] [25][lxxviii]							

[lxxi] Study does not differentiate between Pfizer and Moderna.

[lxxviii] Study does not differentiate between mRNA-based vaccines.

	0.17) against hospitalization 7 days after second dose among people aged 75 and older; which is an **estimated 86% risk reduction**. [France] [25lxxii] VE against death among older population was **75.2%** (95% CI, 54.6-86.4). [France][5] VE was **82%** (95% CI, 69.0-90.0) against hospitalization after full vaccination and **53%** (95% CI, 23.0-71.0) for partially vaccinated.[Lebanon; April to May 2021][26]							
Alpha	Single dose: **83%** (95% CI, 62-93)		Single dose: **76%** (95% CI, 61-85)	***Beta***	No available data	No available data	No available data	No available data

[lxxii] Study does not differentiate between mRNA-based vaccines.

	53% (95% CI, 7-83; England) [Feb-Sep 2021] Two doses: **95%** (95% CI, 78-99) **71%** (95% CI, 12-95; England) [Feb-Sep 2021] *Against death:* **98.2%** (95% CI, 95.9-99.2) [2-9 weeks] **90.4%** (95% CI, 85.1-93.8) [≥20 weeks]	No available data	**3%** (95% CI, -38 – 39; England) [Feb-Sep 2021] Two doses: **86%** (95% CI, 53-96) **26%** (95% CI, -39 – 73; England) [Feb-Sep 2021] *Against death:* **94.1%** (95% CI, 91.8-95.8) [2-9 weeks] **78.7%** (95% CI, 52.1-90.4) [≥20 weeks]	**67%** effective at preventing hospitalizations *Against death:* 96% effective at preventing death				
Gamma	No available data	No available data	No available data	**72.9%** (95% CI, 35.1-91.1) *Against ICU admission:* **92.5%** (95% CI, 54.9-99.6) *Against death:* **90.5%** (95% CI, 31.5-99.6)	No available data	*Against hospitalization:* **95%** (95% CI, 86.9-98.1) *Against death:* **94.9%** (95% CI, 76.4-98.9)	No available data	No available data
Delta	*Single dose:* **94%** (95% CI, 46-99) **91%** (95% CI, 90-93)	*Single dose:* **81%** (95% CI, 81-90.6) *Two doses:*	*Single dose*: **71%** (95% CI, 51-83) **88%** (95% CI, 83-91)	**71%** **85%** (95% CI, 73-91)	*Single dose:* Does not offer clinically meaningful	*Single dose:* Does not offer clinically meaningful	No available data	No available data

	4% (95% CI, -21 – 44; England) [Feb-Sep 2021] *Two doses*: **96%** (95% CI, 86-99) **88%** (95% CI, 78.9-93.2) **75%** (95% CI, 24-93.9) **84%** (95% CI, 79-89) **98.4%** (95% CI, 97.9-98.8) [2-9 weeks] **92.7%** (95% CI, 90.3-94.6) [≥20 weeks] **96%** (95% CI, 95-96) **80%** (95% CI, 73-85) [June-August] **93%** (95% CI, 84-96) **96.8%** (95% CI, 93.9-98.3)[2 months after the second dose]	**84%** (95% CI, 80-87) **95%** (95% CI, 92-97) [Jun-Aug 2021] **96.7%** (95% CI, 93.9-98.2) **97.3%** (95% CI, 95.9-98.4; New York) [Aug 2021] *Individuals ≥65:* **93.7%** (95% CI, 92.9-94.4; New York) [Aug 2021] *Against ICU admission:* **86%** (95% CI, 79-90) **96%** against severe COVID-19 infection Estimated risk of SARS-CoV-2 infection is **4.52 events per 1000**	**2%** (95% CI, -19 – 31; England) [Feb-Sep 2021] *Two doses*: **92%** (95% CI, 75-97) **95.2%** (95% CI, 94.6-95.6) [2-9 weeks] **77.0%** (95% CI, 70.3-82.3) [≥20 weeks] **94%** (95% CI, 92-95) **14%** (95% CI, -5 – 46; England) [Feb-Sep 2021] **63.1%** (95% CI, 51.5-72.1; India) (Apr – May 2021) *Against moderate to severe disease:* **81.5%** (95% CI, 9.9-99.0; India) (Apr – May 2021) *Against ICU admission:*	**91%** (95% CI, 88-94) **93.5%** (95% CI, 89.6-96.1; New York) [Aug 2021] **85%** effective at preventing severe disease and hospitalization *Individuals ≥50:* **84% (**95% CI, 81-85) *Individuals ≥65:* **81.8%** (95% CI, 77.8-85.3; New York) [Aug 2021] *Against ICU admission:* **94%** (95% CI, 88-98)	protection against severe illness[lxxix] *Two doses:* **88%** (95% CI, 55-98) adjusted risk reduction in developing severe illness[lxxx]	protection against severe illness[lxxxi] *Two doses:* **88%** (95% CI, 55-98) adjusted risk reduction in developing severe illness[lxxxii]		

[lxxix] Study does not differentiate between the two inactivated vaccines, BBIBP-CorV and CoronaVac.

[lxxx] Study does not differentiate between the two inactivated vaccines, BBIBP-CorV and CoronaVac.

[lxxxi] Study does not differentiate between the two inactivated vaccines, BBIBP-CorV and CoronaVac.

[lxxxii] Study does not differentiate between the two inactivated vaccines, BBIBP-CorV and CoronaVac.

	93% (95% CI, 84-96) **91.5%** (95% CI, 89.5-93.2) **24%** (95% CI, -2 – 64; England) [Feb-Sep 2021] **95.2%** (95% CI, 93.6-96.5; New York) [Aug 2021] *Individuals ≥65:* **88.6%** (95% CI, 87.4-89.6; New York) [Aug 2021] *Against death:* **90%** (95% CI, 83-94) [≥2 weeks after second dose] *All ages:* **90%** (95% CI, 83-94) *40-59*: **95%** (95% CI, 79-99) *60+:* **87%** (95% CI, 77-93) Estimated risk of SARS-CoV-2 infection is **5.75 events per 1000** persons (95% CI, 5.39-6.23)[32]	persons (95% CI, 4.17-4.84)	*Single dose:* **92%** (95% CI, 84-96) *Two doses*: **96%** (95% CI, 94-98) *Against death:* **91%** (95% CI, 86-94) [≥2 weeks after second dose] *All ages:* **91%** (95% CI, 86-94) *40-59*: **88%** (95% CI, 76-93) *60+:* **90%** (95% CI, 84-94)						

	VE against ED admission waned from **80%** (95% CI, 69.0-87.0) at <3 months to **63%** (95% CI, 57.0-69.0) at ≥6 months after two doses. [United States, 01 Dec 2021 to 11 Jan 2022] [33] VE against hospital admission waned from **88%** (95% CI, 71.0−95.0) at <3 months to **74%** (95% CI, 65.0−80.0) at ≥6 months after two doses.[United States, 01 Dec 2021 to 11 Jan 2022] [33]							
Omicron	Estimated VE against hospitalization **4 to 5-fold increased** compared to Delta[34*]	Estimated VE against hospitalization **4 to 5-fold increased** compared to Delta[34*]	Length hospital stay was significantly shorter than for Delta (**confounding-adjusted difference -4.0**					

	84.9% (95% CI, 83.0-86.6) against Omicron variant for recently vaccinated Pfizer[34] *No differention between mRNA vaccines VE against hospitalization was 70% (95% CI, 62.0-76.0; South Africa)[November 2021 to December 2021]35 VE against ED admission waned from **60%** (95% CI, 43.0−72.0) at <3 months to **41%** (95% CI, 32.0−50.0) at ≥6 months after two doses.[United States, 01 Dec 2021 to 11 Jan 2022] [33]	*No differention between mRNA vaccines Length hospital stay was significantly shorter than for Delta (**confounding-adjusted difference -4.0 days** (95%CI -7.2 to -0.8).[Portugal, 01 December 2021 to 29 December 2021][36lxxxv] Odds of death were **0.14** (95% CI, 0.0011-1.12), representing a reduction in the risk of death of 86% when infected with Omicron (BA.1) compared with Delta (B.1.617.2). [Portugal, 01	**days** (95%CI -7.2 to -0.8).[Portugal, 01 December 2021 to 29 December 2021][36lxxxvii] Odds of death were **0.14** (95% CI, 0.0011-1.12), representing a reduction in the risk of death of 86% when infected with Omicron (BA.1) compared with Delta (B.1.617.2). [Portugal, 01 December 2021 to 29 December 2021][36lxxxviii]						

[lxxxv] Study does not differentiate between ChAdOx1, BNT162b2, or mRNA-1273.

[lxxxvii] Study does not differentiate between ChAdOx1, BNT162b2, or mRNA-1273.

[lxxxviii] Study does not differentiate between ChAdOx1, BNT162b2, or mRNA-1273.

	VE against hospital admission was **68%** (95% CI, 58.0−75.0) after two doses with no waning of effectiveness observed.[United States, 01 Dec 2021 to 11 Jan 2022] [33] Length hospital stay was significantly shorter than for Delta (**confounding-adjusted difference -4.0 days** (95%CI -7.2 to -0.8).[Portugal, 01 December 2021 to 29 December 2021] [36lxxxiii] Odds of death were **0.14** (95% CI, 0.0011-1.12), representing a	December 2021 to 29 December 2021][36lxxxvi]							

[lxxxiii] Study does not differentiate between ChAdOx1, BNT162b2, or mRNA-1273.
[lxxxvi] Study does not differentiate between ChAdOx1, BNT162b2, or mRNA-1273.

	reduction in the risk of death of 86% when infected with Omicron (BA.1) compared with Delta (B.1.617.2). [Portugal, 01 December 2021 to 29 December 2021][36lxxxiv]							
	DURATION OF PROTECTION, TRANSMISSION & BREAKTHROUGH INFECTIONS							
	BNT162b2/ COMIRNATY	**Spikevax/ Moderna COVID-19 Vaccine/ mRNA-1273**	**Vaxzevria/ ChAdOx1 nCoV-19/ AZD1222/ Covishield**	**Janssen COVID-19 vaccine/Johnson & Johnson**	**Covilo/ BBIBP-CorV**	**CoronaVac**	**COVAXIN / BBV152**	**Novavax/ NVX-CoV2373**
Duration of protection (antibodies)	Median time between second dose and infection: **146 days (IQR, 121-167)** *Anti-SARS-CoV-2 Antibodies:* 1 month after 2nd dose: **1762 KU/L (IQR: 933-3761)**	*Preliminary phase I results:* Antibody activity remained high in all age groups at **day 209** (approximately 6 months) GMT were lower in ≥56 years old	*Antibody Response:* After single dose, antibody response declined within one year, but remained above baseline levels. Antibody levels after **day 180**: 0.54 GMR (CI, 0.47-0.61).	*Neutralizing antibodies:* Remained largely stable for **8-9 months** Remained **stable for 8 months**; At 4 weespoks after immunization NAb titre was **146**,	*Antibody Response:* **Unexposed subjects:** After 1st dose: **43.6 IU/mL** (95% CI, 30.3-62.8) After 2nd dose: **377.0 IU/mL** (95% CI: 324.3-438.3) 3 months after 2nd dose: **125.4 IU/mL**	A phase I/II clinical trial found that NAbs titres dropped below the seropositive cut-off of 8, **6 months** after the administration of the first dose **80-90%** of anti-S IgG and Nab titers against wild type	Median anti-S IgG was **342.7 AU/mL** (IQ: 76.1-892.8) which was found to be significantly lower than the Covidshield-induced antibody concentration of **1,299.5 AU/mL** (IQ: 517.9-5,019.07). [India;	No available data

[lxxxiv] Study does not differentiate between ChAdOx1, BNT162b2, or mRNA-1273.

	3 months after 2nd dose: **1086 KU/L (IQR: 629-2155)** 6 months after 2nd dose: **802 KU/L (IQR, 447-1487)** No health worker had antibodies BELOW method-dependent cut-off (0.8 KU/L) *Anti-S antibody titre* 694.6 AU/mL after 8.4 months [37] *Neutralizing antibodies:* At peak immunity, NAb titre was **1,789**, after 8 months titre was **53** *Pseudovirus neutralizing antibodies:* At peak immunity, pseudovirus NAb titre was **700**, after	*Anti-S antibody titre* 1500.8 AU/mL after 8.4 months[37] *Neutralizing antibodies:* At peak immunity, NAb titre was **5,848**, after 8 months titre was **133** VLP neutralization titers were **reduced 2.7-fold** to Delta and **reduced 15.4-fold** to Omicron.[40xc] *Pseudovirus neutralizing antibodies:* At peak immunity, pseudovirus NAb titre was **1,569**, after 8 months titre was **273** *Anti-spike Protein RBD IgG Antibodies:*	Antibody levels after **day 320**: 0.30 GMR (CI, 0.24-0.39) *Cellular Immune Response:* **Day 182** after first dose: median of **237 SFUx10^6 PBMC (IQR, 109-520)** **6 months** after second dose: **(median 1240, IQR 432-2002**) in groups with 15-25 week interval between doses *Anti-spike Protein RBD IgG Antibodies:* **Younger age groups (<60):** 1 month after 2nd dose: 100% seropositivity, **17.1** (IQR, 9.9-23.6)	after 8 months titre was **629** VLP neutralization titers were **reduced 2.7-fold** to Delta and **reduced 15.4-fold** to Omicron.[40xci] *Pseudovirus neutralizing antibodies:* Remained **stable for 8 months**; At 4 weeks after immunization pseudovirus NAb titre was **391**, after 8 months titre was **185** *Binding antibodies:* Remained stable **6 months** irrespective of age group *Humoral & Cellular Immune Response:*	(95% CI: 88.2-178.4) **Exposed subjects:** Before 1st dose: **203.2 UI/mL** (95% CI: 42.9-962.4) After 1st dose: **761.7 UI/mL** (95% CI: 381.1-1522) After 2nd dose: **719.9 UI/mL** (95% CI : 264.6-1959) 3 months after 2nd dose: **484.4 IU/mL** (95% CI: 147.3-1593) *Anti-RBD IgG*: Decreased up to **41.8%** 2 months after second dose and dropped to **42.9%** decrease after 7 months *Binding Antibodies:* Decreased **82.1%** 7 months after second dose	waned **6 months** after second vaccination *Anti-spike Protein RBD IgG Antibodies:* **Younger age groups (<60):** 1 month after 2nd dose: 97% seropositivity, **11.3** (IQR, 6.2-20.7) 3 months after 2nd dose: 76% seropositivity, **2.4** (IQR, 1.0-5.0) **Older age groups (≥60)**: 1 month after 2nd dose: 88% seropositivity, **6.4** (IQR, 2.5-13.6) 3 months after 2nd dose: 60% seropositivity, **1.3** (IQR, 0.5-3.3) *Neutralizing Antibody:*	January to July 2021]	

[xc] Study does not differentiate between BNT162b2, mRNA-1273, or Ad26.COV2.S
[xci] Study does not differentiate between BNT162b2, mRNA-1273, or Ad26.COV2.S

	8 months titre was **160** *Anti-spike Protein RBD IgG Antibodies:* At peak immunity, RBD titre was **21,564**, after 8 months titre was **755** **Younger age groups (<60):** 1 month after 2nd dose: 100% seropositivity, **35.3** (IQR, 27.6-40.0) 3 months after 2nd dose: 100% seropositivity, **19.2** (IQR, 8.2-23.1) **Older age groups (≥60)**: 1 month after 2nd dose: 100% seropositivity, **29.4** (IQR, 22.5-33.3) 3 months after 2nd dose: 100% seropositivity, **14.8** (IQR, 7.4-18.7) *Sub-populations:* **Older age (≥65):**	At peak immunity, RBD titre was **25,677**, after 8 months titre was **1,546** *Humoral & Cellular Immune Response:* CD8+ T cell response was **0.017%** 8 months after full vaccination	3 months after 2nd dose: 97% seropositivity, **6.5** (IQR, 3.5-9.3) **Older age groups (≥60)**: 1 month after 2nd dose: 96% seropositivity, **13.3** (IQR, 6.9-27.7) 3 months after 2nd dose: 90% seropositivity, **3.9** (IQR, 1.9-8.4) Median anti-S IgG was **1,299.5 AU/mL (IQ: 517.9-5,019.07)** which is approximately **4-fold higher than the Covaxin**-induced antibody concentration of 342.7 AU/mL (IQ: 76.1-892.8). [India; January to July 2021]	Antibody responses were detected in all vaccine recipients on **day 239** (stable response for at least 8 months) CD8+ T cell response was **0.12%** 8 months after vaccination *Anti-spike Protein RBD IgG Antibodies:* Remained **stable for 8 months**; At 4 weeks after immunization titre was **1,361**, after 8 months titre was **843**		Decay from **95.08%** 42 days after 2nd dose to **19.7%**160 days after 2nd dose *Anti-RBD Antibody:* Decay from **100%** 42 days after 2nd dose to **54.10%** 160 days after 2nd dose *Anti-spike IgG:* Decay from **100.0%** 42 days after 2nd dose to **50.82%** 160 days after 2nd dose *Anti-spike IgM:* Decay from **59.02%** 42 days after 2nd dose to **3.28%** 160 days after 2nd dose *Anti-spike IgA:* Decay **31.15%** 42 days after 2nd dose to **0.00%** 160 days after 2nd dose		

	38% to **42%** decrease of humoral antibodies compared to 18- to 45-year-old **Older age (≥65) AND men:** **37%** to **46%** decrease compared to 18- to 45-year-old women **Immunosuppression:** **65% to 70%** decrease compared to non-immunosuppressed **Obesity (BMI ≥30):** **31%** increase in neutralizing antibody compared with nonobese While the mean values of anti-RBD-IgG showed a marked decline at 6 months, high					Of 329 participants, 18.5% (61 of 329) results were positive with a 64.47 BAU/mL anti –RDB IgG median quantitative titer (IQR 42.87-125.5) obtained. The negative group comprised of 80% of the group (268 of 329) with a 8.55 anti –RDB IgG median quantitative titer (IQR 5.5-13.92) and the maximum titer was 29.92 BAU/mL (p <0.001).[Brazil]		

	neutralizing bioactivity was maintained at least 6 months after vaccination in almost all study participants (N=57 HCWs) *<u>Humoral & Cellular Immune Response:</u>* CD8+ T cell response was **0.016%** 8 months after full vaccination Decline in Serum Nucleocapsid and RBD Abs from 632.5 U/mL (IQR: 170-1848 U/mL) at 5-weeks post vaccination to 133 U/mL (IQR: 54-337 U/mL) at 6-months post vaccination.[38] IgG levels steadily decreased over the 6-month period in the total tested population and in all age								

	groups. An inverse relationship was found between IgG titer and subsequent PCR-positive infection. Persons vaccinated during the first 2 months of the campaign were more likely to become infected than those subsequently vaccinated.[Israel] [39] VLP neutralization titers were **reduced 2.7-fold** to Delta and **reduced 15.4-fold** to Omicron.[40lxxxix]							
Duration of protection (vaccine effectiveness)	*Against any SARS-CoV-2 Infection:* After reaching peak VE (77.5%) 1 month after 2nd dose, VE dropped to **20%** in **months 5-7** after 2nd dose	**36.4** (95% CI, 17.1-51.5) reduction of observed incidence rate (SARS-CoV-2 infection) if vaccinated from Dec 2020 – Apr 2021 than Jul 2021 – Dec 2020.	VE reduced by 7% (95% CI, -18 - 2) for every 30 days from the second dose for those aged 18 to 64 years[47]. VE reduced from **58%** (95% CI, 51-65) to **27%** (95%	A study observed sustained and stable vaccine effectiveness starting 14 days post vaccination to a maximum of **152** days after vaccination.	No available data	*Against COVID-19 infections:* VE waned from **74.4%** (95% CI 209 70.4, 77.8) to **30.0%** (95% CI 18.4, 39.9) [Malaysia][42] *Against ICU admissions:*	No available data	No available data

