Literature screening report

COVID-19 vaccines in the WHO's Emergency Use Listing (EUL) Report (11)

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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 14 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, 59.6% of the world populations, of which only 9.5% of people in low-income countries, have received at least one dose of a marketed COVID-19 vaccine as of 14 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 14.01.2021).

[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 14 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)

Vaccine immunogenicity

Since the Omicron variant's (B.1.1.529) identification in early November, and its recognition by the WHO's Technical Advisory Group on 26 November 2021 as a variant of concern, Omicron cases have soared worldwide and is on the way to becoming the dominant variant across the globe[5]. The Omicron variant is characterised by its high (30-40) number of mutations in the virus spike (S) glycoprotein[6], leading to higher affinities to the binding angiotensin-converting enzyme 2 (ACE-2) domain of the SARS-CoV-2 virus[7,8], and potential evasions of vaccine-

[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] Weekly epidemiological update on COVID-19 – 11 January 2022. *World Health Organization.* https://www.who.int/publications/m/item/weekly-epidemiological-update-on-covid-19---11-january-2022

[6] In comparison to 7-10 mutations in the other VOCs; Neutralization and Stability of SARS-CoV-2 Omicron variant*. medRxiv.* https://www.biorxiv.org/content/10.1101/2021.12.16.472934v1.full

[7] The Omicron variant increases the interaction of SARS-CoV-2 spike glycoprotein with ACE2. *bioRXiv*. https://www.biorxiv.org/content/10.1101/2021.12.06.471377v2

[8] Structural insights of SARS-CoV-2 spike protein from Delta and Omicron variants. *bioRxiv.* https://www.biorxiv.org/content/10.1101/2021.12.08.471777v1

induced immunity[9,10]. While certain data and knowledge (i.e. real world vaccine effectiveness & transmissibility) regarding the Omicron strain need further clarification and analysis, recently published studies have confirmed that although vaccine-induced immune responses against Omicron is substantially lower than that of the ancestral wild type (Wuhan) strain[11], and the Alpha, Beta and Delta VOCs[12], neutralizing antibody responses remain protective among boosted (three vaccine doses)[13,14] individuals or in previous SARS-CoV-2 infected persons who are double vaccinated[15]. Among plasma specimens of persons recently vaccinated (1.3 months) with either the Pfizer-BioNTech or Moderna vaccines, the 50% neutralization titre (NT_{50}) values were on average **127** (± 66 standard deviations; SD) times lower for the Omicron variant than the ancestral Wuhan strain[16]. Five months post full immunization, the mRNA vaccines' neutralization potency was **27** (±17SD) times lower for Omicron than for wild type. Specimens obtained from Johnson & Johnson vaccine recipients "lacked detectable neutralizing activity against the Omicron variant" at 1- and 5-months post vaccination[17]. Plasma specimens among persons who had prior SARS-CoV-2 infections and were additionally fully (two-dose schedule) vaccinated, NT_{50} values against Omicron were **154 times greater** than the pre-vaccination convalescent phase titres. Likewise, Omicron NT_{50} values from plasma samples of boosted individuals were **38 times greater** than non-boosted individuals[18].

[9] Reduced neutralization of SARS-CoV Omicron B.1.1.529 variant by post-immunization serum. *medRxiv.* https://www.medrxiv.org/content/10.1101/2021.12.10.21267534v1

[10] Reduced neutralization of SARS-CoV Omicron B.1.1.529 variant by post-immunization serum. *medRxiv.* https://www.medrxiv.org/content/10.1101/2021.12.10.21267534v1

[11] Reduced neutralization of SARS-CoV Omicron B.1.1.529 variant by post-immunization serum. *medRxiv.* https://www.medrxiv.org/content/10.1101/2021.12.10.21267534v1

[12] SARS-CoV-2 Omicron Variant neutralization in serum from vaccinated and convalescent persons. *New England Journal of Medicine.* https://www.nejm.org/doi/full/10.1056/NEJMc2119236?query=featured_home

[13] Variable loss of antiboy potency against SARS-CoV-2 B.1.1.529 (Omicron). *medRxiv.* https://www.biorxiv.org/content/10.1101/2021.12.19.473354v1

[14] Neutralization and Stability of SARS-CoV-2 Omicron variant. *medRxiv.* https://www.biorxiv.org/content/10.1101/2021.12.16.472934v1.full

[15] Imprinted SARS-CoV-2-specific memory lymphocytes define hybrid immunity. *medRxiv.* https://www.medrxiv.org/content/10.1101/2022.01.12.22269192v1

[16] Plasma neutralization of the SARS-CoV-w Omicron variant. *The New England Journal of Medicine.* https://www.nejm.org/doi/10.1056/NEJMc2119641

[17] Plasma neutralization of the SARS-CoV-w Omicron variant. *The New England Journal of Medicine.* https://www.nejm.org/doi/10.1056/NEJMc2119641

[18] Plasma neutralization of the SARS-CoV-w Omicron variant. *The New England Journal of Medicine.* https://www.nejm.org/doi/10.1056/NEJMc2119641

Neutralization activities were undetectable in plasma samples of unvaccinated SARS-CoV-2 recovered individuals and of persons with only two doses of an mRNA vaccine, while neutralizing titres ranged from **1,411 to 56,537** in vaccinated convalescent and booster persons[19]. Another study that aggregated and analysed Omicron neutralization data from 23 laboratories across Europe and the United Kingdom observed that Moderna's mRNA-1273 vaccine was the only vaccine to demonstrate an **100%** response rate to Omicron[20]. Response rates were significantly lower for the BNT162b2 (**33%;** interestingly the response rate increased to 47% after six months, indicating Omicron cross-protection over time), AZD1222 (**50%**) and Ad26.CoV2.S (**9%**) vaccines[21]. Geometric mean titres (GMT) against the Omicron strain were reduced by factors of **15.8**, **12.8**, and **28.8**, for the mRNA-1273, AZD1222 and BNT162b2 vaccines, respectively, as compared to the wild type neutralization titres[22]. Another study analysing the neutralizing antibody titres against the Omicron variant observed that the serum samples from vaccinated individuals neutralized the Omicron variant to a much lesser extent than any other variant, including Alpha, Beta, or Delta[23]. Out of all the vaccinated individuals, people who received either a homologous BNT162b2 vaccination or a heterologous ChAdOx1-S/ BNT162b2 vaccination had some cross-neutralization of the Omicron variant[23]. Overall, **1/10** participants who received the mRNA-1273 vaccine 4 to 6 months ago, **0/10** participants who received the ChAdOx1-S vaccine one month ago, **14/20** participants who received the ChAdOx1-S vaccines as their first dose and the BNT162b2 as their second dose one month ago, and **9/20** participants who received the BNT162b2 vaccine one month ago reported to have neutralizing antibodies above the 16 IC_{50} limit[23]. Lastly, studies confirm that despite mutations on the S glycoprotein, T cell reactivity against the