[lxxxix] Study does not differentiate between BNT162b2, mRNA-1273, or Ad26.COV2.S

	VE reduced from **87%** (95% CI, 85-89) to **56%** (95% CI, 53-59) after 4 months VE reduced from **91%** (95% CI, 91-92) in March to **50%** (95% CI, 47-52) in August VE reduced from **89.0%** (95% CI, 84.6-92.1; United States) [May to August] to **62.7%** (95% CI, 62.4-63.1; United States) [May to August][xcii] VE decreased by **18.5% points** (95% CI 8.4-33.4) among all ages and **19.9% points** among older individuals (95% CI; 9.2-36.7) [Overall average from Systematic	**46.0** (95% CI, -52.4-83.2) reduction of observed incidence rate (**severe** SARS-CoV-2 infection) if vaccinated from Dec 2020 – Apr 2021 than Jul 2021 – Dec 2020. VE against the Delta variant declined from **94.1%** (95% CI, 90.5-96.3) 14-60 days after vaccination to **80.0%** (95% CI, 70.2-86.6) 151-180 days after vaccination. **91%** [January-March] **71%** (95% CI, 53-83) [April-May] **63%** (95% CI, 44-76)	CI, 17-37) after 4 months. VE reduced from **88%** (95% CI, 87-89) in March to **3%** (95% CI, -7-12) in August VE decreased by **18.5% points** (95% CI 8.4-33.4) among all ages and **19.9% points** among older individuals (95% CI; 9.2-36.7) [Overall average from Systematic Review and Meta-Regression][cxii] VE reduced from **96.9%** (range, 93.7-98.0) for the week of 1 May 2021 to **77.8%** (range, 70.1-86.8) by the week of August 28 2021 Estimated results show that vaccine	VE decreased from **89.4%** in May to **51.7%** in July VE decreased from **86.4%** (95% CI, 85.2-87.6) in March 2021 to **13.1%** (95% CI, 9.2-16.8) in September 2021 VE decreased by **18.5% points** (95% CI 8.4-33.4) among all ages and **19.9% points** among older individuals (95% CI; 9.2-36.7) [Overall average from Systematic Review and Meta-Regression][cxviii] VE reduced from **86.6%** (range, 77.8-89.7) for the week of 1 May 2021 to **69.4%** (range, 63.4-77.3)		VE declined from **56.1%** (95% CI 51.4, 60.2) to **29.9%** (95% CI 13.9, 43.0) [Malaysia][42] *Against deaths:* Did not wane after three to five months of full vaccination. [Malaysia][42]		

[xcii] Study does not differentiate between the two mRNA vaccines, Pfizer and Moderna.
[cxii] Study does not differentiate between Pfizer/BioNTech-Comirnaty, Moderna-mRNA-1273, Janssen-Ad26.COV2.S and AstraZeneca-Vaxrevria.
[cxviii] Study does not differentiate between Pfizer/BioNTech-Comirnaty, Moderna-mRNA-1273, Janssen-Ad26.COV2.S and AstraZeneca-Vaxrevria.

	Review and Meta-Regression][xciii] VE reduced from **91.3%** (range, 84.1-97) for the week of 1 May 2021 to **72.3%** (range, 63.7-77.5) by the week of August 28 2021. **VE decreased to 66.3% (95% CI, 65.7-66.9)** by 20 weeks after the second dose. Protection **against hospitalization decreased less with a VE of 91.7% (95% CI 90.2-93.0)** and a **VE against death of 91.9% (95% CI, 88.5-94.3)** [England] VE was **94.5% (95% CI, 94.1 to 94.9)** 2 months after the first dose	VE reduced from **90%** (95% CI, 88-91) to **71%** (95% CI, 68-74) after 4 months[44] VE reduced from **91%** (95% CI, 72-98) in January-March to **71%** (95% CI, 53-83) in April-May to **63%** (95% CI, 44-76) in June-August VE reduced from **92%** (95% CI, 92-93) in March to **64%** (95% CI, 62-66) in August VE against infection was **82%** (95% CI, 79-85) 14-90 days after the second dose and appeared to **wane over time** and was **63%** (95% CI, 55-68) 91-180 days after the second dose	effectiveness significantly wanes from 60 days after the second dose [Japan; February 2020 to December 2021] [cxiii] VE of first dose 68% (95% CI 67.0.% - 69.%; Canada) and 88% (95% CI 87.0% - 88.0%; Canada) [December 2020 to October 2021] Risk of infection decreased 4-6 months after the second vaccine dose, but markedly increased after.[cxiv] VE decreased to 44.3% (95% CI, 43.2-45.4) by 20 weeks after the second dose. Protection against hospitalization	by the week of August 28 2021. VE was 74.8% (95% CI, 72.5-76.9) at 1 months and decreased to 59.4% (95% CI, 57.2-61.5) at 5 months. [United States; December 2020 to September 2021] Waning protection against infections started in month 4 for Ad26.COV2.S (OR [95% CI] in month 5+, 1.31 [1.18, 1.47]). No waning of protection was observed at any time for ICU admissions. [United States, January 2021 to September 2021] There was no evidence of				

[xciii] Study does not differentiate between Pfizer/BioNTech-Comirnaty, Moderna-mRNA-1273, Janssen-Ad26.COV2.S and AstraZeneca-Vaxrevria.

[cxiii] Study does not differentiate between Pfizer Moderna, and AstraZeneca.

[cxiv] Study does not differentiate between BNT162b2, mRNA-1273, and ChAdOX-S.

	and **decreased to 66.6% (95% CI 65.2-67.8)** at 7 months. [United States; December 2020 to September 2021] Waning protection against infections started in month 2 for BNT162b2 (OR [95% CI] in month 6+, 2.93 [2.72, 3.15]). No waning of protection was observed at any time for ICU admissions. [United States, January 2021 to September 2021] Estimated results show that vaccine effectiveness significantly wanes from 60 days after the second dose [Japan; February 2020 to December 2021] [xciv]	[27 Dec 2020 – 26 Oct 2021; Finland][cii] VE decreased from **89.2%** (95% CI, 88.8-89.6) in March 2021 to **58.0%** (95% CI, 56.9-59.1) in September 2021[45] VE reduced from **89.0%** (95% CI, 84.6-92.1; United States) [May to August] to **62.7%** (95% CI, 62.4-63.1; United States) [May to August][ciii] VE decreased by **18.5% points** (95% CI 8.4-33.4) among all ages and **19.9% points** among older individuals (95% CI; 9.2-36.7) [Overall average	decreased less with a VE of 80.0% (95% CI 76.8-82.7) and a VE against death of 84.8% (95% CI, 76.2-90.3) [England] *Against symptomatic COVID-19:* VE decreased by **25.4%** (95% CI, 13.7-42.5) among all ages and **32.0%** (95% CI, 11.0-69.0) among older individuals [Overall average from Systematic Review and Meta-Regression][cxv] **50%** (95% CI, 16-69)14-73 days after second dose. Effectiveness did not fall significantly after longer intervals,	waning protection against hospitalization for Ad26.COV2.S (OR [95% CI], 1.25 [0.86, 1.80] in month 5+) [United States, January 2021 to September 2021] Adjusted estimated VE of 1 dose remained greater than **50%** after 2 weeks. [United States; 01 May 2021 to 07 August 2021)[41] VE was lower compared with mRNA vaccines, with no trend observed over time (95% CI, 80.0-90.6%).[United States][15]				

[xciv] Study does not differentiate between Pfizer Moderna, and AstraZeneca.
[cii] Study does not differentiate between COMIRNATY/BNT162b2 and SPIKEVAX/ mRNA-1273.
[ciii] Study does not differentiate between the two mRNA vaccines, Pfizer and Moderna.
[cxv] Study does not differentiate between Pfizer/BioNTech-Comirnaty, Moderna-mRNA-1273, Janssen-Ad26.COV2.S and AstraZeneca-Vaxrevria.

	VE of first dose 68% (95% CI 67.0.% - 69.%; Canada) and 88% (95% CI 87.0% - 88.0%; Canada) [December 2020 to October 2021] Risk of infection decreased 4-6 months after the second vaccine dose, but markedly increased after.[xcv] Adjusted estimated VE against infections **peaked** after 2 weeks **at 92.4%** [95% CI, 91.7%-93.1%] for BNT162b2), then gradually **fell to 78.6%** (95% CI, 78.0%-79.2%) at 2 to 3 months and **66%** (95% CI,	from Systematic Review and Meta-Regression][civ] VE reduced from **96.9%** (range, 93.7-98.0) for the week of 1 May 2021 to **77.8%** (range, 70.1-86.8) by the week of August 28 2021. VE was 95.9% (95% CI, 95.5-96.2) 2 months after the first dose decreased to 80.3% (95% CI 79.3-81.2) at 7 months. [United States; December 2020 to September 2021] Waning protection against infections started in month 2 for mRNA-1273 (OR [95% CI] in month 6+, 2.76	however this could be influenced by the study's small number of participants *Against severe COVID-19:* VE decreased by **8.0%** (95% CI, 3.6-15.20) among all ages and **9.7%** (95% CI; 5.9-14.7) among older individuals [Overall average from Systematic Review and Meta-Regression][cxvi] VE against severe outcomes (hospitalization and death) decreased from 83.7% (95% CI, 79.7-87.0) at 2-3 weeks to **63·7%** (59·6–67·4) at 18–19 weeks after the	*Against symptomatic COVID-19:* VE decreased by **25.4%** (95% CI, 13.7-42.5) among all ages and **32.0%** (95% CI, 11.0-69.0) among older individuals [Overall average from Systematic Review and Meta-Regression][cxix] *Against severe COVID-19:* VE decreased by **8.0%** (95% CI, 3.6-15.20) among all ages and **9.7%** (95% CI; 5.9-14.7) among older individuals [Overall average from Systematic Review and Meta-Regression][cxx]				

[xcv] Study does not differentiate between BNT162b2, mRNA-1273, and ChAdOX-S.
[civ] Study does not differentiate between Pfizer/BioNTech-Comirnaty, Moderna-mRNA-1273, Janssen-Ad26.COV2.S and AstraZeneca-Vaxrevria.
[cxvi] Study does not differentiate between Pfizer/BioNTech-Comirnaty, Moderna-mRNA-1273, Janssen-Ad26.COV2.S and AstraZeneca-Vaxrevria.
[cxix] Study does not differentiate between Pfizer/BioNTech-Comirnaty, Moderna-mRNA-1273, Janssen-Ad26.COV2.S and AstraZeneca-Vaxrevria.
[cxx] Study does not differentiate between Pfizer/BioNTech-Comirnaty, Moderna-mRNA-1273, Janssen-Ad26.COV2.S and AstraZeneca-Vaxrevria.

	64.2%-68.0%) **6 months after the second dose**. [United States; 01 May 2021 to 07 August 2021][41] VE against COVID-19 infections **declined from 90.8%** (95% CI 89.4, 92.0) to **79.1%** (95% CI 75.8, 81.9) in the early group (fully vaccinated in April to June 2021). VE against ICU admission and deaths were comparable. [Malaysia][42] Among patients aged 16 to 64, VE within one to three months after full vaccination was **91.8%** (95% CI, 80.3 to 96.6), and was **86.4%** (95% CI, 56.9 to 95.7) within four to six	[2.51, 3.04]). No waning of protection was observed at any time for ICU admissions. [United States, January 2021 to September 2021] Evidence of waning protection against hospitalization started in month 3 for mRNA-1273 (OR 95% CI, 1.66 [1.26, 2.19] in month 6+) [United States, January 2021 to September 2021] Estimated results show that vaccine effectiveness significantly wanes from 60 days after the second dose [Japan; February 2020 to December 2021][cv] VE of first dose 68% (95% CI	second dose in Scotland. In Brazil, VE decreased from 86·4% (85·4–87·3) at 2-3 weeks, to **42·2%** (32·4–50·6) at 18–19 weeks.[Brazil and Scotland][48] Against variants: Among individuals who received 2 doses of vaccines (with at least 1mRNA vaccine) VE against Delta declined steadily over time from 84% (95%CI, 81-86%) 7-59 days after the second dose to 71% (95%CI, 66-75%) ≥240 days after the second dose, but recovered to 93% (95%CI, 92-94%) ≥7 days after receiving an mRNA vaccine for the third dose.[Canada;	VE after 8.4 months was estimated at **33%** (95% CI, 0-86)[37]				

[cv] Study does not differentiate between Pfizer Moderna, and AstraZeneca.

	months[Japan, 01 July to 30 September 2021][12xcvi] VE declined from **82% (95% CI, 79.0-85.0)** 14 to 90 days after vaccination to **53% (95% CI, 43.0-62.0)** after 6 months.[Finland; December 2020 to October 2021][43xcvii] *<u>Against symptomatic COVID-19:</u>* VE decreased by **25.4%** (95% CI, 13.7-42.5) among all ages and **32.0%** (95% CI, 11.0-69.0) among older individuals [Overall average from Systematic	67.0.% - 69.%; Canada) and 88% (95% CI 87.0% - 88.0%; Canada) [December 2020 to October 2021] Risk of infection decreased 4-6 months after the second vaccine dose, but markedly increased after. [cvi] Adjusted estimated VE against infections peaked after 2 weeks at **96.3%** (95% CI, 95.6%-96.9%) then gradually **fell to 86.8%** (95% CI, 86.2%-87.4%) at 2 to 3 months and **74.2%** (95% CI, 71.6%-76.6%) **6 months after the second dose**. [United States; 01	November 2021 to December 2021]cxvii					

[xcvi] Study does not differentiate between BNT162b2 or mRNA-1273.
[xcvii] Study does not differential between mRNA-based vaccines.
[cvi] Study does not differentiate between BNT162b2, mRNA-1273, and ChAdOX-S.
[cxvii] Study does not differentiate between Pfizer, Moderna, or AstraZeneca.

	Review and Meta-Regression[xcviii] VE reduced by 22% (95% CI, 6-41) for every 30 days from the second dose for those aged 18 to 64 years. VE against infection was **82%** (95% CI, 79-85) 14-90 days after the second dose and appeared to **wane over time** and was **63%** (95% CI, 55-68) 91-180 days after the second dose [27 Dec 2020 – 26 Oct 2021; Finland][xcix] VE decreased from **86.9%** (95% CI, 86.5-87.3) in March 2021 to **43.3%** (95% CI, | May 2021 to 07 August 2021) [41] Among patients aged 16 to 64, VE within one to three months after full vaccination was **91.8%** (95% CI, 80.3 to 96.6), and was **86.4%** (95% CI, 56.9 to 95.7) within four to six months[Japan, 01 July to 30 September 2021][12cvii] VE declined from **82% (95% CI, 79.0-85.0)** 14 to 90 days after vaccination to **53% (95% CI, 43.0-62.0)** after 6 months.[Finland; December 2020 to October 2021][43cviii] VE against infection peaked at 90% months							

[xcviii] Study does not differentiate between Pfizer/BioNTech-Comirnaty, Moderna-mRNA-1273, Janssen-Ad26.COV2.S and AstraZeneca-Vaxrevria.
[xcix] Study does not differentiate between COMIRNATY/BNT162b2 and SPIKEVAX/ mRNA-1273.
[cvii] Study does not differentiate between BNT162b2 or mRNA-1273.
[cviii] Study does not differential between mRNA-based vaccines.

	41.9-44.6) in September 2021 VE declined from **81%** (95% CI, 68-89) 14-73 days after second dose. 4-6 months after second dose, VE remained at **70%** (95% CI, 62-76) and declined to **46%** (95% CI, 22-63) after six months. [second dose was administered ≥6 weeks after first dose]. VE declined from **86%** (95% CI, 73-93) 14-73 days after second dose. 6 months after second dose, VE declined to **61%** (95% CI, 45-73). [second dose was administered ≤6 weeks after first dose]	after the second dose and was **less than 50%** by the seventh month after the second dose.[Qatar; 01 January 2021 to 05 December 2021][46] *Against symptomatic COVID-19:* VE decreased by **25.4%** (95% CI, 13.7-42.5) among all ages and **32.0%** (95% CI, 11.0-69.0) among older individuals [Overall average from Systematic Review and Meta-Regression)[cix] *Against severe COVID-19 disease:* VE decreased by **8.0%** (95% CI, 3.6-15.20) among all ages and **9.7%** (95% CI; 5.9-14.7) among older						

[cix] Study does not differentiate between Pfizer/BioNTech-Comirnaty, Moderna-mRNA-1273, Janssen-Ad26.COV2.S and AstraZeneca-Vaxrevria.

	Against severe COVID-19: VE decreased by **8.0%** (95% CI, 3.6-15.20) among all ages and **9.7%** (95% CI; 5.9-14.7) among older individuals [Overall average from Systematic Review and Meta-Regression][c] *Against Hospitalization and Death:* After reaching peak VE (96.8%) 2 months after 2nd dose, **VE did not decline over time**, except for 7th months (VE 55.6%) with very few cases Evidence of waning protection against hospitalization started in month 2 for BNT162b2 (OR [95% CI], 3.97	individuals [Overall average from Systematic Review and Meta-Regression][cx] *Against hospitalization* VE among **18-64 years of age** remained approximately **greater than 86%** with no obvious time trend regardless of vaccine and **declined** from May through August among **persons 65 years of age or older** who were vaccinated with mRNA-1273, from **97.1 to 93.7%**.[United States][15] *Against variants:* Among individuals who received 2 doses of vaccines							

[c] Study does not differentiate between Pfizer/BioNTech-Comirnaty, Moderna-mRNA-1273, Janssen-Ad26.COV2.S and AstraZeneca-Vaxrevria.
[cx] Study does not differentiate between Pfizer/BioNTech-Comirnaty, Moderna-mRNA-1273, Janssen-Ad26.COV2.S and AstraZeneca-Vaxrevria.

	[3.26, 4.83] in month 6+) [United States, January 2021 to September 2021] *Against variants:* Among individuals who received 2 doses of vaccines (with at least 1mRNA vaccine) VE against Delta declined steadily over time from 84% (95%CI, 81-86%) 7-59 days after the second dose to 71% (95%CI, 66-75%) ≥240 days after the second dose, but recovered to 93% (95%CI, 92-94%) ≥7 days after receiving an mRNA vaccine for the third dose.[Canada; November 2021 to December 2021]ci VE against hospitalization	(with at least 1mRNA vaccine) VE against Delta declined steadily over time from 84% (95%CI, 81-86%) 7-59 days after the second dose to 71% (95%CI, 66-75%) ≥240 days after the second dose, but recovered to 93% (95%CI, 92-94%) ≥7 days after receiving an mRNA vaccine for the third dose.[Canada; November 2021 to December 2021] cxi VE after 8.4 months was estimated at **89%** (95% CI, 67-96)[37]							

[ci] Study does not differentiate between Pfizer, Moderna, or AstraZeneca.
[cxi] Study does not differentiate between Pfizer, Moderna, or AstraZeneca.

	among those 18-64 years of age remained approximately greater than 86% with no obvious time trend regardless of vaccine and declined from May through August among persons 65 years of age or older who were vaccinated with BNT162b2, from 94.8 to 88.6%.[United States][15] VE after 8.4 months was estimated at **87%** (95% CI, 60-96)[37]							
Transmission prevention	*Prior Delta Variant:* Vaccine effectiveness against infectiousness given infections **41.3%** VE against transmission **88.5%**	VE against onwards transmission: **52%** (95% CI, 33-69) VE against transmission from vaccinated index case to unvaccinated contact is **63%** (95% CI, 46-75)	**48%** (limited data) May not be able to block the transmission of the alpha variant as efficiently as the wild type. VE against transmission from vaccinated index	VE against transmissibility was **31%** (95% CI, 26-36) when the secondary case was not vaccinated and **10%** (95% CI, 0-18) when secondary case was fully vaccinated	Unknown	Unknown	No available data	No available data

	VE against onwards transmission of Alpha **57% (95% CI, 5-85**) VE against onwards transmission (VET) of Alpha two weeks after full vaccination was **68%** (95% CI, 52-79); at 12 weeks VET was **52%** (95% CI, 29-67) Proportion of the total effect (mediated by Ct values) of two vaccinations on transmission of the Alpha variant was **18%** (95% CI, 9-64) *<u>During Delta Variant:</u>*	and **40%** (95% CI, 20-54) to a vaccinated contact.[cxxii] VE against transmissibility was **31%** (95% CI, 26-36) when the secondary case was not vaccinated and **10%** (95% CI, 0-18) when secondary case was fully vaccinated Estimated SAR to fully vaccinated household contact was **6.2%** (95% CI, 2.8-13.0)	case to unvaccinated contact is **63%** (95% CI, 46-75) and **40%** (95% CI, 20-54) to a vaccinated contact.[cxxiii] Evidence of fully vaccinated individuals infecting other fully vaccinated individuals 81 breakthrough infections among 1100 HCWs; 32 breakthrough infections among 4000 HCWs VE against onwards transmission of Alpha **35% (95% CI, -26 – 74**) Proportion of the total effect (mediated by Ct	Estimated SAR to fully vaccinated household contact was **42.7%** (95% CI, 13.6-77.9)				

[cxxii] Study does not differentiate between Comirnaty/BNT162b2, Spikevax/ mRNA-1273, and Vaxzevria/ ChAdOz1 nCOV-19.
[cxxiii] Study does not differentiate between Comirnaty/BNT162b2, Spikevax/ mRNA-1273, and Vaxzevria/ ChAdOz1 nCOV-19.