[19] Plasma neutralization of the SARS-CoV-w Omicron variant. *The New England Journal of Medicine.* https://www.nejm.org/doi/10.1056/NEJMc2119641

[20] Diminished neutralization responses towards SARS-CoV-2 Omicron VoC after mRNA or vector-based COVID-19 vaccinations. *medRxiv.* https://www.medrxiv.org/content/10.1101/2021.12.21.21267898v1

[21] Diminished neutralization responses towards SARS-CoV-2 Omicron VoC after mRNA or vector-based COVID-19 vaccinations. *medRxiv.* https://www.medrxiv.org/content/10.1101/2021.12.21.21267898v1

[22] Diminished neutralization responses towards SARS-CoV-2 Omicron VoC after mRNA or vector-based COVID-19 vaccinations. *medRxiv.* https://www.medrxiv.org/content/10.1101/2021.12.21.21267898v1

[23] SARS-CoV-2 Omicron Variant Neutralization in Serum from Vaccinated and Convalescent Persons. *The New England Journal of Medicine.* https://www.nejm.org/doi/full/10.1056/NEJMc2119236

Omicron strain is retained to a greater extent than neutralizing antibodies[24] (the Omicron variant is estimated to be still **83%** recognisable by the cellular and humoral component of the immune system[25]), and that booster vaccinations substantially enhance CD4+ and CD8+ T cell responses to the Omicron strain[26].

It is important to note that given the rapid emergence and global transmission of the B.1.1.529 SARS-CoV-2 strain, some of the reported studies, particularly those related to vaccination neutralization capacities against Omicron, have not been peer-reviewed and findings should be "interpreted with due consideration of this limitation"[27].

Effectiveness and Duration of Protection

As COVID-19 continues to surge worldwide throughout the Winter season, the Omicron VOC has been identified to be the cause of the majority of cases in many countries. Current literature shows that vaccine effectiveness (VE) against the latest VOC is significantly lower than that against earlier VOCs such as Beta and Delta.

Preliminary studies conducted in Canada show evidence that 2-doses of Pfizer, Moderna, or AstraZeneca vaccines were not protective against Omicron at any time points. VE was found to be **-38% (95% CI, -61.0% to -18.0%) 120-179 and -42% (95% CI, –69.0% to –19.0%)** 180-239 days after the second dose.[28] Alternatively, a study in Denmark investigating VE against Omicron contradicts these findings and show that VE was **55.2% (95% CI, 23.5 to 73.7%)** for BNT162b2 and **36.7% (95% CI: -69.9 to 76.4%)** for mRNA-1273 in the first month after primary vaccination.[29] However, these resulting VE were found to be significantly lower compared with Delta infection and

[24] T cell reactivity to the SARS-CoV-2 Omicron variant is preserved in most but not all prior infected and vaccinated individuals. *medRxiv*. https://www.medrxiv.org/content/10.1101/2022.01.04.21268586v1

[25] Preserved T cell reactivity to the SARS-CoV-2 Omicron variant indicates continued protection in vaccinated individuals. *medRxiv*. https://www.biorxiv.org/content/10.1101/2021.12.30.474453v1

[26] T cell reactivity to the SARS-CoV-2 Omicron variant is preserved in most but not all prior infected and vaccinated individuals. *medRxiv*. https://www.medrxiv.org/content/10.1101/2022.01.04.21268586v1

[27] Weekly epidemiological update on COVID-19 – 11 January 2022. *World Health Organization.* https://www.who.int/publications/m/item/weekly-epidemiological-update-on-covid-19---11-january-2022

[28] Effectiveness of COVID-19 vaccines against Omicron or Delta infection. *medRxiv.* *https://www.medrxiv.org/content/10.1101/2021.12.30.21268565v1*

[29] Vaccine effectiveness against SARS-CoV-2 infection with the Omicron or Delta variants following a two-dose or booster BNT162b2 or mRNA-1273 vaccination series: A Danish cohort study. *medRxiv.* https://www.medrxiv.org/content/10.1101/2021.12.20.21267966v3

declined rapidly over time.[30] Results of the Danish study regarding VE of mRNA-1273 against Omicron were further corroborated by a study conducted in the United States which evidenced that VE against Omicron infection was **30.4% (95% CI, 5.0%-49.0%)** at 14-90 days after complete vaccination and declined quickly thereafter.[31]

Further, a study conducted in South Africa investigating the VE of Pfizer against Omicron showed that test positivity rate appeared to be higher during the designated proxy Omicron period **(24.4% positivity)** compared to rates during the dominance of the Delta variant (**6.4% positivity)**. Effectiveness against hospitalization during Omicron period was also found to be significantly different at **VE 70% (95% CI, 62.0-76.0)** compared with **VE 93% (95% CI, 90.0-94.0)** during the Delta period.[32]

While current literature show that VE and protection against Omicron are significantly lower in comparison with other VOCs, investigations must be continued in order to guide decision making regarding booster vaccination campaigns and other health measures.

Breakthrough Infections

A study conducted in the United States using samples collected from 27 November 2021 to 20 December 2021 shows early evidence that while Omicron patients had increased rates of breakthrough infections in comparison with patients infected with Alpha or Delta variants, these individuals were younger and less likely to require hospitalization. Additionally, of Omicron patients who were admitted to the hospital, less intense medical treatments were needed and overall length of stay was shorter.[33]

[30] Vaccine effectiveness against SARS-CoV-2 infection with the Omicron or Delta variants following a two-dose or booster BNT162b2 or mRNA-1273 vaccination series: A Danish cohort study. *medRxiv.* https://www.medrxiv.org/content/10.1101/2021.12.20.21267966v3

[31] Effectiveness of mRNA-1273 against SARS-CoV-2 omicron and delta variants. *medRxiv.* *https://www.medrxiv.org/content/10.1101/2022.01.07.22268919v1*

[32] Effectiveness of BNT162b2 Vaccine against Omicron Variant in South Africa. *The New England Journal of Medicine.* https://www.nejm.org/doi/10.1056/NEJMc2119270

[33] Early signals of significantly increased vaccine breakthrough, decreased hospitalization rates, and less severe disease in patients with COVID-19 caused by the Omicron variant of SARS-CoV-2 in Houston, Texas. *medRxiv.* *https://www.medrxiv.org/content/10.1101/2021.12.30.21268560v2*

These findings are largely consistent with results examining breakthrough infections in the Sisonke Ad.26.COV2.S vaccine trial conducted in South Africa. Among a total of 40,538 breakthrough infections detected during the period of study, it was found that Omicron daily infections were three times the peak observed during predominance of the Delta variant.[34] Of the 1,914 breakthrough infection-related hospitalizations identified, **408 hospitalizations occurred during Omicron** study period in comparison with **77 during the Beta period** and **1,429 during the Delta period**. Patients with Omicron were also found to require significantly less intensive care and intense respiratory support than patients infected with Beta or Delta variants. Among hospitalized HCWs, **3% required intensive care** during the Omicron period compared with **7% during Delta** and **16% during Beta** study periods.[35] Finally, the length of hospital stay was significantly lower with Omicron cases **(median length of 3 days)** compared with Beta and Delta cases **(median length of 5-6 days)**.[36]