	Similar Ct values (<25) were found in both vaccinated and unvaccinated groups VE against onwards transmission (VET) of Delta two weeks after full vaccination was **50%** (95% CI, 35-61); at 12 weeks VET was **24%** (95% CI, 20-28) Proportion of the total effect (mediated by Ct values) of two vaccinations on transmission of the Delta variant was **23%** (95% CI, 17-33) Studies from Scotland and England demonstrated reductions in secondary infections among families of vaccinated		values) of two vaccinations on transmission of the Alpha variant was **16%** (95% CI, 1-80) VE against onwards transmission (VET) of Alpha two weeks after full vaccination was **24%** (95% CI, 18-30); at 12 weeks VET was **2%** (95% CI, -2-6) VE against onwards transmission (VET) of Delta two weeks after full vaccination was **52%** (95% CI, 22-70); at 12 weeks VET was **38%** (95% CI, -1-62) Proportion of the total effect (mediated by Ct values) of two vaccinations on transmission of the Delta variant					

	individuals compared to families of unvaccinated individuals. VE against onwards transmission: **62%** (95% CI, 57-67) VE against transmission from vaccinated index case to unvaccinated contact is **63%** (95% CI, 46-75) and **40%** (95% CI, 20-54) to a vaccinated contact.[cxxi] VE against onwards transmission of Delta **31% (95% CI, -3 – 61**) VE against infection [within a ten-day window] when having a confirmed		was **7%** (95% CI, 5-10) VE against onwards transmission of Delta **42% (95% CI, 14-69**) VE against transmissibility was **31%** (95% CI, 26-36) when the secondary case was not vaccinated and **10%** (95% CI, 0-18) when secondary case was fully vaccinated					

[cxxi] Study does not differentiate between Comirnaty/BNT162b2, Spikevax/ mRNA-1273, and Vaxzevria/ ChAdOz1 nCOV-19.

	household exposure **80.4%** (95% CI, 73.6-85.5) Additional infections occurred in 49.8% (95% CI, 48-51.6) of homogenously unvaccinated household members and 12.5% (95% CI, 9.1-17) of homogenously vaccinated household members [within a ten-day window] VE against transmissibility was **31%** (95% CI, 26-36) when the secondary case was not vaccinated and **10%** (95% CI, 0-18) when secondary case was fully vaccinated Estimated SAR from fully								

	vaccinated index case was **8.3%** (95% CI, 5.6-12.1) and **35.9%** (95% CI, 34.1-37.6) for unvaccinated index cases Estimated SAR to fully vaccinated household contact was **15.8%** (95% CI, 15.0-16.7) VE against susceptibility to infection **80.5%** (95% CI, 78.9-82.1) VE against infectiousness given infection **41.3%** (95% CI, 9.5-73.0) VE against transmission **88.5%** (95% CI, 82.3-94.8)[49] Delta infection: SAR in fully vaccinated household members was **12.5%,** while the SAR in								

	unvaccinated and partially vaccinated individuals was **27.8%** and **25.0%**, respectively[50]							
Transmission prevention: Omicron	Secondary attack rate was **31%** in households infected with the Omicron VOC and **21%** in households with the Delta VOC[51]. Unvaccinated secondary cases demonstrated similar attack rates in households with the Omicron VOC (**29%**) and the Delta VOC (**28%**). Fully vaccinated individuals had a secondary attack rate of **32%** in Omicron infected households and **19%** in Delta infected households[51]. Among individuals who had received a third (booster) shot, secondary attack rate was **25%** for Omicron and **11%** for Delta[51]. The odds ratio (OR) for Omicron infection of unvaccinated persons was **1.04** (95% CI, 0.87-1.24) and **0.54** (95% CI, 0.4-0.71) for boosted individuals[51]. Comparing across variants, unvaccinated individuals in Omicron infected households had an estimated OR of **1.17** (95% CI, 0.99-1.38) compared to Delta infected households. For vaccinated and boosted individuals, the estimated OR was **2.61** (95% CI, 2.34-2.90) and **3.66** (95% CI, 2.65-5.05), respectively[51].							
Breakthrough infections	From 6,161 patients with a positive nasopharyngeal SARS-CoV-2 PCR, 1,120 (18%) were breakthrough infections – 97% of these occurred after 2 May (emergence of	From 6,161 patients with a positive nasopharyngeal SARS-CoV-2 PCR, 1,120 (18%) were breakthrough infections – 97% of these occurred after 2 May	As of 10 June, 1.5 million individuals have been fully vaccinated with Covishield in Odisha Province, India. Between 1 March to 10 June, 239 breakthrough infections (SARS-CoV-2 positive	From 6,161 patients with a positive nasopharyngeal SARS-CoV-2 PCR, 1,120 (18%) were breakthrough infections – 97% of these occurred after 2 May	Of 22 individuals fully vaccinated, 20 were infected. Of 26 individuals who received a single dose, 23 were infected.[Bahrain][58]	Omicron (B.1.1.529) was neutralized less effectively by serum from breakthrough infection patients, with a 6.3-fold reduction	As of 10 June, 380,000 individuals have been fully vaccinated with Covaxin in Odisha Province, India. Between 1 March to 10 June, 35 breakthrough infections (SARS-	No available data

	Delta variant). Of the 1,120 cases, 126 (12%) were hospitalized. Of the 126 breakthrough admissions, 59 were vaccinated with BNT162b2 Individuals vaccinated in January and February had a **51%** (95% CI, 40-68) increased risk for breakthrough infections compared to individuals vaccinated in March and April Breakthrough infections remained under 1% for fully vaccinated individuals (no difference	(emergence of Delta variant). Of the 1,120 cases, 126 (12%) were hospitalized. Of the 126 breakthrough admissions, 36 were vaccinated with mRNA-1273. Breakthrough infections remained under 1% for fully vaccinated individuals (no difference between Pfizer or Moderna recipients between May and August 2021 In a study of 10,412 participants, of which 8,554 were vaccinated, breakthrough | after having received two doses of Covishield) were identified. Of these, 199 (83.3%) were symptomatic, 24 (10.0%) were hospitalized - 59 individuals had comorbidities Median antibody titer: 647.5 AU/ ml Vietnamese study: High viral loads were observed 2-3 days before symptom onset among 49 symptomatic breakthrough cases (out of 62). Their peak viral loads measured at any point in time were higher than that of	(emergence of Delta variant). Of the 1,120 cases, 126 (12%) were hospitalized. Of the 126 breakthrough admissions, 10 were vaccinated with Ad26.COV2.S **4.2%** of fully vaccinated HCWs developed breakthrough infections – all cases were symptomatic but mild, only one case required hospitalization[cxxxiv] Rate of breakthrough infections was comparable to Pfizer and Moderna recipients during	Of 1033 participants, 16 (1.55%) developed PCR positive COVID-19 infection two weeks after the second dose while 3 (0.29%) had re-infection. [Pakistan][59]	compared to delta variants. [57cxxxvii] Of 1401 study participants, 32.9% (461 of 1401) were hospitalized after receiving 2 doses of Sinovac compared with 47.8% (669 of 1401) of unvaccinated hospitalized individuals. [Turkey][60]	CoV-2 positive after having received two doses of Covishield) were identified. Of these, 29 (82.9%) were symptomatic, 3 (8.6%) were hospitalized. 5 individuals had comorbidities Median antibody titer: 213.5 AU/ ml **4.2%** of fully vaccinated HCWs developed breakthrough infections – all cases were symptomatic but mild, only one case required hospitalization [cxxxviii] In a study of 614 of HCW, 13% (81	

[cxxxiv] Study does not differentiate between Covishield (*n*=62.4%) and Covaxin (*n*=37%).

[cxxxvii] Study does not differentiate between inactivated vaccinates, CoronaVac or AZD1222.

[cxxxviii] Study does not differentiate between Covishield (*n*=62.4%) and Covaxin (*n*=37%).

	between Pfizer or Moderna recipients between May and August 2021 In a study of 10,412 participants, of which 8,554 were vaccinated, breakthrough infections were reported by 74 (1.0%) among fully vaccinated individuals and 198 (2.3%) among partially vaccinated. [United States; December 2020 to September 2021][cxxiv] In a case series of 20 HCWs, 90% (18 of 20) had confirmed infection after the	infections were reported by 74 (1.0%) among fully vaccinated individuals and 198 (2.3%) among partially vaccinated. [United States; December 2020 to September 2021][cxxviii] From 126,586 vaccine recipients, 492 (0.39%) were found to have breakthrough infections during the 10-month observational period. 97.2% of the identified breakthrough cases (478 of 492) were asymptomatic or mild and 2.8% (14 of 492) required hospitalization.	asymptomatic cases (IQR: 16.5 log10/mL vs 30.8 log10/mL, respectively). NAbs were measured for 10 breakthrough cases, all 10 cases had lower NAbs at day 14 and 90 post second vaccination compared to controls From 126,586 vaccine recipients, 492 (0.39%) were found to have breakthrough infections during the 10-month observational period. 97.2% of the identified breakthrough cases (478 of 492) were	the initial stages of the study, but increased to 1.96% (2 times the breakthrough rate of mRNA vaccines) In a study of 10,412 participants, of which 8,554 were vaccinated, breakthrough infections were reported by 74 (1.0%) among fully vaccinated individuals and 198 (2.3%) among partially vaccinated. [United States; December 2020 to September 2021][cxxxv] From 126,586 vaccine recipients, 492 (0.39%) were			of 614) had breakthrough infections – within breakthrough infections, 63% (51 of 81**)** were Covaxin recipients. [India; January to July 2021] Out of 355 fully vaccinated HCWs, 16 had symptomatic breakthrough infections >14 days after the second dose. No significant difference was observed between Covishield and Covaxin. [India; 16 January 2021 to 31 July 2021] [56]	

[cxxiv] Study does not differentiate between Pfizer, Moderna, or Johnson & Johnson.
[cxxviii] Study does not differentiate between Pfizer, Moderna, or Johnson & Johnson.
[cxxxv] Study does not differentiate between Pfizer, Moderna, or Johnson & Johnson.

	first dose (47.1% within the first week, 41.2% within the second week, and 11.8% within the third week. 2 HCWs (10.0%) had infection one week after the second dose. [Saudi Arabia; December 2020 to March 2021] From 126,586 vaccine recipients, 492 (0.39%) were found to have breakthrough infections during the 10-month observational period. 97.2% of the identified breakthrough cases (478 of 492) were asymptomatic or mild and 2.8% (14 of 492) required	[Switzerland; December 2021 to October 2021][cxxix] Of 23,697 vaccinated HCPs, 0.58% tested positive for COVID (138 of 23,697 cases that received at least one dose of an mRNA vaccine) – 105 of which only received one dose and 33 (0.15% 33 of 22,458 cases who received both vaccine doses) were among those who completed vaccination. Among the 138 postvaccination cases, 64 were vaccinated with Moderna. Among 1,128 cluster-associated cases of COVID,	asymptomatic or mild and 2.8% (14 of 492) required hospitalization. [Switzerland; December 2021 to October 2021][cxxxii] In a study of 614 of HCW, 13% (81 of 614) had breakthrough infections – within breakthrough infections, 37% (30 of 81**)** were Covishield recipients. [India; January to July 2021] Out of 355 fully vaccinated HCWs, 16 had symptomatic breakthrough infections >14 days after the second dose. No significant difference was	found to have breakthrough infections during the 10-month observational period. 97.2% of the identified breakthrough cases (478 of 492) were asymptomatic or mild and 2.8% (14 of 492) required hospitalization. [Switzerland; December 2021 to October 2021][cxxxvi] Among HCW participating in the Sisonke clinical trial, 40,538 breakthrough infections were confirmed – 609 of which occurred during Beta variant predominance, 22,279 cases during Delta, and				

[cxxix] Study does not differentiate between Pfizer, Moderna, AstraZeneca, or Janssen.
[cxxxii] ***Study does not differentiate between Pfizer, Moderna, AstraZeneca, or Janssen.
[cxxxvi] Study does not differentiate between Pfizer, Moderna, AstraZeneca, or Janssen.

	hospitalization. [Switzerland; December 2021 to October 2021][cxxv] Of 23,697 vaccinated HCPs, 0.58% tested positive for COVID (138 of 23,697 cases that received at least one dose of an mRNA vaccine) – 105 of which only received one dose and 33 (0.15% 33 of 22,458 cases who received both vaccine doses) were among those who completed vaccination. Among the 138 postvacciantion cases, 74 were vaccinated with Pfizer. Among 1,128 cluster-associated cases of COVID,	918 (81%) were identified as breakthrough infections. Of these, 293 (32%) received the Moderna vaccine. Characteristics of breakthrough infection cases were similar across Pfizer, Moderna, and Johnson & Johnson vaccines. Cumulative incidence of breakthrough infection was **0.59%** (95% CI, 0.55-0.64) 6 months after the second dose.[Qatar][52] *Delta (B.1.617.2):* Estimated lower VE against Delta infection since **higher odds of breakthrough**	observed between Covishield and Covaxin. [India; 16 January 2021 to 31 July 2021][56] Omicron (B.1.1.529) was neutralized less effectively by serum from breakthrough infection patients, with a 6.3-fold reduction compared to delta variants. [57] [cxxxiii]	17,650 during Omicron. There were a total of 1,914 hospitalizations (77 in the Beta, 1,429 in the Delta, and 408 in the Omicron periods). During Omicron, 91% hospitalized HCWs required general ward care, 6% high care, and 3% intensive care which were significantly different from the Delta (89% general, 4% high, 7% intensive care) and Beta (78% general, 7% high, 16% intensive care) periods. [South Africa; March 2021 to December 2021] Among 1,128 cluster-associated cases of COVID,				

[cxxv] Study does not differentiate between Pfizer, Moderna, AstraZeneca, or Janssen.
[cxxxiii] Study does not differentiate between inactivated vaccinates, CoronaVac or AZD1222.

	918 (81%) were identified as breakthrough infections. Of these, 504 (55%) received the Pfizer vaccine. Characteristics of breakthrough infection cases were similar across Pfizer, Moderna, and Johnson & Johnson vaccines. Overall test positivity rate was 6.4% during the period of Delta dominance and 24.4% during a proxy Omicron period.[South Africa] Of 365 cases with covid in a long-term care facility, the mean attack rate was **18.0%** (95% CI 12.8-	**infection** were found when comparing Delta and Alpha-infected patients - **odds ratio: 1.96** (95%CI. 1.22-3.14][Portugal, 17 May 2021 to 04 July 2021] [53cxxx] *Omicron (B.1.1529):* Of 111 participants, 59% (66 of 111) had confirmed infection while 14% (15 of 111) were probable cases, the **total attack rate for Omicron was 74%** (81/110).[Norway; November 2021 to December 2021][55cxxxi] Over a period of 8.4 months, **13 out of 387** (3.4%)		918 (81%) were identified as breakthrough infections. Of these, 121 (13%) received the Johnson & Johnson vaccine. Characteristics of breakthrough infection cases were similar across Pfizer, Moderna, and Johnson & Johnson vaccines.				

[cxxx] Study does not differentiate between mRNA vaccines.

[cxxxi] Study does not differentiate between mRNA vaccines.

	23.2) among those fully vaccinated compared with 27.5% (95% CI, 16.3-38.7) among unvaccinated persons. [France][5] Cumulative incidence of breakthrough infection was **0.84%** (95% CI, 0.79-0.89) 6 months after the second dose.[Qatar][52] *Delta (B.1.617.2):* Estimated lower VE against Delta infection since higher odds of breakthrough infection were found when comparing Delta and Alpha-infected patients - odds ratio: 1.96 (95%CI. 1.22-3.14][Portugal, 17	of vaccinated followed up individuals developed a breakthrough infection [37]							

	May 2021 to 04 July 2021] [53] [cxxvi] *Omicron (B.1.1529):* Breakthrough cases described symptoms as mild or moderate, had viral loads ranging from 15,011.2 to over 40,000 AU.mL[54] Of 111 participants, 59% (66 of 111) had confirmed infection while 14% (15 of 111) were probable cases, the **total attack rate for Omicron was 74%** (81/110).[Norway; November 2021 to December 2021][55] [cxxvii]								

[cxxvi] Study does not differentiate between mRNA vaccines.

[cxxvii] Study does not differentiate between mRNA vaccines.

	Over a period of 8.4 months, **8 out of 212** (3.8%) of vaccinated followed up individuals developed a breakthrough infection [37]							
	SAFETY AND ADVERSE EVENTS							
	BNT162b2/ COMIRNATY	**Spikevax/ Moderna COVID-19 Vaccine/ mRNA-1273**	**Vaxzevria/ ChAdOx1 nCoV-19/ AZD1222/ Covishield**	**Janssen COVID-19 vaccine/Johnson & Johnson**	**Covilo/ /BBIBP-CorV**	**CoronaVac**	**COVAXIN / BBV152**	**Nuvaxovid/ NVX-CoV2373/ Covovax**
Common side effects	Pain at the injection site, fatigue, headache, myalgia, chills and fever, arthralgia Optimal safety for asthma patients. More adverse events reported after the first than the second dose for recipients who had prior COVID-19 infections[61]	Pain at injection site, headache, fatigue, myalgia, arthralgia, Covid arm (cutaneous hypersensitivity). The vaccine is considered safe for cancer patients undergoing treatments. Anaphylaxis rates associated with vaccine is comparable to those of other	Fatigue, myalgia, arthralgia, headache, lethargy, fever, & nausea, urticaria[64] Anaphylaxis rates associated with vaccine is comparable to those of other vaccines and is ranked fifth in reported anaphylaxis rates, behind rabies, tick-borne encephalitis,	Headache, fever, chills, fatigue, myalgia, and nausea. Anaphylaxis rates associated with vaccine is comparable to those of other vaccines and is ranked fifth in reported anaphylaxis rates, behind rabies, tick-borne encephalitis, measles-mumps-	Pain at the injection site, dizziness, fever, headache, fatigue, nausea, vomiting, & allergic dermatitis.	Pain at injection site, headache, fatigue, tremors, & flushing, inflammatory reaction, urticaria, myalgia	Pain at injection site, headache, pyrexia, fatigue, myalgia	Pain at injection-site, headache, muscle pain, fatigue

	Acute adverse events (AAE) **17.8** cases of dizziness, **9.7** of headache, **7.1** of nausea and **3.2** of syncope per 10,000 doses administered were observed in Saudi Arabia[62] One in ten AAEs were considered serious, but only 0.1 per 10,000 doses required hospitalization for non-anaphylaxis reasons[62] The vaccine is considered safe for cancer patients undergoing treatments. Anaphylaxis rates associated with vaccine is comparable to those of other vaccines and is ranked fifth in reported anaphylaxis rates,	vaccines and is ranked fifth in reported anaphylaxis rates, behind rabies, tick-borne encephalitis, measles-mumps-rubella-varicella, and human pappilomavirus vaccines[63]	measles-mumps-rubella-varicella, and human pappilomavirus vaccines[63]	rubella-varicella, and human pappilomavirus vaccines[63]					

	behind rabies, tick-borne encephalitis, measles-mumps-rubella-varicella, and human pappilomavirus vaccines[63]							
Risk of developing adverse event[cxxxix]	Cerebral venous sinus thrombosis **OR 4.40*** (95% CI, 3.56-5.44)[65] **Absolute risk 0.6** (95% CI, 0.5-0.7) per million doses [66] Cerebral venous sinus thrombosis with thrombocytopenia **Absolute risk 0.0** (95% CI, 0.0-0.1) per million doses [66] Guillain-Barre syndrome **OR 1.53*** (95% CI, 1.34-1.75)[65]	Cerebral venous sinus thrombosis **OR 2.67*** (95% CI, 1.77-4.03)[65] **Absolute risk 0.6** (95% CI, 0.3-1.1) per million doses [66] Cerebral venous sinus thrombosis with thrombocytopenia **Absolute risk 0.0** (95% CI, 0.0-0.2) per million doses [66] Guillain-Barre syndrome **OR 1.74*** (95% CI, 1.43-2.12)[65]	Cerebral venous sinus thrombosis **OR 15.43*** (95% CI, 13.73-17.34)[65] **Absolute risk 7.5** (95% CI, 6.9-8.3) per million doses [66] Cerebral venous sinus thrombosis with thrombocytopenia **Absolute risk 4.4** (95% CI, 3.9-4.9) per million doses [66] Guillain-Barre syndrome **OR 2.74*** (95% CI, 2.49-3.02)[65]	Cerebral venous sinus thrombosis **Absolute risk 0.7** (95% CI, 0.2-2.4) per million doses [66] Cerebral venous sinus thrombosis with thrombocytopenia **Absolute risk 0.7** (95% CI, 0.2-2.4) per million doses [66] Acute pericarditis **OR 3.33*** (95% CI, 1.29-10.14)[67cxliv] Thrombosis with thrombocytopenia syndrome				

[cxxxix] Values with a * were deemed significant in the report
[cxliv] Study does not differentiate between vaccines

	Haemorrhagic stroke **OR 0.82** (95% CI, 0.66-1.02)[65] Ischemic stroke **OR 2.73*** (95% CI, 2.48-3.01)[65] Transient ischemic attack **OR 1.24*** (95% CI, 1.13-1.36)[65] Acute pericarditis **OR 3.33*** (95% CI, 1.29-10.14)[67cxl] Thrombosis with thrombocytopenia syndrome Reporting rate of **0.0085** per million vaccine doses[cxli68]	Haemorrhagic stroke **OR 0.72** (95% CI, 0.50-1.04)[65] Ischemic stroke **OR 1.56*** (95% CI, 1.28-1.90)[65] Transient ischemic attack **OR 0.99** (95% CI, 0.84-1.16)[65] Acute pericarditis **OR 3.33*** (95% CI, 1.29-10.14)[67cxlii] Thrombosis with thrombocytopenia syndrome Reporting rate of **0.0085** per million vaccine doses[cxliii68]	Haemorrhagic stroke **OR 0.53** (95% CI, 0.41-0.69)[65] Ischemic stroke **OR 2.13*** (95% CI, 1.92-2.37)[65] Transient ischemic attack **OR 1.38*** (95% CI, 1.27-1.50)[65]	Reporting rate of **3.83** per million vaccine doses [68]				

[cxl] Study does not differentiate between vaccines.
[cxli] Does not differentiate between BNT162b2 and mRNA-1273.
[cxlii] Study does not differentiate between vaccines.
[cxliii] Does not differentiate between BNT162b2 and mRNA-1273.

Rare adverse events	Myocarditis & myopericarditis, pericarditis[69], thrombosis [70], anaphylaxis and swelling of the lips, face, and tongue related to anaphylaxis (11 anaphylaxis cases per million doses administered), paroxysmal ventricular arrhythmia, leg paresthesia, pityriasis rosea (lesions improved completely after ~8 weeks), lymphocytic vasculitis, varicella-zoster reactivation, Kikuchi-Fujimoto disease, thrombotic thrombocytopenic purpura, IgA nephropathy flare-up, Guillain-Barré syndrome, psoriasis, immunoglobulin A vasculitis, immune complex vasculitis,	Myocarditis & myopericarditis, pericarditis[69], orofacial swelling & anaphylaxis. Potential risk factor for Bell's palsy (most improve upon follow-up), herpes zoster reactivation, varicella zoster reactivation, herpes zoster ophtalmicus, eczema & urticaria, transverse myelitis, Guillain-Barré syndrome, acute generalized exanthematous pustulosis, rhabdomyolysis, cervical lymphadenopathy, glomerulonephritis , Behçet's disease, neurological autoimmune disease, axillary adenopathy, multiple sclerosis, cutaneous	Transverse myelitis, high fever, cutaneous hypersensitivity, vasculitis, thromboembolism, vaccine induced immune thrombotic thrombocytopenia, intracerebral haemorrhage, small vessel vasculitis, psoriasis, rosacea, raynaud's phenomenon, Ischaemic stroke, anaphylaxis, recurrent herpes zoster, generalized bullous fixed drug eruption, Guillain-Barré syndrome, pityriasis rosea. Vaccination in individuals with adrenal insufficiency can lead to adrenal crises, Dariers disease, vaccine induced acute localized	Thrombosis, thrombocytopenia, increased risk of developing Guillain-Barré syndrome post vaccination, herpes zoster ophtalmicus, pseudothrombocytopenia, vaccine induced thrombocytopic thrombosis, cutaneous reactions, optic neuritis, subacute thyroiditis, CNS demyelination, bullous local reaction[80] 97% of reported reactions after vaccine administration were non-serious.	Cutaneous reactions, herpes zoster, CNS demyelination Rare adverse events were similar among the vaccine groups and control group within 7 days. Pityriasis rosea, uveitis	Myalgia, fever, pityriasis rosea (lesions improved completely after ~8 weeks), reactivation of herpes zoster and herpes simplex. Most reactions improved without treatment within a few weeks, Guillain-Barré syndrome, subacute thyroiditis, erythema multiforme, uveitis, vaccine induced thrombotic thrombocytopenia, serum sickness-like reaction, cutaneous reactions, neuromyelitis optica spectrum disorders (transverse myelitis or optic neuritis), bullous pemphigoid, CNS demyelination, deafness[81],	Subacute thyroiditis, herpes zoster	Cutaneous reactions Myocarditis was reported in one vaccine recipient, occurring 3 days after second dose

	Rhabdomyolysis, subacute thyroiditis, Bell's Palsy, erythema multiforme, vaccine induced interstitial lung disease, macular neuroretinopathy, brachial neuritis, thyroid eye disease, exacerbation of subclinical hyperthyroidism, rhabdomyolysis, internal jugular vein thrombosis, herpes simplex, herpes zoster, virus keratitis, cervical lymphadenopathy, glomerulonephritis, Ramsay-Hunt syndrome, Sweet's syndrome, neurological autoimmune disease, axillary adenopathy, multiple sclerosis, meningoencephalitis, intracerebral haemorrhage due	reactions, Löfgren's syndrome, erythema multiforme, pemphigus vulgaris, graft rejection (corneal), thrombotic thrombocytopenic purpura, reactivation of BCG scars, urticarial vasculitis, CNS demyelination, thrombocytopenia, thyroiditis[74], thyrotoxicosis[73], polymyalgia rheumatic [75]	exanthematous pustulosis, Henoch-Schönlein Purpura, rhabdomyolysis, Grave's disease, acute demyelinating polyradiculoneuropathy, erythema nodosum, polyarthralgia, recurrence of cutaneous T-cell lymphoma, neurological autoimmune disease, multiple sclerosis, sudden sensorineural hearing loss, acute-onset polyradiculoneuropathy, cutaneous reactions, leukocytoclastic vasculitis, Löfgren's syndrome, acute eosinophilic pneumonia, bullous sweet syndrome, neuralgic amyotrophy of the lumbosacral			glomerulonephritis[82]		

	to vasculitis, cutaneous reactions, pigmented purpuric dermatosis, graft rejection (corneal), flexural exanthema, severe non-anaphylatic allergic reaction, uveitis, erythroderma, Behçet's disease, brachial plexus neuritis, systemic capillary leak syndrome, chronic graft-versus-host-disease flare up, vaccine-induced pneumonitis, reactivation of BCG scars, CNS demyelination, urticarial reactions[71], transverse myelitis[72], thyrotoxicosis [73] Systemic allergic symptoms were more common in BNT162b2 than		plexus, sudden sensorineural hearing loss, graft rejection (corneal), erythema annulare centrfugum, graft rejection (stromal), leukocytoclastic vasculitis, subacute thyroiditis[76], vaccine-induced pneumonitis[77], myositis[77], glomerulopathy[78], nephrotic syndrome [79]					

	mRNA-1273, however, anaphylaxis rates were similar for both mRNA vaccines, could potentially worsen migraines in people who already suffer from migraines Having adverse reactions is associated with enhanced SARS-CoV-2 IgG antibody response							
Potential associated adverse events (causal links not yet proven)	Cerebral venous sinus thrombosis and intracranial haemorrhage, aseptic meningitis, autoimmune hepatitis, multiple sclerosis relapse, myeloperoxidase anti-neutrophil cytoplasmic antibody-positive optic perineuritis, central retinal vein occlusion, paracentral acute middle	Cerebral venous sinus, Autoimmune hepatitis, myocardial infarction, autoimmune haemolytic anaemia, hypophysitis & panhypopituitarism, erythema nodosum, pulmonary embolism, minimal change disease, encephalomyelitis, lupus nephritis,	Autoimmune hepatitis, Acute hyperglycaemic crisis, Facial nerve palsy, cervical myelitis, alopecia areata, takotsubo (stress) cardiomyopathy, acute disseminated encephalomyelitis, cerebral venous sinus thrombosis (higher risk for women), ophthalmic vein thrombosis, retinal	Facial Diplegia, acute macular neurotinopathy, cerebral venous sinus thrombosis, oral lichen planus	Cerebral venous sinus thrombosis [91], Longitudinally extensive transverse myelitis	Cerebral venous sinus thrombosis [91], Likely vaccine associated disease enhancement (VADE), autoimmune hepatitis	No available data	No available data

	maculopathy & acute macular neurotinopathy, Stevens-Johnson syndrome/ toxic epidermal necrolysis, lichenoid cutaneous skin eruption, acute mania and psychotic features, acute psychosis due to anti-N-methyl-D-aspartate receptor (anti-NMDAR) encephalitis, alopecia areata, rhombencephalitis, multisystem inflammation and organ dysfunction, aplastic anaemia, bullous pemphigoid, minimal change disease, miller fisher syndrome, unilateral acute foveolitis, encephalomyelitis, acute posterior multifocal placoid pigment epitheliopathy,	retinal vein occlusion, takotsubo syndrome, encephalitis[85], status epilepticus [85], pleuropericardial diffusion [86] One case developed IgA Nephropathy after receiving the second dose of mRNA-1273.	vein occlusion, Still's disease, autoimmune encephalitis, acute abducens palsy, lichenoid eruption, multisystem inflammatory syndrome[87], parosmia[88], encephalopathy [89], reactivation of bipolar mania[90]					

	trigeminal neuralgia, vestibular neuritis, autoimmune acquired factor XIII/13 deficiency, Still's disease, autoimmune acquired factor XIII/13 deficiency, Still's disease, cranial nerve palsy, inflammatory bowl disease[83], pancreatitis [84]							
Myocarditis data	Mainly reported in young adults and adolescents *First dose (1-28 days post vaccination):* Incidence rate ratio of **1.37** (95% CI, 1.12-1.67)[92] *Second dose:* Incidence rate ratio of **1.60** (95% CI, 1.31-1.97)[92] *Third dose:* Incidence rate ratio of **2.02** (95% CI, 1.40-2.91)[92]	Mainly reported in young adults and adolescents *First dose (1-28 days post vaccination):* No association[92] *Second dose:* Incidence rate ratio of **13.71** (95% CI, 8.46-22.20)[92] *Third dose:* No association[92] (small sample size)	*First dose (1-28 days post vaccination):* Incidence rate ratio of **1.27** (95% CI, 1.05-1.55)[92] *Second dose:* No association[92] *Third dose:* No association[92] (small sample size) *Males <40 years: Second dose [1-28 days post vaccination]:*	No available data	No available data	No available data	No available data	Myocarditis was reported as viral myocarditis. Participant fully recovered after 2 days of hospitalisation. No episode of anaphylaxis or vaccine-associated enhanced COVID-19 was reported

	<u>Males <40 years:</u> *First dose [1-28 days post vaccination]:* Incidence rate ratio of **1.66** (95% CI, 1.14-2.41)[92] *Second dose [1-28 days post vaccination]:* Incidence rate ratio of **3.41** (95% CI, 2.44-4.78)[92] *Third dose [1-28 days post vaccination]:* Incidence rate ratio of **7.60** (95% CI, 2.44-4.78)[92] <u>Israeli study:</u> Estimated incidence within 42 days after receipt of first dose per 100,000 vaccinated persons was **2.13** cases (95% CI, 1.56-2.7) <u>Male patients</u>	*<u>Males <40 years:</u>* *First dose [1-28 days post vaccination]:* Incidence rate ratio of **2.34** (95% CI, 1.03-5.34)[92] *Second dose [1-28 days post vaccination]:* Incidence rate ratio of **16.52** (95% CI, 9.10-30.0)[92] *<u>Females <40 years</u>* *Second dose [1-28 days post vaccination]:* Incidence rate ratio of **7.55** (95% CI, 1.67-34.12)[92] 5.8 cases per 1 million second dose administrations **95.4** (95% CI, 52.1-160.0) **cases** per 1 million second dose	Incidence rate ratio of **2.57** (95% CI, 1.52-4.35)[92]					

	Incidence of **4.12** (95% CI, 2.99-5.26) per 100,000 vaccinated **3.19** cases (95% CI, 2.37-4.02) per 100,000 vaccinated <u>Female patients</u> Incidence of **0.23** (95% CI, 0-0.49) per 100,000 vaccinated[93] **0.39** cases (95% CI, 0.10-0.68) per 100,000 vaccinated <u>≥30 years</u> Incidence of **1.13** (95% CI, 0.66-1.60) per 100,00 vaccinated **5.8 cases** per 1 million second dose administrations **95.4** (95% CI, 52.1-160.0) **cases** per 1 million second dose administrations in	administrations in patients aged 12-39[94] *<u>12–39-year-olds (within 28 days of vaccination:</u>* <u>Female patients</u> **2.0** (95% CI, 0.7-4.8) per 100,000 vaccinated[95] <u>Male patients</u> **6.3** (95% CI, 3.6-10.2) per 100,000 vaccinated[95]							

	patients aged 12-39[94] **5.07** cases per 100,000 <u>Disease severity</u> Mild: **1.62** (95% CI, 1.12-2.11) Intermediate: **0.47** (95% CI, 0.21-0.74) Fulminant: **0.04** (95% CI, 0-0.12) <u>Risk per 100,000 persons</u> 1st dose (male): **0.64** 2nd dose (male); **3.83** 1st dose (female): **0.07** 2nd dose (female): **0.46** 1st dose (male 16-19): **1.34** 2nd dose (male 16-19): **15.07** *<u>12–39-year-olds (within 28 days of vaccination:</u>* <u>Female patients</u>								

	1.3 (95% CI, 0.8-1.9) per 100,000 vaccinated[95] <u>Male patients</u> **1.5** (95% CI, 1.0-2.2) per 100,000 vaccinated[95]							
	CHILDREN VACCINATION							
	BNT162b2/ COMIRNATY	**Spikevax/ Moderna COVID-19 Vaccine/ mRNA-1273**	**Vaxzevria/ ChAdOx1 nCoV-19/ AZD1222/ Covishield**	**Janssen COVID-19 vaccine/Johnson & Johnson**	**Covilo/ /BBIBP-CorV**	**CoronaVac**	**COVAXIN / BBV152**	**Nuvaxovid/ NVX-CoV2373/ Covovax**
Efficacy	*<u>Adolescents (12-15):</u>* After one dose had efficacy of **75% (CI, 7.6-95.5)** After second dose efficacy of **100% (CI, 78.1-100)** *<u>Children (5-11):</u>* After second dose efficacy of **90.7% (CI, 67.7-98.3)**	*<u>Adolescents (12-17):</u>* 14 days after one dose had efficacy of **92.7% (CI, 67.8-99.2)** After second dose efficacy of **93.3% (CI, 47.9-99.9)** ***Against SARS-CoV-2 Infection:*** 14 days after first dose efficacy of **68.9% (95% CI, 49.9-82.1)**	No available data Paused ongoing trials in children aged 6-17 due to concerns over rare blood clots reported in adult population	No available data Announced at beginning of April ongoing study in adolescents but paused to investigate blood clots in adult population	*<u>Children (3-17):</u>* Unknown. Ongoing clinical trial only looked at safety, tolerability, and immunogenicity[cxlv] * * The study design administered **three doses** of 2 µg, 4 µg, or 8 µg of vaccine	*<u>Children (3-17):</u>* Unknown. Clinical trial only looked at safety, tolerability and immunogenicity	No available data	*<u>Adolescents (16-17):</u>* PREVENT-19 clinical trial[cxlvi] expanded to assess efficacy, safety, and immunogenicity in 12–17-year-old adolescents

[cxlv] Safety and immunogenicity of an inactivated COVID-19 vaccine, BBIBP-CorV, in people younger than 18 years: a randomised, double-blind, controlled, phase 1/2 trial. *The Lancet Infectious Diseases.* https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(21)00462-X/fulltext

[cxlvi] A Study to Evaluate the Efficacy, Immune Response, and Safety of a COVID-19 Vaccine in Adults ≥18 Years With a Pediatric Expansion in Adolescents (12 to <18 Years) at Risk for SARS-CoV-2. *ClinicalTrials.gov*. ClinicalTrials.gov Identifier: NCT04611802. https://clinicaltrials.gov/ct2/show/NCT04611802?term=Novavax&cond=Covid19&draw=2

	Children (Under 5 years): Ongoing trials[96]	14 days after second dose efficacy of **55.7% (95% CI, 16.8,82.1)** ***Against asymptomatic:*** 14 days after first dose efficacy of **59.5% (95% CI, 28.4-77.3)** 14 days after second dose efficacy of **39.2 (95% CI, -24.7-69.7)** *Children (6month-11):* Ongoing trials[97]						
Effectiveness	*Adolescents Against SARS-CoV-2 infection:* **91.5%** (95% CI, 88.2-93.9)[98] **91%** (95% CI, 88-93) **92%** (95% CI, 79%–97%)" from July-Dec 2021[99] *Adolescents Against hospitalisation:*	No available data	No available data	No available data	No available data	No available data	No available data	No available data