Alternatively, a study examining infectious viral load among unvaccinated and vaccinated individuals infected with Alpha, Delta, and Omicron variants was conducted in Switzerland to gain insight regarding viral shedding kinetics and understand viral load in vaccine breakthrough infections. Results showed that among vaccinated, Delta infected individuals, infectious viral titers (IVTs) were significantly lower and virus cleared faster compared with unvaccinated individuals. Interestingly, vaccinated individuals infected with Omicron exhibited similar IVTs to those with Delta. Based on these early findings, researchers suggest that factors other than increased viral load may explain high infectiousness of the Omicron variant.[37]

[34] Breakthrough Covid-19 infections during periods of circulating Beta, Delta and Omicron variants of concern, among health care workers in the Sisonke Ad26.COV2.S vaccine trial, South Africa. *medRxiv.* https://www.medrxiv.org/content/10.1101/2021.12.21.21268171v2.full.pdf

[35] Breakthrough Covid-19 infections during periods of circulating Beta, Delta and Omicron variants of concern, among health care workers in the Sisonke Ad26.COV2.S vaccine trial, South Africa. *medRxiv.* https://www.medrxiv.org/content/10.1101/2021.12.21.21268171v2.full.pdf

[36] Breakthrough Covid-19 infections during periods of circulating Beta, Delta and Omicron variants of concern, among health care workers in the Sisonke Ad26.COV2.S vaccine trial, South Africa. *medRxiv.* https://www.medrxiv.org/content/10.1101/2021.12.21.21268171v2.full.pdf

[37] Infectious viral load in unvaccinated and vaccinated patients infected with SARS-CoV-2 WT, Delta and Omicron. *medRxiv.* https://www.medrxiv.org/content/10.1101/2022.01.10.22269010v1

At this point in time, early research findings show that breakthrough infections with the Omicron variant are more common, but are less severe compared with other VOCs. Further investigations are needed to confirm disease character from these preliminary studies.

Transmissibility

While the substantial increase of Omicron cases throughout the world "may indicate a higher rate of transmission compared to other variants"[38], few studies have analysed Omicron's true transmissibility rate in real-life populations, thus far. A model-inference system estimated B.1.1.529 transmission dynamics (adjusting for under-detection of infection, seasonality, vaccination rates, and implementation of nonpharmaceutical measures) using real life data from the Guateng province (first identified epicentre of the Omicron outbreak) in South Africa[39]. Based on the study's real-life estimates, the Omicron variant is **100.3%** (95% CI, 74.8-140.4) more transmissible than the ancestral wild type (Wuhan) strain and **36.5%** (95% CI, 20.9-60.1) more transmissible than the Delta VOC. Additionally, the Omicron variant was estimated to evade **63.7%** (95% CI, 52.9-73.9) of the populations' pre-existing immunity (i.e., those recovered from SARS-CoV-2 and/or are vaccinated against SARS-CoV-2)[40]. A Danish study corroborates the South-African data: Danish households infected with the Omicron VOC demonstrated secondary attack rates of **31%,** while Delta-infected households' secondary attack rates were **21%**[41]. Whereas unvaccinated secondary cases had similar infection rates in Omicron-infected households (**29%**) to Delta-infected households (**28%**), fully vaccinated individuals had a secondary attack rate of **32%** in Omicron households and **19%** in Delta infected households[42], demonstrating the variant's ability to evade vaccine immunity. Nevertheless, the secondary attack rate

[38] Neutralization and Stability of SARS-CoV-2 Omicron variant. *medRxiv.* https://www.biorxiv.org/content/10.1101/2021.12.16.472934v1.full

[39] SARS-CoV-2 transmission dynamics in South Africa and epidemiological characteristics of the Omicron variant. *medRxiv.* https://www.medrxiv.org/content/10.1101/2021.12.19.21268073v1.full-text

[40] SARS-CoV-2 transmission dynamics in South Africa and epidemiological characteristics of the Omicron variant. *medRxiv.* https://www.medrxiv.org/content/10.1101/2021.12.19.21268073v1.full-text

[41] SARS-CoV-2 Omicron VOC Transmission in Danish Households. *medRxiv.* https://www.medrxiv.org/content/10.1101/2021.12.27.21268278v1.full-text#T3

[42] SARS-CoV-2 Omicron VOC Transmission in Danish Households. *medRxiv.* https://www.medrxiv.org/content/10.1101/2021.12.27.21268278v1.full-text#T3

diminished for boosted (three-dose schedule) individuals; the attack rate was **25%** for Omicron and **11%** for Delta[43]. The odds ratio (OR) for becoming infected with Omicron was **1.04** (95% CI, 0.87-1.24) for unvaccinated persons and **0.54** (95% CI, 0.4-0.71) for boosted individuals[44]. Lastly, a case report described a possible airborne transmission of the Omicron variant "between 2 fully vaccinated persons [who had no contact whatsoever] across the corridor of a quarantine hotel" in Hong Kong[45].

Booster Dose

The variant Omicron (B.1.1.529), first detected in South Africa and Botswana and with a large number of accumulated spike mutations, has rapidly spread over seas and has overthrown other variants of concern, such as Delta, by becoming the predominant variant in many nations. With the massive and rapid transmission of Omicron, various countries have expanded, accelerated, and encouraged the administration of a booster dose in the general population with the hopes of boosting the decreasing number of neutralization antibodies in individuals vaccinated over 5 to 6 months ago. Thus far, the administration of a booster dose, regardless of it being homologous or heterologous to the primary schedule, has shown to re-establish and provide an increased protection against the Omicron variant compared to the two initial doses in terms of neutralizing antibodies and effectiveness. Despite this increase, a reduction in neutralizing antibodies and effectiveness is reported for Omicron when comparing it to the wild type and previous variants.

Booster Doses (Homologous & Heterologous)

Although the longevity of vaccine-induced immunity remains an ongoing discussion and continues to spark debate for the use of booster doses, multiple studies and a great deal of evidence have demonstrated that the immunogenicity of fully vaccinated

[43] SARS-CoV-2 Omicron VOC Transmission in Danish Households. *medRxiv.* https://www.medrxiv.org/content/10.1101/2021.12.27.21268278v1.full-text#T3

[44] SARS-CoV-2 Omicron VOC Transmission in Danish Households. *medRxiv.* https://www.medrxiv.org/content/10.1101/2021.12.27.21268278v1.full-text#T3

[45] Probable transmission of SARS-CoV-23 Omicron variant in quarantine hotel, Hong Kong, China, November 2021. *Emerging Infectious Diseases*. https://wwwnc.cdc.gov/eid/article/28/2/21-2422_article

individuals wanes over time, especially in immunocompromised and older individuals. This issue has been highlighted after the exponential increase in breakthrough infections with the Omicron variant. Multiple countries have approved and started implementing booster vaccination programs to prioritize risk-groups and older individuals, all while expanding the program to include all individuals. New WHO EUL approved vaccines such as the Novavax (NVX-CoV2373) and the Covaxin (BBV152) vaccines have published their results on the administration of booster doses. Based on the results, the administration of a third dose of Covaxin **increased** the neutralizing antibodies against SAR-CoV-2 by a **19- to 97-fold** and the neutralizing antibodies against Delta by a **174-fold** compared to the initial two doses[46]. Additionally, the third dose was proven to be safe and well tolerated amongst the participants. As for Novavax's booster dose, the results reported to enhance the immune response by increasing the neutralizing antibodies against SAS-CoV-2 and its variants of concern (Alpha, Beta, Delta, and Omicron) all while remaining safe and well tolerable[47]. Regarding the administration of heterologous booster doses, a similar and at times higher increase in antibodies and immune response can be seen in participants receiving heterologous booster doses.