	81% (95% CI, -55-98)[100] **93%** (95% CI,83-97) **94%** (95% CI, 91 to 97) *Adolescents against ICU care:* **98%** (95% CI, 93 to 99)[101] *Waning VE in Adolescents 12-16:* VE against breakthrough infection reduced to **75% (95% CI: 71%, 79%)** after 90-149 days after second dose and **58% (95% CI: 52%, 64%**) 150-180 days after second dose VE against symptomatic infection was 78% **(95% CI: 73%, 82%)** after 90-140 days and **65% (95% CI: 58%, 71%)** after 150-180 days[102]								

	effectiveness of 2 doses against MIS-C was **91%** (95% CI, 78%–97%)[103]							
Immunogenicity	*Adolescents (12-15) serum-neutralizing titer:* 1 month after 2nd dose had **1283.0 GMN_{50} (CI, 1095.5-1402.5)** *Adolescents/young adult (16-25) serum-neutralizing titer:* 1 month after 2nd dose had **705.1 GMN_{50} (CI, 621.4-800.2)** *Children (5-11):* 1 month after 2nd dose had **1,197.6 GMT (95% CI, 1106.1-1296.6)** SARS-CoV-2-neutralizing antibody *Children (Under 5):* Ongoing trials[96]	*Adolescents (12-17):* Neutralizing antibody titer after 2nd dose was **1401.7 GMN_{50} (CI, 1276.3-1539.4)** Serological response was **98.8% (CI, 97.0-99.7)** *Children (6-11):* Seroreponse of **99.3%**[105] *Children (6month-11):* Ongoing trials[97] *Adolescents (12-17) Against Omicron:* **11.8-fold reduction** in GMT compared to wild-type	No available data	No available data	*Children (3-17):* Neutralizing antibodies after 28 days after 2nd dose ranged from **105.3-180.2 GMT** in 3-5 years cohort, **84.1-168.6 GMT** in 6-12 years cohort, and **88.0-155.7 GMT** in 13-17 years cohort Neutralizing antibodies after 28 days after 3rd dose ranged from **143.5-224.5 GMT** in 3-5 years cohort, **127-184.8 GMT** in 6-12 years cohort, and **150.7-199 GMT** in 13-17 years cohort GMC of anti-RBD antibody in adolescent cohort aged 12-17 was	*Children (3-17):* Neutralizing antibody response after 2nd dose **(100%)** with GMT ranging from **45.9-212.6**	Ongoing clinical trial[107] Neutralizing antibodies after 56 days after 2nd dose was **358.6 GMT (95% CI, 287.2-447.8)** in 2-6 years group, **366.9 (95% CI, 297.0-453.3)** in 6-12 years group, and **317.4 (95% CI, 224.4-449.2)** in 12-18 years group	Ongoing clinical trial[108]

	Adolescents (11-16) Against Omicron: **3-4-fold reduction** in neutralization detectable titers in only **3 of 15** adolescents GMT for WA1 were **329** (range 94-1096)**.** For Omicron, was **39** (range 25-64)[104]	*Children (6012) Against Omicron:* **22.1 fold reduction** in GMT compared to wild-type[106]			**102.9 BAU/mL (95%CI; 91.0-116.4)** after 4 weeks since 2nd dose			
Safety and Adverse events	Rare possibility of developing multisystem inflammatory syndrome *Adolescents (12-15):* Local and systemic events were generally mild to moderate Severe injection-site pain **(1.5%)** Fever **(20%)** High Fever **(0.1%)** Adverse events **(6%)**	Rare possibility of developing multisystem inflammatory syndrome *Adolescents (12-17):* Solicited local reactions after 2nd dose **(93.4%)** Most common solicited adverse reactions were Injection-site pain **(92.7%)** Headache **(70.2%)**	No available data	Rare possibility of developing multisystem inflammatory syndrome	*Children (3-17):* Most common adverse reaction was pain at injection site in 3–5-year group **(4%)**, 6-12-year group **(1.2%)**, and 13-17-year group **(7.9%)** Most common systemic reactions in all three age cohorts were mild to moderate **fever** and **cough**	*Children (3-17):* Adverse reactions in 12–17 year group **(35%)**, 3-5 year group **(26%)**, and 6-11 year group **(18%)** Reported at least one adverse event **(27%)** Most reported events were mild and moderate and only **(<1%)** grade 3 events Injection-site pain **(13%)** Fever **(25%)**	Ongoing clinical trial[107] Most common local reaction of mild injection site pain in no more than **35%** of all age groups Most frequent solicited systemic adverse event was mild-to-moderate fever- **5%** of 12-18 group, **10%** of 6-12 group, and **13%** of 2-6 group	Ongoing clinical trial[108]

	Severe adverse events **(0.6%)** *Adolescent/young adults (16-25):* Local and systemic events were generally mild to moderate Severe injection-site pain **(3.4%)** Fever **(17%)** Adverse events **(6%)** Severe adverse events **(1.7%)** *Children (5-11):* Pain at injection site, fatigue, headache, chills were reported. Overall, the vaccine is safe and tolerable *Children (Under 5):* Ongoing trials[96] Additional reports of rare cases of multisystem inflammatory syndrome	Fatigue **(67.8%)** Grade 3 adverse events **(6.8%)**) Most common solicited local reaction: injection-site pain after first injection **(93.1%)** and second injection **(92.4%)** Most common systemic **reactions: fatigue, myalgia,** and **chills** *Children (6-11):* Vaccine was generally well tolerated *Children (6month-11):* Ongoing trials[97]			Adverse events were mostly mild to moderate in severity **18.1%** reactogenicity reported on day 1 in adolescents 12-17, most common immediate local events were **mild pain and tenderness** at injection site, No serious adverse events			

	Among 8,113,058 doses administered to 4,079,234 12–17-year-old children, 9 developed multisystem inflammatory syndrome in France. Reporting rate was 1.1 (95% CI, 0.5-2.1) per million doses administered. [109] Out of 4,249 VAERS reports of adverse events, 4,149 **(97.6%)** were **nonserious events**.[110] *Adverse events cases:* 15-year old boy developed nephrotic syndrome							
Myocarditis Data	Few reported cases of acute myocarditis and pericarditis in 16-25 year olds (mainly in males)	Few reported cases of acute myocarditis and pericarditis (mainly in males)	No available data	No available data	No available data	No available data	No available data	No available data

	From large VAERS cohort, 11 verified reports of myocarditis [111] **4.3 cases per 100,000** (95% C.I. 2.6–6.7) 18 year olds after second dose[112] <u>Male patients 12-17 years</u> **97 cases per million** (1 in 10,000 males) <u>Female patients 12-17 years</u> **16 cases per million** (1 in 63,000 females) <u>16-29 years</u> Incidence of **5.49** (95% CI, 3.59-7.39) per 100,00 vaccinated <u>Male patients (16-29 years)</u> Incidence of **10.69** (95% CI, 6.93-14.46) per	*<u>16-17 year old boys in US</u>*: *Second dose*: 31.2 cases per million doses administered							

	100,000 vaccinated Incidence of **13.6 cases** (95% CI, 9.30-19.20) per 100,000 vaccinated *12-15 year old boys in US*: *First dose*: 4.8 cases per million doses administered *Second dose*: 42.6 cases per million doses administered *12-15 year old girls in US*: *First dose*: 0.5 cases per million doses administered *Second dose*: 4.3 cases per million doses administered *16-17 year old boys in US*: *First dose*: 5.2 cases per million								

	doses administered *Second dose*: 71.5 cases per million doses administered *<u>16-17 year old girls in US</u>*: *First dose*: 0.0 cases per million doses administered *Second dose*: 8.1 cases per million doses administered							
Vaccine Schedule	**HETEROLOGOUS VACCINATION**							
	BNT162b2/ChAdOx1 Administration of ChAdOx1 as second/booster dose	**ChAdOx1/mRNA-1273** Administration of mRNA-1273 as second/booster dose	**ChAdOx1/BNT162b2** Administration of BNT162b2 as second/booster dose	Not Applicable (one dose schedule) For more information refer to booster section	**BBIBP/BNT162b2**	**CoronaVac/ChAdOx1** Press releases have confirmed that Thailand will use the AstraZeneca vaccine as the second dose for individuals whose	**ChAdOx1/BBV152** Administration of Covaxin as second/booster dose	Ongoing trial[113] (Com-Cov2)[cxlviii]

[cxlviii] Comparing COVID-19 Vaccine Schedule Combinations. *University of Oxford.* https://comcovstudy.org.uk/about-com-cov2

						first dose was Sinovac[cxlvii] **CoronaVac/Convidecia**		
Immunogenicity	*GMCs of SARS-CoV-2 anti-spike IgG at 28 days post booster:* Heterologous **(7133 ELU/mL, CI 6415-7932)** vs. Homologous **(14080 ELU/mL, CI 12491-15871)** *SFC frequency (T0cell ELISpot):* Heterologous **(99 SFC/10^6 PBMCs)** vs. Homologous **(80 SFC/10^6 PBMCs)** ***Heterologous mRNA:*** **84.7%** effectiveness (95% CI, 83.1-86.1)	**Spike-specific IgG antibodies:* Heterologous **(3602 BAU/mL)** vs. Homologous **(4189 BAU/mL)** **Neutralizing antibodies:* Heterologous **(100%)** vs. Homologous **(100%)** ***Heterologous mRNA:*** **84.7%** effectiveness (95% CI, 83.1-86.1) *Results based on immunosuppressed population	*RBD antibody titres:* Heterologous **(7756.68 BAU/mL, CI 7371.53-8161.96)** vs. Homologous **(99.84 BAU/mL, CI 76.93-129.59)** at day 14 *IgG antibody titres:* Heterologous **(3684 BAU/mL)** vs. Homologous **(101.2 BAU/mL)** at day 14 *Neutralizing antibodies:* Heterologous **(100%)** at day 14 vs.	Not Applicable (one dose schedule) For more information refer to booster section	Unknown (on-going clinical trial)[49]	**CoronaVac/ChAdOx1 :** *Anti-S Antibodies:* Heterologous **(797 U/mL; 95% CI, 598.7-1062)** vs. Homologous CoronaVac **(94.4 U/mL; 95% CI : 76.1-122.1)** vs. Homologougous ChAdOx1 **(818 U/mL; 95% CI: 662.5-1010)** **CoronaVac/Convidecia** *Neutralizing antibodies :* Heterologous **54.4 GMT** (95% CI, 37.9-78) vs. Homologous CoronaVac	*RBD antibody titres:* Heterologous **(1866 GMT; 95% CI, 1003-3472)** vs. Homologous Covishield **(2260 GMT; 95% CI, 1881-2716)** vs. Homologous Covaxin **(710 GMT, 95% CI, 461-1092)** *N-protein IgG:* Heterologous **(1145 GMT; 95% CI, 520.7-2520)** vs. Homologous Covishield **(353.7 GMT; 95% CI, 219.9-568.9)** vs.	No available data Ongoing trial[113]

[cxlvii] Malaysia to stop using Sinovac vaccine after supply ends - minister. *Reuters* [press release]. https://www.reuters.com/world/asia-pacific/malaysia-stop-using-sinovac-vaccine-after-supply-ends-minister-2021-07-15/

			Homologous **(30%)** at day 14 Heterologous **(median 99%)** vs. Homologous (BNT162b2/BNT162b2) **(median 62%)**			**12.8 GMT** (95% CI, 9.3-17.5)	Homologous Covaxin **(742.4 GMT; 95% CI, 485.8-1134)** *Neutralizing antibody titres :* Heterologous **(171.4 GMT; 95% CI, 121.3-242.3)** vs. Homologous Covishield **(111 GMT; 95% CI, 98.59-124.9)** vs. Homologous Covaxin **(86 GMT; 95% CI, 138.2-252.0)**	
Immunogenicity against variants	No available data	No available data	*Neutralizing Antibodies for Alpha, Beta, Gamma, and Delta:* Heterologous **2.3-fold to 3.6-fold** higher neutralizing antibodies than homologous *Omicron (B.1.1.529):*	No available data	No available data	No available data	*Neutralizing antibody titres **B.1.539.4:*** **GMT (95% CI, 263.9-1103)** *Neutralizing antibody titres **Alpha:*** **396.1 GMT (95% CI, 199.1-788)** *Neutralizing antibody titres **Beta:***	No available data

			13/20 seropositive against Omicron[114]				**151 GMT (95% CI, 80.21-284.3)** *Neutralizing antibody titres* ***Delta***: **241.2 GMT (95% CI, 74.99-775.9)**	
Reactogenicity	Observed increase in systemic reactogenicity after boost in heterologous schedules in comparison with homologous schedules *Adverse events in heterologous:* Adverse events **(90)** Grade 1 **(54.4%)** Grade 2 **(37.8%)** Grade 3 **(7.8%)** Grade 4 **(0%)** Arthralgia, Migraine, Back Pain *Adverse events in homologous:*	*Adverse events in heterologous and homologous vaccination groups were very similar *Majority of adverse events self-reported were Pain at injection site, Swelling at injection site, Fever, Headaches, Fatigue, Chills, GI effects, Myalgia, Arthralgia *Results based on immunosuppressed population	*Adverse events in heterologous:* Headache **(44%)**, Myalgia **(43%)**, Malaise **(42%)**, Fever **(2%)**, Injection site pain **(88%)**, Induration **(35%)**, Erythema **(31%)** *Severity of adverse events in heterologous:* Mild **(68%)**, Moderate **(30%)**, Severe **(2%)**	Not Applicable (one dose schedule) For more information refer to booster section	Unknown (on-going clinical trial)[115]	**CoronaVac/ChAdOx1:** Unknown **CoronaVac/Convidecia:** Convidecia recipients reported more adverse reactions and reported higher occurrence of solicited injection-site pain)	*Most common local adverse events:* Pain at injection site **(11.1%)** *Most common systemic adverse events:* Pyrexia **(27.77%, 11.1%)** after 1st and 2nd dose Malaise **(33.3%, 5.5%)** after 1st and 2nd dose	No available data Ongoing trial[113]

	Adverse events **(81)** Grade 1 **(59.3%)** Grade 2 **(39.5%)** Grade 3 **(1.2%)** Grade 4 **(0%)**							
BOOSTER DOSES								
Vaccine Schedule	**BNT162b2/BNT162b2**	**mRNA-1273/mRNA-1273**	**ChAdOx1/ChAdOX1**	**Ad26.CoV.2.S/ Ad26.CoV.2.S**	**Covilo/ Covilo**	**CoronaVac/CoronaVac**	**Covaxin/Covaxin**	**NVX-CoV2373/ NVX-CoV2373**
Approved Administration	*Israel:* 12-year-old and over can received homologous booster shot 5 months after full jab[cxlix] *United States:* Starting September, adults who received mRNA vaccine 8	Phase II booster trial of three booster doses are ongoing[116] Moderna sought FDA approval of its COVID-19 vaccine booster[cli] *United States:* Starting September, adults who received	Preliminary results on tolerability and immunogenicity of third dose of ChAdOx1 vaccines showed strong boost to the immune response[117]	Johnson & Johnson has said it will submit all of their new data to the FDA for potential consideration for adding a booster dose and consideration to authorize two-dose regimen[clii]	*UAE:* Offering booster doses of Pfizer and Sinopharm to people who received full Sinopharm jab ≥6 months ago	**Turkey** and the **United Arab Emirates** began homologous booster shots **Indonesia** and **Thailand** are considering giving homologous booster shot to HCW[cliii]	**India** has started administering homologous booster doses	Ongoing phase II trials[118] Results below are based on ongoing phase II trial

[cxlix] Israel offers COVID-19 booster to all vaccinated people. *Reuters* [press release]. https://www.reuters.com/world/middle-east/israel-offers-covid-19-booster-shots-all-vaccinated-people-2021-08-29/

[cli] Moderna seeks U.S. authorization for COVID-19 vaccine booster. *Reuters* [press release]. https://www.reuters.com/business/healthcare-pharmaceuticals/moderna-submits-initial-data-covid-19-vaccine-booster-us-fda-2021-09-01/

[clii] Two dose version of Johnson & Johnson shot 94% effective against Covid-19, study finds. *CNN*. https://edition.cnn.com/2021/09/21/health/johnson-vaccine-two-doses-booster/index.html

[cliii] Indonesia and Thailand consider booster shots amid doubts over Sinovac vaccine. *Reuters* [press release]. https://www.reuters.com/world/china/indonesia-thailand-consider-booster-shots-amid-doubts-over-sinovac-vaccine-2021-07-08/

	months ago are eligible for booster *Europe:* Starting in fall, most European countries are planning on rolling out booster shots to immunocompromised and elder populations with some countries administering to overall population[cl]	mRNA vaccine 8 months ago are eligible for booster						
Time-to-booster dose	**6 months to 8 months** after initial two-dose regimen Israel offers up to **5 months** after initial two-dose regimen UK has shortened time interval up to **3 months** after initial two-dose regimen due to	**6 months to 8 months** after initial two-dose regimen	**6-9 months** after initial two-dose regimen	**2 months** after one dose regimen[119]	**6 months** after initial two-dose regimen	**6 months to 12 months** After primary vaccination **8 months** after the primary vaccination to healthy adults ≥60 years	**6 months** after initial two-dose regimen	**6 months** after initial two-dose regimen (**189 days**)[118]

[cl] A country-by-country guide to coronavirus vaccine booster plans. *POLITICO* [press reléase]. https://www.politico.eu/article/vaccine-booster-coronavirus-covid-19-europe-delta-varian-who/

	new Omicron variant[cliv]							
Efficacy	*Symptomatic COVID-19:* **95.6%** during Delta prevalent period **95.3% (**95% CI, 89.5-98.3) **96.5%** (95% CI, 89.3-99.3) in *16-55 year old* **93.1%** (95% CI, 78.4-98.6) in *≥55 year old*	No available data	No available data	No available data	No available data	No available data	Ongoing clinical trials[xxxvii]	No available data
Effectiveness	*Effectiveness against testing positive:* **12%** (95% CI, 8-17) in first 7 days after booster **58%** (95% CI, 56-61) 14 days after booster **85%** (95% CI, 83-86) 28 days after booster	*Effectiveness against infection:* **94%** (95% CI, 91-95) **91%** (95% CI, 90-92) **87%** (95% CI, 83-91) *Effectiveness against hospitalization:*	No available data	No available data	No available data	*Effectiveness against symptomatic infection:* **78.8%** (95% CI, 76.8-80.6) *Effectiveness against hospitalization:* **86.3%**	No available data	No available data

[cliv] UK's minimum gap for Covid-19 booster jabs to be halved to three months. *The Guardian* [press release]. Accessed on 12 December 2021. https://www.theguardian.com/world/2021/nov/29/covid-booster-jabs-to-be-offered-to-all-uk-adults-after-three-month-gap

	Effectiveness against symptomatic infection: **92%** (95% CI, 91-92) **85.6%** (95% CI, 79.2-90.1) relative to two doses **88%** (95% CI, 87-88) **82%** (95% CI, 79-85) *Effectiveness in ≥50:* **84.4%** (95% CI, 82.8-85.8) against symptomatic COVID-19 **94.0%** (93.4-94.6) against symptomatic COVID-19 compared with unvaccinated *Effectiveness against hospitalization:* **87%** 0-6 days after receiving booster dose **92% to 97% lower** than those	**86%** (95% CI, 82-89)				*Effectiveness against ICU admission:* **92.2%** *Effectiveness against COVID-19 related death:* **86.7%**		

	who received 2 doses **88%** (95% CI, 86-90)							
Effectiveness against Variants	**Delta (B.1.617.2):** **77%** (95% CI, 75.0-79.0) against infection [USA; 01-31 December 2921][11] ***Omicron (B.1.1.529):*** **75.5%** (95% CI, 56.1-86.3) effectiveness against symptomatic infection[17] If assuming 25-fold decrease compared to wild-type, **81%** (95% CI, 59-95) **54.6%** (95% CI, 30.4-70.4) effectiveness against symptomatic infection in ≥60-year-old[19]	**Delta (B.1.617.2):** 95.2% (93.4%-96.4%) **Omicron (B1.1.529):** 62.5% (95% CI 56.2-67.9%)[21]		***Omicron (B.1.1.529):*** **63%** (95% CI, 31-81) against hospitalization 0-13 days post booster **84%** (95% CI, 67-92) against hospitalization 14-27 days post booster **85%** (95% CI, 54-95) against hospitalization 1-2 months post booster[120]				