Currently, literature regarding the duration and possible waning of antibodies induced by the booster doses remains limited. One study examining the durability of the response to the third dose of the BNT162b2 vaccine in adults aged 60 years and older demonstrated that the **anti-spike IgG and neutralizing antibody levels remain adequate 3 months after the booster dose**[48]. On the other hand, another study examining the viral-dose reduction effectiveness of the BNT162b2 booster dose over

[46] Persistence of immunity and impact of a third (booster) dose of an inactivated SAR-CoV-2 vaccine, BBV152; a phase 2, double-blind, randomized controlled trial. *medRxiv.* https://www.medrxiv.org/content/10.1101/2022.01.05.22268777v1

[47] Immunogeneicity and Safety following a Homologous Booster Dose of a SARS-CoV-2 recombinant spike vaccine (NVX-CoV2373): A Phase 2 Randomized Placebo-Controlled Trial. *medRxiv.* https://www.medrxiv.org/content/10.1101/2021.12.23.21267374v1

[48] Durability of response to the third dose of the SARS-CoV-2 BNT162b2 vaccine in adults aged 60 years and older: Three-month follow-up. *medRxiv.* https://www.medrxiv.org/content/10.1101/2021.12.25.21268336v1

time, reported a **significant decline within months after the booster dose**[49]. While the duration of protection of the booster doses remains relatively unknown, countries such as Israel begun vaccinating citizen aged 60 years and over and health-care workers with the fourth dose of a COVID-19, on 2 January 2022, amid the rapid spread of Omicron and the increasing spike of COVID-19 infections[50].

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 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. Interim findings from a US study assessing the effectiveness of the BNT162b2 vaccine against hospitalization and severe Covid-19 among adolescents aged 12-18 showed that effectiveness against hospitalization was **94% (95% CI, 90-96)**. Vaccine effectiveness against requiring ICU services was **98% (95% CI, 93-99)**, and vaccine effectiveness against requiring life support was similar.[51] Falling in line with the trend of waning vaccine duration over time seen in adults, an Israeli study evaluated the duration of protection provided by the BNT162b2 vaccine among adolescents aged 12-16 and found that vaccine effectiveness against breakthrough infection reduced to **75% (95% CI: 71%, 79%)** after 90-149 days after receipt of a second dose and was reduced to **58% (95% CI: 52%, 64%)** 150-180 days after the second dose. Vaccine effectiveness against symptomatic infection was **78% (95% CI: 73%, 82%)** after 90-140 days since receipt of a second dose and **65% (95% CI: 58%, 71%)** after 150-180 days since receipt of a second dose.[52]

[49] Waning of SARS-CoV-2 booster viral-load reduction effectiveness. *medRxiv.* https://www.medrxiv.org/content/10.1101/2021.12.27.21268424v1

[50] 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

[51] Olson SM, Newhams MM, Halasa NB, et al. Effectiveness of BNT162b2 Vaccine against Critical Covid-19 in Adolescents. New England Journal of Medicine. 2022;doi:10.1056/NEJMoa2117995

[52] Prunas O, Weinberger DM, Pitzer VE, Gazit S, Patalon T. Waning Effectiveness of the BNT162b2 Vaccine Against Infection in Adolescents. medRxiv. 2022:2022.01.04.22268776. doi:10.1101/2022.01.04.22268776

Previous reports have mentioned the rare yet concerning adverse event of multi-inflammatory syndrome in children (MIS-C). A US study identified 21 potential cases of MIS-C after vaccination through a national surveillance program and found that of the 21 adolescents with MIS-C, 15 (71%) had evidence of SARS-CoV-2 infection. Of these 15 cases, 47% (7) were aged 12-15, 33% (5) were aged 16-17, 20% (3) were aged 18-20. 66% of these patients had only received one dose of the vaccine. The remaining 6 cases had no evidence of SARS-CoV-2 infection. All patients observed showed clinical improvement, did not have major complications beyond MIS-C, and were sent home.[53]

Studies on the safety and immunogenicity of both the BBIP-CorV and BBV152/Covaxin vaccines in children showed mild to moderate immediate local side effects, with the most common being injection site pain/tenderness for both studies. The study on Covaxin stated the most common systemic adverse event as mild to moderate fever, with no age group reaching more than 15% occurrence. Both studies showed robust immunogenic responses to the vaccines among adolescent recipients when compared to adult recipients. This study further confirms the finding of improved immunogenicity of children as opposed to adults for other vaccines as well.[54] [55]

Vaccine Safety and Adverse Events

The first case of thrombotic thrombocytopenic purpura was reported in a 25-year-old male patient, after receiving the Spikevax vaccine (mRNA-1273, Moderna BioTech, USA)[56].

[53] Yousaf AR, Cortese MM, Taylor AW, et al. Reported Cases of Multisystem Inflammatory Syndrome in Children (MIS-C) Aged 12–20 Years in the United States Who Received COVID-19 Vaccine, December 2020 through August 2021. medRxiv. 2022:2022.01.03.22268681. doi:10.1101/2022.01.03.22268681

[54] Tawinprai K, Siripongboonsitti T, Porntharukchareon T, et al. Safety and immunogenicity of the BBIBP-CorV vaccine in adolescents aged 12-17 years in Thai population, prospective cohort study. medRxiv. 2022:2022.01.07.22268883. doi:10.1101/2022.01.07.22268883

[55] Vadrevu KM, Reddy S, Jogdand H, et al. Immunogenicity and safety of an inactivated SARS-CoV-2 vaccine (BBV152) in children from 2 to 18 years of age: an open-label, age-de-escalation phase 2/3 study. medRxiv. 2021:2021.12.28.21268468. doi:10.1101/2021.12.28.21268468

[56] First diagnosis of thrombotic thrombocytopenic purpura after SARS-CoV-2 vaccine – case report. *BMC Nephrology*. https://bmcnephrol.biomedcentral.com/articles/10.1186/s12882-021-02616-3