	62% (95% CI, 59.0-65.0) against infection [USA; 01-31 December 2021][11] **91%** (95 CI, 85.0-94.0) against hospitalization [USA; 01-31 December][11] **96%** (95% CI, 91.0-98.0) against death [USA; 01-31 December][11]							
Immunogenicity	*Neutralizing titers:* Elicits **>5-8 more** for wild type after 6 months after 2nd dose **6.1-fold increase** (95% CI, 5.5-6.8) following booster compared to 2-initial doses **97.6%** (mean 95.9%) inhibition one month after booster[121]	Booster doses (mRNA1273 or mRNA1273.351) increased neutralizing antibody titers against wild-type	*Antibody Levels:* Higher levels after third dose (tIgG EU **3746**; IQR: 2047-6420) *Spike Cellular Immune Response:* Increased from **200 SFUx10^6 PBMC (IQR, 127-389)** after the second dose to **399 SFUx10^6 PBMC (IQR, 314-662)** after the third one	5X10^{10} vp booster dose elicited **9-fold** increase at day 7 compared to first dose after 29 days in 18-55-year-olds 1.25X10^{10} vp booster dose elicited **6-7.7-fold** increase at day 28 compared to first dose after 29 days in 18-55 and ≥65-year-old	*Specific Antibodies:* **99.66%** participants had detectable antibodies 28 days after the booster *IgG Seroconversion:* **175/176** vaccinees were seropositive for IgG 14 days after receiving third dose	*Seropositivity:* **Adults (≥18):** **98%** (95% CI, 90.76-99.96) in participants who received their 2nd dose 14 days apart and 3rd dose 2 months afterwards[125] **100%** (95% CI, 93.51-100.00) in participants who received their 2nd dose 14 days apart and 3rd dose	*Neutralizing Antibodies ($PRNT_{50}$):* **30-fold increase** with **746 GMT** (95% CI, 515-1081) 4 weeks after booster *S-protein IgG:* Increase of IgG to **11,119 GMT** (95% CI, 8,689-14,229) 4 weeks after booster dose *Anti-RBD & Anti-nucleocapsid IgG:*	*Anti-spike IgG:* Increase of **4.6-fold** compared to peak response after 2nd dose (**Day 217 GMEU = 200408**; 95% CI: 159796-251342) *Wild-type Neutralizing Response:* Increase of **4.3-fold** compared to peak response after 2nd dose **(IC50 = 6231;**

	18104 GMT (95% CI, 13911-23560)[122] *IgG Antibodies:* **1.7-fold increase** (95% CI, 1.6-1.9) following booster compared to 2-initial doses ***≥ 60 years:*** *Neutralizing antibody:* **9.34 times higher** than second dose *IgG Antibodies in* **97%** seroconversion with increase in IgG antibody titers **33-fold increase** in IgG after booster dose			*S-binding Antibodies:* Higher levels in booster group (**beta coefficient: 0.64** [98.3% CI< 0.41-0.81]) **97%** response[123] *Neutralizing Antibodies:* Increase observed after booster **98%** response[123] *Interferon-γ/ T Cells Levels:* **Increase** in T cell recall **72.7%** response[123]	Mean IgG value increased **8.00-fold** compared to before third vaccination **6.1-fold increase** 28 days after booster dose compared to 28 days after second dose[124] *Anti-RBD IgG:* Increased by **8.14-fold** higher than before third vaccine *Memory B cells:* Third dose increased the percentage of RBD-specific memory B cells **(0.96%)**	8 months afterwards[125] **100%** (95% CI, 92.60-100.00) in participants who received their 2nd dose 28 days apart and 3rd dose 2 months afterwards[125] **100%** (95% CI, 92.60-100.00) in participants who received their 2nd dose 28 days apart and 3rd dose 8 months afterwards[125] **Older adults (≥60):** **96%** (95% CI, 81.65-99.91)[125] *Neutralizing Antibodies:* **60%** higher NAbs activity against wild-type compared to 2-doses **Adults (≥18):** **74.2 GMT** (95% CI, 59.0-93.3) in participants 14d-	**Increase** in IgG antibodies 4 weeks after booster dose	**95% CI: 4738-8195)** *Serum IgG:* **4.7-fold increase** from **43,905 EU** following primary vaccination to **204,367 EU** following booster *Older Participants (60-84):* **5.4-fold** increase in antibody response **5.1-fold increase** in serum IgG *Younger Participants (18-59):* **3.7-fold** increase in antibody response **4.1-fold increase** in serum IgG

						2m 28 days after booster [125] **175.1 GMT** (95% CI, 138.221.0) in participants 14d-8m 28 days after booster [125] **51.9 GMT** (95% CI, 41.3-65.3) in participants 28d-2m 28 days after booster [125] **215.7 GMT** (95% CI, 162.6-286.2) in participants 28d-8m 28 days after booster [125] **Older Adults (≥60):** **178.9 GMT** (95% CI, 125.2-255.6) in participants 28d-8m 28 days after booster [125] *<u>Anti-S IgG and NAbs:</u>* **20-fold** increase 4 weeks post booster vaccination NAbs were maintained **60** to **180 days** post booster		

Immunogenicity against variants	**Beta (B.1.351):** Elicits **15-21** more neutralizing titers for Beta variant after 6 months after 2nd dose **Delta (B.1.671.2):** **>5-fold** increase in neutralizing titers against Delta compared to dose 2 titers in 18–55-year-olds **>11-fold** increase in neutralizing titers against Delta compared to dose 2 titers in 65–85-year-olds **Omicron (B.1.1.529):** **37.0-fold decrease** in neutralization compared to Delta after 0.5 months after booster **24.5-fold decrease** in neutralization compared to Delta after 3 months after booster	Preliminary results of booster doses of mRNA-1273 vaccine show robust antibody response against Delta variant **Beta (B.1.351):** **6.7-fold** increase in neutralization against Beta compared to 2-initial doses **Omicron (B.1.1.529):** **12-fold increase** in neutralization titer (GMT) against Omicron compared to 2-initial doses[128]	Third dose provided higher antibody titters against Alpha, Beta, and Delta variants	No available data	**Beta (B.1.351):** **71.6%** plasma inhibitions against Beta variant **215.7 pVNT** neutralizing antibodies against Beta variant 14 days after booster[129] **Delta (B.1.671.2):** **83.4%%** plasma inhibitions against Delta variant **250.8 pVNT** neutralizing antibodies against Delta 14 days after booster[129] **Lambda:** **89.0%** plasma inhibitions against Lambda variant **Omicron:** **4-fold increase** in neutralization titer against Omicron compared to 2-dose vaccination[128]	**Beta (B.1.351):** **3.0-fold** decrease in neutralizing antibodies compared to wild type **Gamma (P.1):** **3.1-fold** decrease in neutralizing antibodies compared to wild type **Delta (B.1.671.2):** **2.3-fold** decrease in neutralizing antibodies compared to wild type **2.5-fold** higher neutralizing potency than 2-dose vaccination	**Alpha (B.1.1.7):** **161-fold increase** with **338 GMT** (95% CI, 188-607) 4 weeks after booster dose **Beta (B.1.351):** **265-fold increase** with **147.3 GMT** (95% CI, 75-289) 4 weeks after booster dose **Delta (B.1.671.2):** **32.6-fold increase** with **252 GMT** (95% CI, 133-482) 4 weeks after booster dose **Delta Plus:** **174-fold increase** with **174 GMT** (95% CI, 64-474) 4 weeks after booster dose	High levels of functional antibodies against Alpha (B.1.1.7), Beta (B.1.351), and Delta (B.1.671.2) **Alpha (B.1.1.7):** **21.9-fold increase** in anti-S IgG compared to 2-initial doses **Beta (B.1.351):** **40.6-fold increase** in serum IgG[130] **24.5-fold increase** in anti-S IgG compared to 2-initial doses **Delta (B.1.671.2):** Increase of **6.6-fold** in antibody response compared to Delta response observed with primary vaccination **24.4-fold increase** in anti-S

	17-fold increase in neutralization titer compared to 2-initial doses[126] **41-fold increase** (95% CI, 30-56) in neutralizing antibodies compared to 2-initial dose in **younger participants**[127] **43-fold increase** (95% CI, 32-58) in neutralizing antibodies compared to 2-initial doses in **middle-aged**[127] **27-fold increase** (95% CI, 20-36) in neutralizing antibodies compared to 2-initial doses in **older participants**[127]				**11-fold decrease** in neutralization titer 14 days after booster dose compared to wild type[128] **3.3-fold increase** in neutralizing activity 28 days after booster compared to 2-initial doses against Omicron[124] **48.73 pVNT** neutralizing antibodies against Omicron 14 days after booster[129]			IgG compared to 2-initial doses **Omicron (B.1.1.529): 20.1-fold increase** in anti-S IgG compared to 2-initial doses[130]
Reactogenicity	Preliminary results show consistent tolerability	Similar safety and tolerability compared to second dose	Lower reactogenicity after third dose compared to first dose	No available data	Ongoing trial	The third shot is considered to be safe *Common side effects:*	Most reported adverse events were **mild and resolved within 24 hours**	Booster dose was **well tolerated** Local and systemic **reactogenicity increased**

	25% reported at least one adverse event *Common solicited AE:* Injection site pain, injection site redness, injection site swelling, fatigure, muscle pain, fever *≥Grade 3 AE:* **6.6%** reported grade 3 or higher reactogenicity with **0.7%** being local reactions and **5.9%** systemic events	*Common solicited local adverse events:* Injection-site pain **(68.4% for mRNA-1273.351, 90% for mRNA-1273)** fatigue **(36.8% for mRNA-1273.351, 70% for mRNA-1273)** headache **(36.8% for mRNA1273.351, 55.0% for mRNA-1273)** myalgia **(31.6% for mRNA-1273.351, 45.0% for mRNA-1273)** arthralgia **(21.1% for mRNA-1273, 50.0% for mRNA-1273)**				Pain at the injection site. *Adverse events:* Unrelated to the vaccination	*Solicited Adverse Events:* **8** solicited adverse events were reported **5.4%** care of pain, **2.1%** itching **1%** redness	between Dose 1, Dose 2, and Dose 3 **90%** of symptoms were rated as mild or moderate
Protection against COVID-19	***Confirmed Infection:*** Adults (≥18): **93% relative reduction** in symptomatic infection (hazard ratio: 0.07; 95% CI, 0.02-0.20)[131]	No available information	No available information	No available information	No available information	No available information	Ongoing clinical trials[xxxvii]	No available information

	92% relative reduction in asymptomatic infection (hazard ratio: 0.08; 95% CI, 0.01-0.48)[131] Youngest age group (16-29): **17.2 (95% CI, 15.4-19.2) lower rate** in booster group 30-39 age group: **9.0 (95% CI, 8.4-9.7) lower rate** in booster group 40-49 age group: **9.7 (95% CI, 9.2-10.3) lower rate** in booster group 50-59 age group: **12.2 (95% CI, 11.4-13.0) lower rate** in booster group Oldest age group (≥60): **12.3 (95% CI, 10.4-12.3) lower rate** in booster group								

	12.3 (95% CI, 11.8-12.8) lower rate in booster group ***Severe Illness:*** 40-59 age group: **21.7 (95% CI, 10.6-44.2) lower rate** in booster group Older population (≥60): **19.5 (95% CI, 12.9-29.5) lower rate** in booster group **17.9 (95% CI, 15.1-21.2) lower rate** in booster group ***Mortality:*** ≥60 years old: **14.7 (95% CI, 10.0-21.4) lower rate** in booster group ≥50 years old: Adjusted hazard ratio for death due								

	to COVID-19 in booster compared to non-booster was **0.10 (95% CI, 0.07 to 0.14)** or **90% lower** mortality rate							
Duration of Protection	*≥60 years old:* 3 months after booster dose, neutralizing antibody levels remained adequate although significant decrease is reported **(25,429 AU/mL to 8306 AU/mL)** *Viral Load:* **52% decrease** in Ct-reduction post the booster shot over time (decline in reducing viral loads over time)	No available data	No available data	No available data	No available data	No available data	No available data	No available data
Other	Detailed report from Pfizer regarding booster doses can be found here: https://www.fda.gov/media/152161/download					For more detailed information regarding immunogenicity of		

	14-20 days after booster, marginal effectiveness increases to **70-84%** ***<u>Incidence Rate:</u>*** <u>Infection in individuals <60:</u> **0.22 (95% CI, 0.22-0.23) incidence rate** in booster compared to non-booster <u>Infection in individuals ≥60:</u> **0.16 (95% CI, 0.15-0.17) incidence rate** in booster compared to non-booster <u>Severe illness in individuals <60:</u> **0.33 (95% CI, 0.21-0.52) incidence rate** in booster compared to non-booster					third dose refer to study[clv]		

[clv] A third dose of inactivated vaccine augments the potency, breadth, and duration of anamnestic responses against SARS-CoV-2. *medRxiv.* *https://www.medrxiv.org/content/10.1101/2021.09.02.21261735v1*

	Severe illness in individuals ≥60: **0.12 (95% CI, 0.10-0.14) incidence rate** in booster compared to non-booster							
	HETEROLOGOUS BOOSTER DOSES							
Vaccine Schedule	*Heterologous 1:* **mRNA1273/BNT162b2** *Heterologous 2:* **Ad26.CoV.2.S/BNT162b2** *Heterologous 3:* **ChAdOx1/BNT162b2** *Received BNT162b2 as booster dose	*Heterologous 1:* **BNT162b2/mRNA1273** *Heterologous 2:* **Ad26.CoV.2.S/mRNA1273** *Heterologous 3:* **ChAdOx1/mRNA1273** *Received mRNA1273 as booster dose	*Heterologous 1:* **BNT162b2/ChAdOx1*** *Received ChAdOx1 as booster dose	*Heterologous 1:* **BNT162b2/Ad26.CoV.2.S** *Heterologous 2:* **mRNA1273/Ad26.CoV.2.S** *Heterologous 3:* **ChAdOx1/Ad26.CoV.2.S.** *Received Ad26.CoV.2 as booster dose	*Heterologous 1:* **SinoPharm/BNT162b2**	*Heterologous 1:* **CoronaVac/ChAdOx1** *Heterologous 2 :* **CoronaVac/BNT162b2** *Heterologous 3 :* **CoronaVac/SinoPharm** *Heterologous 4:* **CoronaVac/mRNA1273** *Received CoronaVac as initial regimen	No available data	*Heterologous 1:* **BNT162b2/NVX-CoV2373** *Heterologous 2:* **ChAdOx1/NVX-CoV2373** *Received NVX-CoV2373 as booster dose
Time-to-booster dose	At least **3 months** after receiving two dose regimen	At least **3 months** after receiving two dose regimen	**6 months** after initial two-dose regimen	**4 months** after initial two-dose BNT162b2 regimen At least **3 months** after receiving two dose regimen	**6 months** after initial two-dose regimen	*Heterologous 1:* **21 to 26 days** after full jab of CoronaVac *Heterologous 2:*	No available data	**6 months** after initial two-dose regimen

Effectiveness	*Heterologous 1:* **94%** (95% CI, 91-96) effectiveness against infection *Heterologous 2 – Effectiveness in ≥50:* **87.4%** (95% CI, 84.9-89.4) against symptomatic COVID-19[132] **93.1%** (95% CI, 91.7-94.3) against symptomatic COVID-19 compared to unvaccinated	*Heterologous 1:* **92%** (95% CI, 88-95) effectiveness against infection *Heterologous 3:* **91%** (95% CI, 63-98) effectiveness against infection	No available data	No available data	No available data	**6 months** after primary vaccination of CoronaVac *Heterologous 3:* **6 months** after primary vaccination of CoronaVac *Heterologous 4:* **6 months** after primary vaccination of CoronaVac *Heterologous 1:* **93.2%** (95% CI, 92.9-93.6) against symptomatic infections **97.7%** against hospitalization **98.9%** against ICU admission **98.1%** against COVID-19 related death *Heterologous 2:*	No available data	No available data

Effectiveness against Variants	*Heterologous 3:* **82%** (95% CI, 68-90) effectiveness against infection No available data	No available data	***Omicron (B.1.1.529):*** *Heterologous 1:* **71.4%** (95% CI, 41.8-86.0) against symptomatic infection[17]	No available data	No available data	**96.5%** (95% CI, 96.2-96.7) against symptomatic infections **96.1%** against hospitalization **96.2%** against ICU admission **96.8%** against COVID-19 related death No available data	No available data	No available data
Immunogenicity	*Binding Antibody Responses:* **2-fold or greater rise** in bAb noted in **98-100%** of BNT162b2 recipients *Neutralizing Antibody Responses:*	*Binding Antibody Responses:* **2-fold or greater rise** in bAb noted in **96-100%** of mRNA1273 recipients *Neutralizing Antibody Responses:*	***Heterologous 1:*** *Anti-spike IgG:* In individuals <70: **12440 ELU/mL** (95% CI, 10420-14852) In individuals ≥70: **14961 ELU/mL** (95% CI, 12065-18551)	***Heterologous 1:*** **14.8 to 32.4-fold** increase in neutralization titers against wild-type virus *Binding Antibody Responses (bAb):*	No available data	***Heterologous 1:*** Heterologous vaccination had a **9-fold greater GMT** (7,947 U/mL) than fully patients fully vaccinated with AZD1222 and the	No available data	***Heterologous 1:*** *Anti-spike IgG:* In individuals <70: **14961 ELU/mL** (95% CI, 12065-18551) In individuals ≥70: **9130 EUL/mL** (95% CI, 6783-12289)

	341.3-677.9 IU50/mL 15 days after booster with BNT162b2 Participants who received mRNA-based booster vaccination had four-fold increase compared to Ad26.COV2.S. ***Heterologous 2:*** *S-binding Antibodies:* **Higher levels** after booster **(beta coefficient: 0.73,** [98.3% CI, 0.57-0.90])[123] *Neutralizing Antibodies:* **Higher levels** in booster compared to 2 doses **100%** response[123] *T-Cell/ Interferon-γ:* **Higher levels** in booster compared to 2 doses **91.5%** response[123]	**676.1-901.8 IU50/mL** 15 days after booster with mRNA1273 Participants who received mRNA-based booster vaccination had four-fold increase compared to Ad26.COV2.S. ***Heterologous 1:*** *Anti-spike IgG:* In individuals <70: **44547 ELU/mL** (95% CI, 38424-51645) In individuals ≥70: **25118 ELU/mL** (95% CI, 17698-35650) *Cellular Response :* In individulas <70 : **143 (95% CI, 82-250)** In individuals ≥70: **88 (95% CI, 46-168)** ***Heterologous 2:***	*Cellular Response :* In individuals <70 : **105** (95% CI, 67-164) In individuals ≥70: **84** (95% CI, 45-156)	**2-fold or greater rise** in bAb noted in **98-100%** of Ad26.COV2.S. recipients *Neutralizing Antibody Responses:* **31.2-382.2 IU50/mL** 15 days after booster with Ad26.COV2.S. *Anti-spike IgG:* In individuals >70: **17312 ELU/mL** (95% CI, 13678-21911) In individuals ≥70: **16855 ELU/mL** (95% CI, 13360-21264) *Cellular Response:* In individuals <70: **114** (95% CI, 55-236) In individuals ≥70: **109** (95% CI, 64-187) ***Heterologous 3 :*** *Anti-spike IgG:*		highest antibody response, IgA, and neutralizing antibodies than other groups *Neutralizing Antibody Responses:* **12.4-fold** increase in neutralizing response[134] *Anti-RBD Antibody:* **9865 U/mL** 14-days after booster **7947 BAU/mL** (95% CI, 7277,8679) 14-days after booster leading to **9-fold** greater than individuals fully vaccinated with ChAdOx1[135] *Anti-RBD IgG:* **1492 BAU/mL** (95% CI, 1367-1629) 14-days after booster[135]		*Cellular Response:* In individuals <70: **69** (95% CI, 45-156) In individuals ≥70: **45** (95% CI, 22-92) ***Heterologous 2:*** *Anti-spike IgG:* In individuals <70: **8389 ELU/mL** (95% CI, 6599-10665) In individuals ≥70: **5822 ELU/mL** (95% CI, 4495-7541) *Cellular Response:* In individuals <70: **137** (95% CI, 88-213) In individuals ≥70: **55** (95% CI, 35-89)

	Heterologous 3: *Anti-spike IgG:* In individuals <70: **22479 ELU/mL** (95% CI, 18276-27648) Individuals ≥70: **19091 EUL/mL** (95% CI, 15554-23432) **2364 BAU/mL** 14-days after booster[133] *Cellular Response:* In individuals <70 : **119 (95% CI, 83-169)** sport forming cells per 10^6 peripheral blood mononuclear cells In individuals ≥70: **113 (95% CI, 64-200)** sport forming cells per 10^6 peripheral blood mononuclear cells	*S-binding Antibodies:* **Higher levels** after booster **(beta coefficient: 0.94,** [98.3% CI, 0.85-1.12])[123] *Neutralizing Antibodies:* **Higher levels** in booster compared to 2 doses **100%** response[123] *T-Cell/ Interferon-γ:* **Higher levels** in booster compared to 2 doses **91.7%** response[123] ***Heterologous 3:*** *Anti-spike IgG:* In individuals <70: **35522 ELU/mL** (95% CI, 29205-43204) In individuals ≥70: **27702 ELU/mL** (95% CI, 21337-35966)		In individuals <70: **5582 ELU/mL** (95% CI, 4415-7057) In individuals ≥70: **5464 ELU/mL** (95% CI, 4266-6998) *Cellular Response:* In individuals <70: **141** (95% CI, 100-200) In individuals ≥70: **82** (95% CI, 54-124)		**1358 BAU/mL** 14-days after booster[133] *Anti-S1-IgA:* **5.25 OD/CO** (IQR, 3.94-9.00) 14-days after booster[135] ***Heterologous 2:*** Median values of IgG-S titers were higher in group that received BNT162b2 as booster than CoronaVac BNT162b2 boosted IgG-S median titers by **factor of 46.6** but IgG-N titers decreased by **factor of 6.5** *Neutralizing Antibody Responses:* **11.2-fold increase** in neutralizing response[134]		

		Cellular Response: In individuals <70: **228** (95% CI, 177-294) In individuals ≥70: **101** (95% CI, 54-187)				*Anti-spike RBD:* Single booster dose of BNT162b2 induced higher anti-spike RBD IgG antibody levels, compared to single booster dose of CoronaVac **20,787 U/mL** 14 days after booster **5152 BAU/mL** 14 days after booster[133] ***Heterologous 3:*** *Anti-spike RBD:* **1073 U/mL** 14 days after booster **154 BAU/mL** 14 days after booster[133] ***Heterologous 4:*** *IgG:* **9.3-fold increase** in median IgG titer compared to 2-		

						initial doses **(250 to 2313 BAU/mL)** *Seropositivity:* Increase from **96.4% to 100%** after booster dose		
Immunogenicity against variants	*Binding Antibody Responses:* Baseline bAb levels for **Delta** were **34-45% lower** compared to Wa-1 strain Following boost, bAB levels for **Delta** were **15-36% lowe**r compared to Wa-1 strain ***Heterologous 1:*** *Neutralizing Ab:* **22.7-fold decrease** in neutralization after 0.5 months after booster compared to **Delta** ***Heterologous 3:***	*Binding Antibody Responses:* Baseline bAb levels for **Delta were 34-45% lower** compared to Wa-1 strain Following boost, bAB levels for **Delta** were **15-36% lower** compared to Wa-1 strain *Neutralizing Antibody Responses:* **Delta and Beta** variants were only available in those boosted with mRNA-1273 ***Heterologous 1:***	*AZD1222/ BNT162b2* Demonstrated **80%** response rate against Omicron serum sample & **14.7-fold** decrease in GMT[137] *AZD1222/ mRNA-1273* Demonstrated **82%** response rate against Omicron serum sample & **17.5-fold** decrease in GMT *Pseudovirus neutralizing antibody NT_{50}:* **260 GMT** (95% CI, 217-313) against **Delta**	***Heterologous 1:*** **10.9 to 21.2-fold** increase in pseudo virus neutralization assay (one volunteer did not have any against B.1.351) *Binding Antibody Responses:* Baseline bAb levels for **Delta** were **34-45% lower** compared to Wa-1 strain Following boost, bAB levels for **Delta** were **15-36% lower** compared to Wa-1 strain *Pseudotype virus neutralizing antibody NT_{50}:*	No available data	***Heterologous 1:*** *Neutralizing antibodies*: **wild type > B.1.617.2 > B.1.1.7 > B.1.351** **B.1.351 > wild type > B.1.1.7 > B.1.617.2** Individuals boosted had higher neutralizing antibodies compared to two doses of either vaccine ($p<0.0001$)[135] **271 $PRNT_{50}$** 14 days after booster against **Delta** variant[133] ***Heterologous 2:***	No available data	***Heterologous 1:*** *Pseudotype neutralizing antibody NT_{50}:* **165 GMT** (95% CI, 131-209) against **Delta** ***Heterologous 2:*** *Pseudotype neutralizing antibody NT_{50}:* **124 GMT** (95% CI, 99-156) against **Delta**

	Pseudotype virus neutralizing antibody NT_{50}: **315 GMT** (95% CI, 1314–1998) against **Delta** **470 $PRNT_{50}$** 14 days after booster against **Delta** variant[133] **521 $PRNT_{50}$** 14 days after booster against **Omicron** variant[133]	*Pseudotype virus neutralizing antibody NT_{50}:* **508.7 GMT** (95% CI, 408.6-633.4) against **Delta**[136] ***Heterologous 3:*** *Pseudotype virus neutralizing antibody NT_{50}:* **559.7 GMT** (95% CI, 441.3-709.9) against **Delta**		**418 GMT** (95% CI, 330-530) against **Delta** **41-fold increase** against **Omicron** compared to 2-initial doses ***Heterologous 3:*** *Pseudotype virus antibody NT_{50}:* **125 GMT** (95% CI, 99-159) against **Delta**		**6.3-fold increase** in neutralization titers against **Delta** 28 days after booster dose compared to 2-initial doses **6.3-fold decrease** in neutralization titers against **Omicron** 28 days after booster dose compared to wild type **411 $PRNT_{50}$** 14 days after booster against **Delta** variant[133] **543 $PRNT_{50}$** 14 days after booster against **Omicron** variant[133] ***Heterologous 3:*** **61.3 $PRNT_{50}$** 14 days after booster against **Delta** variant[133]		

Reactogenicity	*Adverse Events:* **72-92%** participants reported local pain or tenderness Malaise, myalgias, and headaches were commonly reported **14.4%** of the participants reported unsolicited adverse events	*Adverse Events:* **75-86%** participants reported local pain or tenderness Malaise, myalgias, and headaches were commonly reported **15.6%** of participants reported unsolicited adverse events	No available data	*Adverse Events:* **71-84%** participants reported local pain or tenderness Malaise, myalgias, and headaches were commonly reported **12%** of participants reported unsolicited adverse events	No available data	Similar results to homologous booster administration Reactogenicity of mRNA1273 booster was acceptable and better tolerated with increasing age and shorter time since booster dose	No available data	No available data
Other						Ongoing clinical trial examining immunogenicity and safety of third dose vaccination with ChAdOx1 or BNT162b2 vaccine among adults who received full jab of CoronaVac[clvi]		

[clvi] Third Dose Vaccination with AstraZeneca or Pfizer COVID-19 Vaccine Among Adults Received Sinovac COVID-19 Vaccine. *ClinicalTrials.gov.* https://clinicaltrials.gov/ct2/show/NCT05049226

ANNEXES

	BNT162b2/ COMIRNATY (Pfizer-BioNTech, USA)	Spikevax/ Moderna COVID-19 Vaccine/ mRNA-1273 (Moderna, USA)	Vaxzevria/ ChAdOx1 nCoV-19/ AZD1222/ Covishield (AstraZeneca/Oxford, UK, India)	Janssen COVID-19 vaccine/Johnson & Johnson (Janssen, USA)	Covilo/ BBIBP-CorV (Sinopharm, China)	CoronaVac (Sinovac, China)	COVAXIN/ BBV152 (Bharat Biotech, India)	Nuvaxovid/ NVX-CoV2373/ Covovax (Novavax, Czech Republic, India)
	FURTHER INFORMATION							
Storage conditions	2°C to 8 °C (for 1 month)	2°C to 8 °C (for 1 month)	2°C until 8 °C	2°C to 8 °C (for 3 months)	2°C until 8 °C	2°C until 8 °C	2°C until 8 °C	2°C to 8 °C
Approving authorities	FDA (11.12.20)[clvii]; EMA (21.12.20); WHO EUL (31.12.20); and list of 137 countries (including Switzerland – approved on 20.12.20)	FDA (18.12.20); EMA (06.01.21); WHO EUL (30.04.21); and list of 85 countries (including Switzerland – approved 12.01.21)	FDA (awaiting on approval); EMA (29.01.21); WHO EUL (15.02.21); and list of 137 (Vaxzevria) and 47 (Covishield) countries (Switzerland	FDA (27.02.21); EMA (11.03.21), WHO EUL (12.03.21), and list of 106 countries (including Switzerland – approved 22.03.21)	WHO EUL (07.05.21); and list of 88 countries (e.g., Argentina, Bahrain, Brazil, China, Indonesia, United Arab Emirates, Zimbabwe)	WHO EUL (01.06.21), and list of 53 countries (e.g., Albania, Chile, Egypt, Hong Kong, Malaysia, Tunisia, Turkey, Ukraine)	WHO EUL (03.11.21) and list of 13 countries (Guyana, Inidia, Iran, Mauritius, Mexico, Nepal, Paraguay, Philippines & Zimbabwe)	WHO EUL (17-20.12.21) and list of 32 countries (Nuvaxovid) and 3 countries (Covovax)

[clvii] Pfizer-BioNTech's Comirnaty Vaccine received full FDA approval on 23 August 2021 for people age 16 and above, moving it beyond emergency use status. https://www.fda.gov/news-events/press-announcements/fda-approves-first-covid-19-vaccine

			awaiting on approval)					
IMMUNOGENICITY								
Immunogenicity	*Single Dose (≥4 weeks):* **79.4% IgG seropositivity** (95% CI, 75.7-83.1)[138] *Second dose (≥4 weeks):* **96.5% IgG seropositivity** (95% CI, 94.9-98.1) to **92% IgG seropositivity onwards**[138] *7-14 days after second dose:* *18-55 years*: GMT ranged from **1.7 to 4.6** times the GMT of the convalescent serum. *65-85 years*: GMT ranged from **1.1 to 2.2** times	*14 days after second dose:* *18-55 years*: $PRNT_{80}$ GMT **654.3 (95% CI, 460.1-930.5**). *56-70 years:* $PRNT_{80}$ GMT **878 (95% CI, 516-1494**). *≥71 years*: $PRNT_{80}$ GMT **317 (95% CI, 181-557**). *8 months after second dose:* Anti-S antibody titre median **1539.5 AU/ mL** (IQR: 876.7-2626.7)[37]	*28 days after second dose median antibody titres:* *18–55 years*: **20,713 AU/mL [IQR 13,898 - 33,550**] *56–69 years*: 1**6,170 AU/mL [IQR 10,233 - 40,353]**. *≥70 years*: **17,561 AU/mL [IQR 9,705 - 37,796]**.	*IgG Antibodies:* **1299.5 AU/mL** highest median[139] *29 days after vaccination:* *18-55 years:* GMC **586 (95% CI, 445-771**); GMT **224 (95% CI, 168-298**). *≥65 years*: GMC **312 (95% CI, 246-396);** GMT **212 (95% CI, 163-266**). *57 days after vaccination:* *18-55 years*: **754 (95% CI, 592-961**); GMT **288 (95% CI, 221-376**). *8 months after second dose:*	*14 days after second dose:* *18-55 years:* GMT ***211.2*** **(95% CI, 158.9-280.6**). *≥60 years: GMT* ***131.5*** **(95% CI, 108.2-159.7**).	*Single dose (≥4 weeks)*: **37.7±57.08 IU/ml (min: 0, max: 317.25);** 57.02% of participants did not develop sufficient antibody titres (<25.6 IU ml) **28.1% IgG seropositivity** (95% CI, 25.0-31.2)[138] *Two doses (2 weeks):* **164.4 BAU/ mL** *Two doses (≥4 weeks)*: **194.61±174.88 IU/ml (min: 0, max: 677.82);** 11.48% of participants did not develop sufficient antibody	*IgG Antibodies:* **342.7 AU/mL** highest median[139] *Single dose (≥4 weeks:* **43.8%** seropositive for anti-spike antibody > 15 AU/mL GMT **16.8 (95% CI, 15.80-17.88)** for SARS-CoV-2 spike antibody titre *Two doses (≥4 weeks)*: **80.0%** seropositive for anti-spike antibody > 15 AU/mL GMT **48.3 (95% CI, 47.46-48.92)**	

	the GMT of the convalescent serum. *8 months after second dose:* Anti-S antibody titre median **751.2 AU/ mL** (IQR: 422.0-1381.5)[37]			Anti-S antibody titre median **451.6 AU/ mL** (IQR: 103.0-2396.7[37]		titres (<25.6 IU ml) **94.8 BAU/ mL** **77.4% IgG seropositivity** (95% CI, 75.5-79.3)[138] *Two doses (8-12 weeks):* 34.7 BAU/ mL	for SARS-CoV-2 spike antibody titre	
Immunogenicity against Delta variant	**7.77-fold reduction** in neutralization titres for **Delta (B.1.617.1)** when compared with wild-type[140] **11.30-fold reduction** in neutralization titres for **Delta (B.1.617.2)** when compared with wild-type[140] **157 $PRNT_{50}$** neutralization against **Delta (B.1.617.1)**[141]							

	355 $PRNT_{50}$ neutralization against **Delta (B.1.617.2)**[141]							
Immunogenicity against the Mu variant	6.8-fold decrease in neutralizing titres when compared to convalescent sera	Neutralizing titre similar to that of BNT162b2 sera	Neutralizing titre similar to that of BNT162b2 sera	No available data	No available data	No available data	No available data	No available data
Immunogenicity against Omicron variant (not specific to vaccines)	Fully vaccinated **17-fold** decrease in neutralization against Omicron when compared to wild type[142] Boosted (3-dose schedule) **7-fold** decrease in neutralization against Omicron when compared to wild type[142]							
Immunogenicity against Omicron variant	**29.8-fold decrease** in mean neutralizing titres compared to wild-type, **10.3-fold decrease** compared to Beta, **25.1-fold decrease** compared to Delta[143] Plasma specimens one month after full mRNA vaccination, NT_{50} values were 127±66 times	**20-fold decrease** in neutralization 6 months after vaccination compared to Delta[143] **1/10 seropositive** against Omicron[114] Plasma specimens one month after full mRNA vaccination, NT_{50} values were 127±66 times lower for Omicron	Mean neutralizing titres drop to below the detectable threshold in all but one participant[143] **0/20 seropositive** against Omicron[114] The mean Omicron titre estimate in the infected + double vaccinated group suggests protection against symptomatic	Vaccine lacked detectable neutralizing activity against Omicron.[144] Demonstrated **9%** response rate against Omicron serum sample[137]		Not a single serum sample demonstrated neutralizing antibodies against the Omicron VOC among 25 blood samples[149]	Only 5/20 live virus samples exhibited neutralization titres above the lower limit of quantification.[148]	

	lower for Omicron than the wild type (Wuhan) strain. After 5 months, the neutralization potency was 27±17 lower for Omicron.[144] Persons who had prior SARS-CoV-2 infections and then were fully (two-dose) vaccinated had NT_{50} values **154** times greater than the pre-vaccination convalescent phase titres[144] A third booster dose increased the neutralization capacity against Omicron by **38** times.[144] **11.4-fold decrease** in neutralization 6 months after vaccination compared to Delta	than the wild type (Wuhan) strain. After 5 months, the neutralization potency was 27±17 lower for Omicron.[144] Persons who had prior SARS-CoV-2 infections and then were fully (two-dose) vaccinated had NT_{50} values **154** times greater than the pre-vaccination convalescent phase titres[144] A third booster dose increased the neutralization capacity against Omicron by **38** times.[144] The mean Omicron titre estimate in the infected + double vaccinated group suggests protection against symptomatic	Omicron disease is **80%**[142] Demonstrated **50%** response rate against Omicron serum sample & **12.8-fold** decrease in GMT[137] Only 5/20 live virus samples exhibited neutralization titres above the lower limit of quantification.[148] No neutralizing antibodies were observed in serum samples obtained 1 months after the receipt of the second dose[147]					

	25-fold decrease in neutralization titers against Omicron variant compared to wild-type[145] **41-fold decrease** in neutralization level against Omicron[146] **9/20 seropositive** against Omicron [114] Demonstrated **33%** response rate against Omicron serum sample[137] **9/20 participants** neutralized Omicron variant 1 month after 2nd dose[147]	Omicron disease is **91%**[142] Demonstrated **100%** response rate against Omicron serum sample & **15.8-fold** decrease in GMT[137] No neutralizing antibodies were observed in serum samples obtained 4-6 months after the receipt of the second dose[147]							
EFFICACY									

Single dose[clviii]	**52%** (95% CI, 29.5 to 68.4; starting at 12 days) or 82.2% (75.1 to 87.3; starting at ≥14 days). **91%** (95% CI, 85-94). ≥80 years : **71.4%** (95% CI, 46.5-90.6) vaccine efficacy for symptomatic disease 14 days after one dose [United Kingdom, 18 Dec 2020 – 26 Feb 2021] ≥65 years : **56%** (95% CI 19-76) at 28-34 days and **62%** (95% CI 23-81) at 35-48 days post-vaccination [United Kingdom,	**95.2%** (95% CI, 91.2.8 to 97.4; starting at >14 days)[150].	**72.8%** (starting at 22 days up to 60 days). **88%** (95% CI, 75-94).[clx] ≥80 years : **80.4%** (95% CI, 36.4-94.5) vaccine efficacy for symptomatic disease 14 days after one dose [United Kingdom, 18 Dec 2020 – 26 Feb 2021 ≥65 years : **56%** (95% CI 19-76) at 28-34 days and **62%** (95% CI 23-81) at 35-48 days post-vaccination [United Kingdom, 8 Dec 2020 – 15 Mar 2021] [clxi]	Single dose vaccine	Unknown	**35.1%** (95% CI, -6.6 to -60.5) [conducted in a setting with high P.1 transmission].	No available data	**83.4%** (95% CI, 73.6-89.5) starting at ≥14 days

[clviii] Against SARS-COV-2 infection
[clx] Conducted between 8 December 2020 and 8 February 2021. Study sample = ≤1 million participants.
[clxi] Does not differentiate between BNT162b2 and ChAdOx1 nCoV-19.