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

Synoptic Table

Synoptic table about SARS-CoV-2 vaccines accepted in the WHO's Emergency Use Listing (as of 14 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)	BBIBP-CorV, (Sinopharm, China)	CoronaVac (Sinovac, China)	COVAXIN / BBV152 (Bharat Biotech, India)	Novavax/ NVX-CoV2373
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
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

[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

Approving authorities	FDA (11.12.20)[ii]; EMA (21.12.20); WHO EUL (31.12.20); and list of 112 countries (including Switzerland – approved on 20.12.20)	FDA (18.12.20); EMA (06.01.21); WHO EUL (30.04.21); and list of 79 countries (including Switzerland – approved 12.01.21)	FDA (awaiting on approval); EMA (29.01.21); WHO EUL (15.02.21); and list of 127 countries (Switzerland awaiting on approval)	FDA (27.02.21); EMA (11.03.21), WHO EUL (12.03.21), and list of 85 countries (including Switzerland – approved 22.03.21)	WHO EUL (07.05.21); and list of 72 countries (including Argentina, Bahrain, Brazil, China, Indonesia, United Arab Emirates, Zimbabwe)	WHO EUL (01.06.21), and list of 47 countries (including Albania, Chile, Egypt, Hong Kong, Malaysia, Tunisia, Turkey, Ukraine)	WHO EUL (03.11.21) and list of 12 countries (including Guyana, Inidia, Iran, Mauritius, Mexico, Nepal, Paraguay, Philippines & Zimbabwe)	Waiting on approval (Not-yet-approved by countries or WHO for emergency use)
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] Swissmedic approves booster	EMA authorised booster dose for immunocompromised individuals[v] FDA approved third booster dose for individuals >65 and high-risk individuals, 6 months after the 2nd dose[vi] Swissmedic approves booster dose for adults	-	-	-	-	-	-

[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

	dose for everyone aged 16 and over[iv]	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**	**BBIBP-CorV,**	**CoronaVac**	**COVAXIN / BBV152**	**Novavax/ NVX-CoV2373**
Effectiveness single dose	*Against any SARS-CoV-2 infection:* **70%**[2]. **77.6%** (95% CI, 70.9-82.7)[3] **36.8%** (95% CI, 33.2-40.2) [3 weeks after first dose][4] **57%** (95% CI, 52-61; Spain) [Apr-Aug][5] **72%** (pooled meta-analysis)[6] **64%** (95% CI, 59%-68%; United	*Against SARS-CoV-2 infection:* **60%** (95% CI, 57-64; >2 weeks after dose)[10].[ix] **88.9%** (95% CI, 78.7-94.2)[3] **66%** (95% CI, 56-73; Spain) [Apr-Aug][5] **69%** (pooled meta-analysis)[6] **64%** (95% CI, 59%-68%; United States) [May to July 2021][7x] **39.6%** (95% CI, 36.3-42.8;	*Against SARS-CoV-2 infection:* **31.4%** (95% CI, 25.7-36.7; Norway) [Jan-Sep][8] *Symptomatic disease:* **67%**[11] **49%** (95% CI, 32.0-62.0; India) [Apr-Jun][12] **41%** (95% CI, 34-48; Spain) [Apr-Aug][5] **51%** (pooled meta-analysis)[6]	*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][13]; **79%** (95% CI, 77-80) (when corrected for under-recording, VE was estimated to be **69%** (95% CI, 67-71)[14].	Partial protection[26].[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[27]. **18.6%** (95% CI, 17.6-19.6) against SARS-CoV-2 infection, **28.1%** (95% CI, 26.3-	*Against symptomatic disease*: **45%** (95% CI,6.0-68.0; India) [Apr-Jun][12] **40%** (95% CI, -21-71; India) less than 7 days after first dose [April-May][29] **1%** (95% CI, -30-25); India) at least 7 days after first dose [April-May][29]	Ongoing studies in South Africa[30] and the United Kingdom[31]

[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).

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

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

	States) [May to July 2021][7viii] **19.6%** (95% CI, 17.3-21.9; Norway) [Jan-Sep][8] *Against symptomatic disease*: **66%** (95% CI, 60-71; Spain) [Apr-Aug][5] *Individuals ≥70:* Symptomatic disease: **58%**[9].	Norway) [Jan-Sep][8] *Against symptomatic disease*: **71%** (95% CI, 61-79; Spain) [Apr-Aug][5] *Individuals ≥70:* Symptomatic disease: **64%** (95% CI, 46-78; >2 weeks after dose)[10].[xi]	**46%** (95% CI, 37-54; Spain) [Apr-Aug][5] *Individuals ≥70:* Symptomatic disease: **58%**[9].	**71%** (95% CI, 56-81) [11 March – 15 August][15]. **61%** (95% CI, 29-84) [January-June][16] **50.9%** (95% CI, 35.1-63.0) [June-September; Brazil][17] **50.0%** (95% CI, 42.0-57.0; Spain) [Apr-Aug][5] **73.6%** (95% CI, 65.9-79.9; US) [Feb-Jul][18] **82.3%** (95% CI, 75.1-87.4%; USA) [16 Dec 2020 to 30 Sep 2021][19xii] 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		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][28]	**-1%** (95% CI, -51-33; India) at least 21 days after first dose [April-May][29]	

[viii] 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][20] *Symptomatic disease*: **54%** (95% CI, 45-62; Spain) [Apr-Aug][5] **81%** (95% CI, 79-84) for preventing hospitalization when corrected for under-recording, VE was estimated to be **73%** (95% CI, 69-76)[14]. **75%** (95% CI, 65-82) against severe critical COVID-19[21] **66.1%** against moderate to severe-critical COVID-19 cases after 28 days [ENSEMBLE study; Sep 2020-Nov 2021)[22] **85.4%** against severe COVID-19 cases after 28 days [ENSEMBLE					

				study; Sep 2020-Nov 2021)[22] *Individuals ≥50:* 68% (95% CI, 50-79)[23]. 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][24][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][24xiv] 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				

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

				States; February 2021 to September 2021][25xv]				
Effectiveness of two doses	*SARS-Cov-2 infection:* **85%**[2]. **94.6%**[32]. **94.5%**[33]. **76%** (95% CI, 69-81) [Jan-Jul][34]. **88.8%** (95% CI, 84.6-91.8) [Dec 2020-May][3] **74%** (95% CI, 72-76) [Jan-Jun][16] **77.5%** (95% CI, 76.4-78.6) [first month after second dose][4] **47%** (95% CI, 43-51) [5 months after second dose][35] **56%** (95% CI, 53-59) [4 months after second dose][36] **69%** (95% CI, 66-72; Spain) [Apr-Aug][5]	*SARS-Cov-2 infection:* **100%**[32]. **86%** (95% CI, 81-90.6) [January-July][34]. **96.3%** (95% CI, 91.3-98.4) [December-May][3] **85%** (95% CI, 80-90) [January-June][16] **71%** (95% CI, 68-74) [4 months after second dose][36] **63%** (95% CI, 44-76) [June-August][50]	*Asymptomatic efficacy:* 61.9%[51] *SARS-CoV-2 infection*: **53%** (95% CI, 12-84) [January-June][16] **27%** (95% CI, 17-37) [4 months after second dose][36] **88%** (95% CI, 79.0-94.0; India) [Apr-Jun][12] **54.0%** (95% CI, 48-60; Spain) [Apr-Aug][5] **43.4%** (95% CI, 4.4-66.5; Norway) [Jan-Sep][8]	Not Applicable (one dose schedule)	Partial protection[26].[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[27]. **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][28]	*Against symptomatic disease*: **71%** (95% CI, 41-85; India) [Apr-Jun][12] 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][54] *Effectiveness of full vaccination:* **69%** (95% CI; 54-79; India) [May - July 2021][52] **50%** (95% CI, 33-62; India) 14 days	Ongoing studies in South Africa[30] and the United Kingdom[31] **89.7%** protection against SARS-CoV-2 infection (95% CI, 80.2-94.6; United Kingdom)[55]