	8 Dec 2020 – 15 Mar 2021] [clix]							
Two doses[clxii]	**95.0%** (95% CI, 90.3-97.6) starting at ≥7 days in population without prior SARS-CoV-2 infection **94.6%** (95% CI, 89.9-97.3) starting at ≥7 days in population with or without prior infection	**94.1%** (95% CI, 89.3-96.8) after median follow-up of less than 63 days **93.2%** (95% CI, 91.0-94.8) Against severe disease: **98.2%** (95% CI, 92.8-99.6) *Prevention against COVID-19 illness:* **93.2%** (95% CI, 91.0-94.8; United States) [151] *Prevention against severe disease:* **98.2%** (95% CI, 92.8-99.6; United States) [151]	**63.1% (**95% CI, 51.8-71.7) starting at ≥14 days for two standard doses **80.7%** (95% CI, 62.1-90.2) starting at ≥14 days for first low dose and standard second dose **66.7%** (95% CI, 57.4-74.0) starting at ≥14 days for pooled analysis efficacy *Against mild-to-moderate symptomatic COVID-19 >14 days after second injection*: **21.9%** (95% CI, -49.9 to 59.8; South Africa) [24	**66.9%** (95% CI 59.0-73.4) after 14 days and **66.1%** (95% CI 55.0-89.1) after 28 days for VE against moderate-severe-critical COVID-19 **76.7%** (95% CI 54.6 to 89.1) after 14 days and **85.4%** (95% CI 54.2 to 96.9) after 28 days for VE against severe-critical COVID-19	After 14 days, efficacy against symptomatic cases was **72.8%** (95% CI 58.1-82.4; in WIV04 vaccine) or **78.1%** (95% CI 64.8 to 86.3; in HBO2 vaccine).	After 14 days, efficacy against symptomatic cases was **50.7%** (95% CI 35.9 to 0-62.0). 99.17% of NAb titres were above or equal to the Nab positivity cut-off (20 units) against wild-type.	*Symptomatic SARS-CoV-2 infection:* **77.8%** (95% CI, 65.2-86.4) *Severe symptomatic SARS-CoV-2 infection:* **93.4** (95% CI, 57.1-99.8) *Symptomatic COVID-19 in ≥60 years old:* **67.8%** (95% CI, 65.2-86.4) against symptomatic COVID-19 *Symptomatic COVID-19 in 18-59 years old:* **79.4%** (95% CI, 66.0-88.2) against symptomatic COVID-19	**89.7%** (95% CI, 80.2-94.6) starting at ≥7 days **90.4%** (95% CI, 82.9-94.6) **100%** (95% CI, 87-100) against moderate-to-severe COVID-19 **100%** (95% CI, 34.6-100) against severe COVID-19 **90%** (95% CI, 80-95) (≥7 days after second dose)

[clix] Does not differentiate between BNT162b2 and ChAdOx1 nCoV-19.
[clxii] Against SARS-CoV-2 infection.

		Prevention against asymptomatic infection starting 14 days after second infection: **63.0%** (95% CI, 56.6-68.5; United States) [151]	June – 09 November 2020][152]					
Against asymptomatic infection	**90%** (starting at 14 days) regardless of symptom status	**63.0%** (95% CI, 56.6-68.5)	Statistically non-significant **reduction of 22.2%** (95% CI -9.9 to 45.0) for asymptomatic cases **61.9%** efficacy[153]	At day 71, vaccine efficacy against asymptomatic infections was **65.5%** (95% CI 39.9 to 81.1).	Efficacy against symptomatic and asymptomatic cases was **64%** (95% CI 48.8 to 74.7; in WIV04 vaccine) or 73.5% (95% CI 60.6 to 82.2; in HBO2 vaccine).	Unknown	**63.6** (95% CI, 29.0-82.4) efficacy against asymptomatic cases	Unknown
	EFFICACY AGAINST VARIANTS							
Alpha (B.1.1.7)	Two doses of the vaccine **effectively neutralize** the B.1.1.7 variant and the D614G substitution.	**NAbs remained high** and consistent with titres of the wildtype for the B.1.1.7 variant.	**70.4%** (95% CI, 43.6-84.5) against symptomatic infection with alpha variant (B.1.1.7); **28.9%** (95% CI, -77.1 to 71.4) against asymptomatic infection with B.1.1.7.	**3.6-fold** reduction in neutralization capacity when compared to wild-type.	Demonstrated reduced neutralizing capacity. However, there were no differences in the NAbs titres against B.1.351 in vaccinated individuals vs. those naturally infected,	**10.4-fold** reduction in neutralization capacity when compared to natural infection sera[154]. **85.83%** of NAb titres were above or equal to the Nab positivity cut-	$PRNT_{50}$ **0.8** when compared with wild type against Alpha (no significant difference in neutralization capacity)	Two dose efficacy against the B.1.1.7 variant **86.3%** (95% CI, 71.3-93.5)[155] **93.6%** (95% CI, 81.7-97.8) against the Alpha variant *Against non-B.1.1.7 variant*

					suggesting the vaccine has a similar level of protection against infection as natural infections.	off (20 units) against wild-type. Neutralization decreased by **4.1-fold** when compared to wild-type.		**96%** (95% CI, 74-99.5) (≥7 days after second dose) *Against B.1.1.7 variant* **86%** (95% CI, 71-94) (≥7 days after second dose)
Beta (B.1.351)	Neutralization was **diminished by a factor of 5**. Despite this, the BNT162b2 mRNA vaccine still provides some protection against B.1.351 **100%** (95% CI, 53.5-100).	NAbs were **6-fold** lower. Nevertheless, NAbs were still found to be protective.	Two doses of the vaccine had no efficacy against the B.1.351 (VE = **21.9%;** 95% CI, -49.9 to 59.8). *Against mild-to-moderate symptomatic COVID-19 associated with B.1.351 variant >14 days after second injection*: **10.4%** (95% -76.8 to 54.8; South Africa) [24 June – 09 November 2020]	Efficacy against moderate-severe-critical Covid-19 due to the variant was **52.0%** (>14 days) and **64.0%** (>28 days). Efficacy against severe-critical COVID-19 was **73.1%** (>14 days) and **81.7%** (>28 days). Demonstrated **3.6-fold** reduction in neutralization sensitivity. Neutralization titres were decreased by **6.7-fold**.	No published data	NT_{GM} **35.03 (95% CI, 27.46-44.68**); **8.75-fold** reduction in neutralization capacity when compared to natural infection sera. **82.5%** of NAb titres were above or equal to the Nab positivity cut-off (20 units) against wild-type.	GMT **61.57 (95% CI, 36.34-104.3)** against Beta variant with significant reduction in neutralization titre	**51.0%** (95% CI, -0.6-76.2) efficacy against B.1.351 variant

Gamma (P.1)	*Single dose:* *≥21 days*: **83%** against hospitalization and death. *Two doses*: *≥14 days*: **98%** against hospitalization and death.	**3.2-fold** reduction in neutralization capacity when compared to wild-type.	*Single dose:* *≥21 days*: **94%** against hospitalization and death[156]. *Two doses:* **64%** (95% CI, -2-87) [n=18] Efficacy against Zeta (P.2) [2 doses]: **69%** (95% CI, 55-78)[157]	Demonstrated **3.4-fold** reduction in neutralization sensitivity.	No published data	**49.6%** against P.1 (>14 days after 1st dose). Neutralization decreased by **7.5-fold** when compared to wild-type.	No available data	No available data
Delta (B. 1.671.2)	**Reduced NAb activity** relative to B.1.1.7 strain.	**2.1-fold** reduction in neutralization capacity when compared to wild-type.	*Single dose:* *≥21 days*: **90%** against hospitalization and death.	Demonstrated **1.6-fold** reduction in neutralization sensitivity. Neutralization titres were decreased by **5.4-fold**.	Demonstrated **reduced neutralizing capacity**. However, there were no differences in the NAbs titres against B.1.617.2 in vaccinated individuals vs. those naturally infected, suggesting the vaccine has a similar level of protection against infection as natural infections.	NT_{GM} **24.48** (95% CI,19.2-31.2). **69.17%** of NAb titres were above or equal to the Nab positivity cut-off (20 units) against wild-type.	**65.2** (95% CI, 33.1-83.0) estimated efficacy GMT **68.97** (95% CI, 24.72-192.4) against Delta variant with significant reduction in neutralization titre	No available data

Omicron (B.1.1.529)	**22.5%** (95% CI, 8.5-40.7) against symptomatic infection							
	PHASE III TRIALS RESULTS [clxiii]							
Number of participants (vaccine/ placebo)	43,448 (21,720/ 21,728)	30,420 (15,210/15,210)	17,178 (8597/8581)	39,321 (19,630/19,691)	26,917 (13,459/13458); or 26,914 (13,465/13,458)	9,823 (4,953/4,870)	25,798 (12,899/12899)	14,039 (7,020/7,019)
Total COVID-19 cases (vaccine/ control)	170(8/162)	196 (11/185)	332 (84/248)	464 (116/348)	121(26/95) or 116(21/95)	253(85/168)	130 (24/106)	106(10/96)
Efficacy estimates in Phase III trials	Starting from 7 days after 2nd dose: **95.0%** (95% CI, 90.3 to 97.6) in population without prior SARS-CoV-2 infection. Efficacy of **94.6%** (95% CI, 89.9 to 97.3) in population with or without prior infection. **100%** among	After a median follow-up of less than 63 days: Efficacy of **94.1%** (95% CI, 89.3 to 96.8; P<0.001). **100%** among adolescents (12 to <18 years old).	Two standard doses: efficacy was **63·1%** (95% CI 51.8 to 71.7; ≥14 days) while those with first low dose and standard 2nd dose the efficacy was **80.7%** (95% CI 62.1 to 90.2). Pooled analysis efficacy was	VE against moderate-severe-critical Covid-19 was **66.9%** (95% CI 59.0 to 73.4) after 14 days post vaccine administration, and **66.1%** (95% CI 55.0 to 89.1) after 28 days. VE against severe-critical COVID-19 cases was **76.7%**	After 14 days, efficacy against symptomatic cases was **72.8%** (95% CI 58.1 to 82.4; in WIV04 vaccine) or **78.1%** (95% CI 64.8 to 86.3; in HBO2 vaccine).	After 14 days, efficacy against symptomatic cases was **50.7%** (95% CI 35.9 to 0-62.0).	**77.8%** (95% CI, 65.2-86.4) against symptomatic COVID-19 starting at ≥14 days after second dose	**83.4%** (95% CI, 73.6-89.5) starting at ≥14 days after first dose **89.7%** (95% CI, 80.2-94.6) starting at ≥7 days after second dose

[clxiii] Phase III trials were conducted between 27 July and 14 November 2020 for BNT162b2/ COMIRNATY, 27 July and 23 October 2020 for Spikevax/ Moderna, 23 April and 6 December 2020 for Vaxzevria/ ChAdOx1 nCoV-19/ AZD1222/ Covishield, 21 September 2020 and 22 January 2021 for Janssen Covid-19 vaccine/ Johnson & Johnson, 16 July and 20 December 2020 for Sinopharm/ BBIB-CorV, 21 July and 16 December 2020 for the Sinovac/ CoronaVac vaccine, 16 November 2020 and 7 January 2021 for the COVAXIN vaccine, and 28 September 2020 and 28 November 2020 for the Novavax vaccine. All trials were conducted prior to the transmission of the more contagious variant strains, particularly the delta variant (B.1.617.2). Studies are currently ongoing to determine the effectiveness of the vaccines against the delta variant.

	adolescents (12-15 years old).		**66.7%** (95% CI 57.4 to 74.0). For any nucleic acid amplification test-positive swab: efficacy was 54.1% (95% CI 44.7 to 61.9).	(95% CI 54.6 to 89.1) after 14 days and **85.4%** (95% CI 54.2 to 96.9) after 28 days. SII-ChAdOx1 nCoV-19 has a non-inferior immune response compared to AZD1222 and an acceptable safety/ reactogenicity profile[158]				
Efficacy against hospitalization and death	**100%** (after 7 days)	**100%** (≥14 days)	**100%** (after 21 days)	**76.7%** (≥14 days) or **85.4%** (≥28 days)	**100%** (>14 days)	**100%** (>14 days)	**93.4%** (>14 days) against severe COVID-19	**100%** (after 7 days).
Phase III clinical trial serious adverse events	Serious adverse events were observed in a similar proportion of vaccine (0.6%) and placebo (0.5%) recipients. These events also occur at a similar frequency within the general population.	The frequency of grade 3 adverse events was similar in both the vaccine (1.5%) and placebo groups (1.3). Serious adverse events were observed in a similar proportion in both groups (0.6%). 3 Bell's Palsy cases occurred in the vaccine group and	Serious adverse events were balanced across the study arms. 79 cases occurred in the vaccine group and 89 cases in the placebo group – 3 cases were considered related to the experimental or control vaccine (out of 11 636 vaccine recipients):	Serious adverse events were reported in 0.4% of vaccine recipients and 0.4% of placebo recipients. Seven of the serious adverse events were considered to be related to the vaccine: Guillain-Barré syndrome (1), pericarditis (1), brachial radiculitis	A cross-sectional survey collected data on adverse events following vaccination in the UAE - none of the symptoms were of serious nature or required hospitalization.	Overall incidence of serious adverse events was 0.5% (31 in placebo group and 33 in vaccine group). All adverse events were determined to be unrelated to the vaccine.	Rates of local and systemic AEs reported in the BBV152 group as mild (11·2%), moderate (0·8%), or severe (0·3%) were comparable to the placebo group 15 deaths, none considered related to the vaccine or placebo	<u>Phase II:</u> Nine serious adverse events were reported, only one of which was assessed as related to the vaccine: acute colitis.

		one Bell's Palsy case occurred in the placebo group.	transverse myelitis, haemolytic anaemia and a case of fever higher than 40°C.	(1), hypersensitivity (1), Bell's Palsy (2), & severe generalized weakness, fever & headache (1).				
	PHASE III TRIAL OTHER							
Comments	Specific populations were excluded (HIV and immunocompromised patients, and pregnant women).	Calculation of efficacy were not based on the total number of confirmed Covid-19 cases.		**2-DOSE EFFICACY** *Efficacy against symptomatic (moderate to severe/ critical) SARS-CoV-2 infection:* **94%** (95% CI, 58-100) in the US. **75%** (95% CI, 55-87) globally. *Efficacy against severe/ critical SARS-CoV-2 infection:* **100%** (95% CI, 33-100)	Only 2 severe cases occurred in the control group and none in the vaccine group (very few cases to get a reliable estimate).	-	-	Novavax is currently awaiting FDA and EMA approval.

	VACCINE PRODUCTION SITES

	BNT162b2/ COMIRNATY (Pfizer-BioNTech, USA)[clxiv]	**Spikevax/ Moderna COVID-19 Vaccine/ mRNA-1273 (Moderna, USA)**[clxv]	**Vaxzevria/ ChAdOx1 nCoV-19/ AZD1222/ Covishield (AstraZeneca/Oxford, UK, India)**[clxvi]	**Janssen COVID-19 vaccine/Johnson & Johnson (Janssen, USA)**[clxvii]	**Sinopharm/BBIBP-CorV, China**[clxviii]	**Sinovac CoronaVac, China**[clxix]	**COVAXIN / BBV152 (Bharat Biotech, India)**	**Nuvaxovid/ NVX-CoV2373/ Covovax**
EUL holder	BioNTech Manufacturing GmbH (Germany)	ModernaTX, Inc. (USA) Moderna Biotech (Spain)	AstraZeneca AB (Sweden)	Janssen-Cilag International NV (Belgium)	Beijing Institute of Biological Products Co., Ltd. (BIBP) (China)	Sinovac Life Sciences Co., Ltd. (China)	Bharat Biotech International Limited (India)	Novavax CZ a.s. (Czech Republic) Covovax Serum Institute of India Pvt. Ltd. (India)
Production sites (Drug substance)	BioNTech Manufacturing GmbH (Mainz, Germany) BioNTech Manufacturing Marburg (Marburg, Germany) Rentschler Biopharma SE	Lonza Biologics, Inc., (USA) Moderna TX, Inc. (USA) Lonza AG (Switzerland)	Henogen S.A (Belgium) Catalent Maryland, Inc. (USA) Oxford Biomedica (UK) Ltd. (United Kingdom)	Janssen Vaccines & Prevention B.V. (The Netherlands) Janssen Biologics B.V. (The Netherlands) Emergent Manufacturing Operations Baltimore LLC (USA)	Beijing Institute of Biological Products Co., Ltd. (China)	Sinovac Life Sciences Co., Ltd. (China)	-	Novavax (Bohumil, Czech Republic)

[clxiv] WHO recommendation BioNTech Tozinameran – COVID-19 mRNA vaccine (nucleoside modified) – COMIRNATY. *WHO.* https://extranet.who.int/pqweb/vaccines/who-recommendation-covid-19-mrna-vaccine-nucleoside-modified-comirnaty

[clxv] 1. WHO recommendation ModernaTX, Inc/USFDA COVID-19 mRNA vaccine (nucleoside modified). *WHO*. https://extranet.who.int/pqweb/vaccines/who-recommendation-modernatx-incusfda-covid-19-mrna-vaccine-nucleoside-modified
2. WHO recommendation Moderna COVID-19 mRNA Vaccine (nucleoside modified). *WHO*. https://extranet.who.int/pqweb/vaccines/covid-19-mrna-vaccine-nucleoside-modified

[clxvi] WHO recommendation AstraZeneca/ EU approved sites COVID-19 vaccine (ChAdOx1-S) [recombinant]. *WHO.* https://extranet.who.int/pqweb/vaccines/covid-19-vaccine-chadox1-s-recombinant-0

[clxvii] WHO recommendation Janssen-Cilag International NV (Belgium) COVID-19 Vaccine (Ad26.COV2-S [recombinant]). *WHO*. https://extranet.who.int/pqweb/vaccines/who-recommendation-janssen-cilag-international-nv-belgium-covid-19-vaccine-ad26cov2-s

[clxviii] WHO recommendation COVID-19 vaccine BIBP/Sinopharm. *WHO.* https://extranet.who.int/pqweb/vaccines/who-recommendation-covid-19-vaccine-bibp

[clxix] WHO recommendation of Sinovac COVID-19 vaccine (Vero Cell [Inactivated]) – CoronaVac. *WHO*. https://extranet.who.int/pqweb/vaccines/who-recommendation-sinovac-covid-19-vaccine-vero-cell-inactivated-coronavac

	(Laupheim, Germany) Wyeth BioPharma Division of Wyeth Pharmaceuticals (USA)		SK Bioscience (Republic of Korea) Halix B.V (Netherlands) WuXi Biologics (China)					
Production sites (Drug product)	Baxter Oncology GmbH (Halle/ Westfallen, Germany) BioNTech Manufacturing GmbH (Mainz, Germany) Pfizer Manufacturing Belgium NV (Belgium) Novartis Pharma Stein AG (Switzerland) Mibe GmbH Arzneimittel (Brehna, Germany) Delpharm Saint-Remy (France)	Baxter Pharmaceutical Solutions, LLC. (USA) Catalent Indiana, LLC. (USA) Rovi Pharma Industrial Services, S.A. (Spain)	Catalent Anagni (Italy) CP Pharmaceuticals (United Kingdom) IDT Biologika (Germany) SK Bioscience (Republic of Korea) Universal Farma, S.L. ("Chemo") (Spain) Amylin Ohio LLC (USA)	Janssen Biologics B.V. (The Netherlands) Janssen Pharmaceutica NV (Belgium) Aspen SVP. (South Africa) Catalent Indiana LLC. (USA) Grand River Aseptic Manufacturing Inc. (USA) Catalent Anagni S.R.L. (Italy)	Beijing Institute of Biological Products Co., Ltd. (China)	Sinovac Life Sciences Co., Ltd. (China)	-	Novavax (Bohumil, Czech Republic)

	Sanofi-Aventis Deutschland GmbH (Germany)							
Diluent suppliers	Pfizer Perth, Australia Fresenius Kabi, USA	-	-	-	-	-	-	-

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