[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

	88% (pooled meta-analysis)[6] **84%** (95% CI, 40-96; Italy) [27 Dec 2020 – 24 Mar 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[37] **95%** (95% CI, 93%-96%; United States) [May to July 2021][7xvii] **69.7%** (95% CI, 68.6-70.8; Norway) [Jan-Sep][8] **82.3%** (95% CI, 75.1-87.4%; USA) [16 Dec 2020 to 30 Sep 2021][19xviii] **75%** (95% CI, 73-77; Sweden) [27 Dec 2020-2 Nov 2021][38]	**82%** (95% CI, 78-86; Spain) [Apr-Aug][5] **80%** (pooled meta-analysis)[6] **95%** (95% CI, 93%-96%; United States) [May to July 2021][7xxvii] **78.2%** (95% CI, 76.7-79.6; Norway) [Jan-Sep][8] **82.3%** (95% CI, 75.1-87.4%; USA) [16 Dec 2020 to 30 Sep 2021][19xxviii] **85%** (95% CI, 82-87; Sweden) [27 Dec 2020-2 Nov 2021][38] For those fully vaccinated the observed effectiveness of the Moderna	**80%** (95% CI; 73-86; India) [May - July 2021][52] **60%** (95% CI, 50-67; Sweden) [27 Dec 2020-2 Nov 2021][38] 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][40] VE was approximately **96.7%** (95% CI, 87.9-99.9) 7 days after the second dose [France; December 2020 to June 2021][43xxxvi]			Among individuals with history of infection, VE against symptomatic infection ≥ 14 days from vaccine series completion was 39.4% (95% CI, 36.1-42.6) for CoronaVac. [Brazil][20] 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][24] VE against infection in the	after second dose [April-May][29] **47%** (95% CI, 29-61; India) 14 days after second dose – excluding participants with previous SARS-CoV-2 infections [April-May][29] **46%** (95% CI, 22-62; India) 28 days after second dose [April-May][29] **57%** (95% CI, 21-76; India) 42 days after second dose [April-May][29]	

[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

	VE was 49% (95% CI 22.0%-67.0%)[England][39] Higher dose two VE was observed 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	vaccine was 98.1%. [Overall average from literature review and meta-analysis] [24] 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][45] 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	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](24xxxvii VE against infection in the general population aged ≥16 years was 86.1% (95% CI 77.8–94.4%), for the elderly VE			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][24xlii] 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		

[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.

	than AZD1222. [England] [40] 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] [40] VE greater than 26 weeks from a second dose was 45% (95% CI, 44.0-47.0) for Pfizer.[United States][41] For those fully vaccinated the observed effectiveness of the Pfizer-BioNTech vaccine was 91.2%. [Overall average	Moderna.[United States][41] 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] [42] [xxix] VE against severe acute respiratory syndrome coronavirus 2	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] [24xxxviii] *Symptomatic disease*: **90%**[11]. **56%** (95% CI, 48-63; Spain) [Apr-Aug][5] 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][46] [xxxix]			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[24]][xliii] *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 **75%** (95% CI 27.9-91.2; Brazil)[53]		

[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.

	from literature review and meta-analysis] [24] 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][42] [xix] VE was approximately **96.7%** (95% CI, 87.9-99.9) 7 days after the second	(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][24xxx] 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	VE against symptomatic SARS-CoV-2 infection was estimated at 92% (95% CI, 78–97%) for ChAdOx.[Based on estimations from a Rapid Review][45] 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][20] VE was approximately 96.7% (95% CI, 87.9-99.9) 7 days after the second dose [France;						

[xix] Study does not differentiate between Moderna or Pfizer-BioNTech.

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

	dose [France; December 2020 to June 2021][43xx] 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	95.3% (95% CI 92.0–98.6%).[Overall average from literature review and meta-analysis][24 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][25 xxxii] *Symptomatic disease*: **91%** (95% CI, 89-93;	December 2020 to June 2021] [43xl]						

[xx] Study does not differentiate between Comirnaty and Vaxrevria.
[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.

	review and meta-analysis](24xxi 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]24xxii Adjusted VE was 71% (95% confidence interval, 49%-83%) among fully vaccinated participants	>2 weeks after dose)10.xxxiii **85%** (95% CI, 80-89; Spain) [Apr-Aug]5 *Asymptomatic SARS-CoV-2 infection:* **90.6%**47.xxxiv **71%** (95% CI, 61-78) [January-August]50 *Hospitalization:* **91.6%** (95% CI, 81-97) [January-July]34. **93%** (95% CI, 91-95) [11 March – 15 August)15. **89%** (95% CI, 87-91) for individuals ≥50 years [1 January-22 June23. xxxv							

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

	reporting contact with persons with COVID-19 versus 80% (95% CI, 72%-86%) among those without contact.[United States; February 2021 to September 2021] [25] [xxiii] *Symptomatic disease*: **72%** (95% CI, 69-75; Spain) [Apr-Aug][5] Adjusted VE was 59% (95% CI 23.0%-78.0%)[England][44] VE against symptomatic SARS-CoV-2 infection was estimated at 89–97% BNT162b2.[Based on estimations from a Rapid Review] [45]									

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

	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] [20] 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][46xxiv] *Asymptomatic SARS-CoV-2 infection:* **90.6%**[47].[xxv] **73.1** (95% CI, 70.3-75.5)[4] *Hospitalization:*								

[xxiv] Study does not differentiate between Pfizer and AstraZeneca

[xxv] Results do not disaggregate between BNT162b2 and mRNA-1273

	85% (95% CI, 73-93) [January-July][34]. **88%** (95% CI, 85-91) [11 March – 15 August][15]. **89%** (95% CI, 87-91) for individuals ≥50 years [1 January-22 June][23]. [xxvi] **90%** (95% CI, 89-92) [Dec 2020 – Aug 2021][35] 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][41] VE against hospitalization or death ≥ 14 days from vaccine series completion was 89.7% (95%								

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

	CI, 54.3-97.7) for BNT162b2. [Brazil] [20] VE against hospitalization 14–119 days following second Pfizer-BioNTech dose was 86.0% (95% 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] [48] *Individuals ≥65:* **61%** (95% CI, 57-65) against SARS-CoV-2 infection and **86%** (95% CI, 82-88) against hospitalizations[35] *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][49]							
	EFFECTIVENESS AGAINST VARIANTS[xliv]							
	BNT162b2/ COMIRNATY	**Spikevax/ Moderna COVID-19 Vaccine/ mRNA-1273**	**Vaxzevria/ ChAdOx1 nCoV-19/ AZD1222/ Covishield**	**Janssen COVID-19 vaccine/Johnson & Johnson**	**BBIBP-CorV,**	**CoronaVac**	**COVAXIN / BBV152**	**Novavax/ NVX-CoV2373**
Alpha (B.1.1.7)	*Single dose:* **48.7%** (95% CI, 45.5 to 51.7)[56] **66%** (95% CI,64-68)[57]. **54.5%** (95 CI, 50.4-58.3)[58] *Two doses:* **93.7%** (95% CI, 91.6 to 95.3)[56] **92%** (95% CI, 90-93)[59]. **89%** (95% CI, 86-91)[57]. **78%** (95% CI, 68-84)[60] **84.4%** (95 CI, 81.8-86.5)[58]	*Single dose:* **88.1%** (95% CI, 83.7 to 91.5)[61] **83%** (95% CI, 80-86)[57]. *Two doses:* **100%** (95% CI, 91.8 to 100)[61] **92%** (95% CI, 86-96)[57]. **98.4%** (95% CI, 96.9-99.1)[62]	*Single dose:* **48.7%** (95% CI 45.5 to 51.7)[56] 6**4%** (95% CI, 60-68)[57]. *Two doses:* **74.5%** (95% CI, 68.4 to 79.4)[56] **73%** (95% CI, 66-78)[59]. 79% (95% CI, 56-90)[60].	-	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[30] and the United Kingdom[31] 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.**[55]

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

Beta (1.351)	*Against SARS-CoV-2 infection:* *Single dose:* **60%** (95% CI, 52-67)[57]. *Two doses:* **84%** (95% CI, 69-92)[57]. **72%** (95% CI, -5-97; Israel) [Dec 2020-Mar 2021][63] *Against symptomatic infection:* **100%** (95% CI, 19-100; Israel) [Dec 2020-Mar 2021][63]	*Single dose:* **61.3%** (95% CI, 56.5 to 65.5)[61] **77%** (95% CI, 69-92)[57]. *Two doses:* **96.4%** (95% CI, 91.9 to 98.7)[61]	*Single dose:* **48%** (95% CI, 28-63)[57].	-	No published data	Neutralization capacity was decreased by factor **5.27**[64].	No available data	No available data
Gamma (P.1)	Neutralization activity reduced by **3.3-fold**[65].	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[66]. **50.2%** against P.1 (>14 days after 2nd dose)[67].	No available data	No available data

						Neutralization was decreased by factor **3.92**[64]. *Against symptomatic COVID-19:* **80.5%** (95% CI, 75.1-84.7)[68]		
Delta (1.617.2)	*Single dose:* **30.7%** (95% CI, 25.2 to 35.7)[56]; **57%** (95% CI, 50-63)[60] **22.5%** (95 CI, 17.0-27.4)[58] **22%** (95% CI, 10-32; France) [May-August 2021][69] *Two doses:* **88.0%** (95% CI, 85.3 to 90.1)[56]; **80%** (95% CI, 77-83)[60] **79%** (95% CI,75-82)[59]. **80%** (95% CI, 77-83)[60] **40.5%** (95% CI, 8.7-61.2)[70]. **42%** (95% CI, 13-62)[34].	*Single dose:* **72%** effective against symptomatic SARS-Cov-2 infection[78]. *≥14 days after second dose:* **76%** (95% CI, 58-87)[34]. **94.5%** (95% CI, 94.1-95) [2-9 weeks after second dose][71]. **50.6%** (95% CI, 45.0-55.7) [among nursing home residents][72]. **86.7%** (95% CI, 84.3-88.7)[62] **56.6%** (95% CI, 42.0-67.5) *against infection*[79]	*Single dose:* **30.7%** (95% CI 25.2 to 35.7)[56] **73%** (95% CI, 64-80; India) [May – July 2021][52] *Two doses:* **67.0%** (95% CI, 61.3 to 71.8)[56] **67%** (95% CI, 62-71)[60]. **60%** (95% CI, 53-66)[59]. **66.7%** (95% CI, 45-49.6) [2-9 weeks after second dose][71]. **47.3%** (95% CI, 66.3-67.0) [≥20 weeks after second dose][71].	**78%** (95% CI, 73-82) against SARS-CoV-2 infection[14]. **3%** (95% CI, -7-12) [August][73] **76.5%** (95% CI, 40.9-90.6; USA) [01 Jul 2021 to 30 Sep 2021][19][lii] *Individuals ≥50:* **83% (**95% CI, 81-85)[14]	No available data	*Single dose:* **13.8%** (95% CI, -60.2-54.8)[81]. *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[81].	*Single dose*: **44%** (95% CI, 0-71; India) [May – July 2021][52] *Two doses:* **64%** (95% CI, 40-79; India) [May – July 2021][52]	No available data

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

	89.8% (95% CI, 89.6-90.0) [2-9 weeks after second dose][71]. **69.7%** (95% CI, 68.7-70.5) [≥20 weeks after second dose][71]. **64.6%** (95 CI, 60.6-68.2)[58] **52.4%** (95% CI, 48.0-56.4) [among nursing home residents][72]. **53%** (95% CI, 39-65) [4 months after second dose][35] **50%** (95% CI, 47-52) [August; elderly Veteran population][73] **76.5%** (95% CI, 40.9-90.6; USA) [01 Jul 2021 to 30 Sep 2021][19xlv] **67%** (95% CI, 63-71; France) [May-August 2021][69] VE against Delta variant-related symptomatic infection was 88%	**84.2%** (95% CI, 56.4-94.3) *against symptomatic infection*[79] **64%** (95% CI, 62-66) [August; elderly Veteran population][73] **76.5%** (95% CI, 40.9-90.6; USA) [01 Jul 2021 to 30 Sep 2021][19xlviii] *10-14 weeks after second dose:* **90.3%** (95% CI, 67.2-97.1)[71]. 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][45] Among early recipients of mRNA-1273, VE	**81%** (95% CI, 71-88; India) [May – July 2021][52] 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 [80]. 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				

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

	(95% CI, 85.3–90.1%) by BNT162b2 after full vaccination.[Based on estimations from a Rapid Review][45] VE against hospitalization was 93% (95% CI, 90.0-94.0); South Africa)[September 2021 to October 2021] [74] Among early recipients of BNT162b2, VE decreased an estimated 15 percentage when the Delta variant became dominant. [75] Among individuals who received 2 doses of vaccines (with at least 1mRNA vaccine) VE against Delta	decreased an estimated 10 percentage when the Delta variant became dominant. [75] 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] [76] [xlix]	mRNA vaccine for the third dose.[Canada; November 2021 to December 2021] [76] [li]						

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

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

	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] [76] [xlvi] 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	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.[77] [l] One dose VE was 77.0% (95% CI, 60.7-86.5%).[62] Two dose VE was 86.7% (95% CI 84.3%-88.7%).[62] VE against hospitalization was 97.5% (95% CI 92.7%-99.2%).[62] VE against infection declined from 94.1% (95%							

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

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

	pre-Delta period.[77xlvii] *Against severe COVID-19:* **91.4%** (95% CI, 82.5-95.7)[70].	CI 90.5%-96.3%) 14-60 days after vaccination to 80.0%(95% CI, 70.2-86.6%) 151-180 days after. [62] VE against infection was lower for ≥ 65 years at 75.2% (95% CI 59.6%-84.8) than those 18-64 years at 87.9%(95% CI, 85.5%-89.9%). [62]						
Mu (B.1.621)	Mu variant is 9.1 times more resistant than the wild type strain when vaccinated with BNT162b2[82]	*Two doses:* **90.4%** (95% CI, 73.9-96.5)[62] (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,	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	No protective effect of vaccination against symptomatic disease with Omicron from 15 weeks after the second dose[83]					

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

	34-37% from 15 weeks after second dose[83] If assuming a 25-fold decrease in pseudovirus neutralization **66%** (95% CI, 42-86)[84] VE against the Omicron variant 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][85] 2 doses of COVID-19 vaccines was not protective against	to December 23 2021][86] 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. [Denmark, November 2021 to December 2021][85] 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	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] [76] [lv]						

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

	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] [76] [liii]	mRNA vaccine for the third dose.[Canada; November 2021 to December 2021] [76] [liv] VE was **30.4% (95% CI, 5.0%-49.0%)** 14-90 days after vaccination and declined thereafter.[86]						
	EFFECTIVENESS AGAINST HOSPITALIZATION							
	BNT162b2/ COMIRNATY	**Spikevax/ Moderna COVID-19 Vaccine/ mRNA-1273**	**Vaxzevria/ ChAdOx1 nCoV-19/ AZD1222/ Covishield**	**Janssen COVID-19 vaccine/Johnson & Johnson**	**BBIBP-CorV,**	**CoronaVac**	**COVAXIN / BBV152**	**Novavax/ NVX-CoV2373**
Any SARS-CoV-2 infection	*Single dose:*	*Single dose:*	*Single dose:*	VE against hospitalization or	No available data	*Against ICU admission*:	No available data	No available data

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

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

	85% (pooled meta-analysis)[6] Hospitalization risk reduced by 35-**45%**[9]. Risk of death reduced by **54%**[9]. *Individuals ≥50:* ≥14 days after first dose: **54%** (95% CI, 47-61) [1 Jan-22 Jun[23]. [lvi] *Two doses:* **91%** (pooled meta-analysis)[6] **91%** (95% CI, 93%-96%; United States) [May to July 2021][7][lvii] **89%** (95% CI, 84-93; Sweden) [27 Dec 2020-2 Nov 2021][38] *Against ICU admission*:	**73%** (pooled meta-analysis)[6] *Individuals ≥50:* ≥14 days after first dose: **54%** (95% CI, 47-61) [1 Jan-22 Jun[23].[lxi] *Two doses:* **88%** (pooled meta-analysis)[6] **91%** (95% CI, 93%-96%; United States) [May to July 2021][7][lxii] **79%** (95% CI, 60-89; Sweden) [27 Dec 2020-2 Nov 2021][38] 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%	**56%** (pooled meta-analysis)[6] Hospitalization risk reduced by **35-45%**[9]. *Two doses:* **91%** (pooled meta-analysis)[6] **92%** (95% CI, 80-97; Sweden) [27 Dec 2020-2 Nov 2021][38] VE against hospitalization or death ≥ 14 days from vaccine series completion was 89.9% (95% CI, 83.5-93.8) for ChAdOx1. [Brazil][20] *Against ICU admission*:	death ≥ 14 days from vaccine series completion was 57.7% (95% CI, −2.6-82.5) for Ad26.COV2.S. [Brazil][20]		**72.0%** (95% CI, 69.9-73.9; Malaysia) [Apr-Sep 2021][87] *Against death:* **82.4%** (95% CI, 81.0-83.7; Malaysia) [Apr-Sep 2021][87] VE against hospitalization or death ≥ 14 days from vaccine series completion was 81.3% (95% CI, 75.3-85.8) for CoronaVac. [Brazil] [20] Adjusted odds ratios of COVID hospitalisation or death were significantly increased from 98 days since series completion, compared to individuals vaccinated 14-41		

[lvi] mRNA-aggregated data (results do not disaggregate between BNT162b2 and mRNA-1273).
[lvii] Results do not disaggregate between mRNA vaccines, BNT162b2 and mRNA-1273.
[lxi] mRNA-aggregated data (results do not disaggregate between BNT162b2 and mRNA-1273).
[lxii] Results do not disaggregate between mRNA vaccines, BNT162b2 and mRNA-1273.

	90.3% (95% CI, 88.8-91.6; Malaysia) [Apr-Sep 2021][87] *Against death:* **92.7%** (95% CI, 91.7-93.6; Malaysia) [Apr-Sep 2021][87] 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] [88] [lviii] Fully vaccinated patients had a shorter overall length of stay in hospitals (aHR for discharge: 1.61,	(95% CI, 83.0%-88.0%) risk reduction in people aged 75 and older [France] [88] [lxiii] 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,	**95.6%** (95% CI, 88.3-98.4; Malaysia) [Apr-Sep 2021][87] *Against death:* **95.3%** (95% CI, 91.3-97.4; Malaysia) [Apr-Sep 2021][87]			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 September 2021] [91]		

[lviii] Study does not differentiate between Pfizer/BioNTech and Moderna.
[lxiii] Study does not differentiate between Pfizer/BioNTech and Moderna.

	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] [89][lix] VE was observed to increase after the first dose of mRNA vaccines with week 6 effectiveness approximating 84% (95% CI	February 2021 to November 2021] [89][lxiv] 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] [90][lxv] VE against hospitalization 14–119 days following second Moderna vaccine dose was 89.6% (95% CI = 80.1%–94.5%) at ≥120 days VE was 86.1% (95% CI = 77.7%–							

[lix] Study does not differentiate between mRNA vaccines Pfizer and Moderna.
[lxiv] Study does not differentiate between mRNA vaccines Pfizer and Moderna.
[lxv] Study does not differentiate between Pfizer and Moderna.

	72.0-91.0) for COVID-19 infection and 86% (95% CI, 69.0-95.0) for COVID-19-associated hospitalization.[United States] [90] [lx]	91.3%).[United States; February 2021 to September 2021][48]						
Alpha	Single dose: **83%** (95% CI, 62-93) **53%** (95% CI, 7-83; England) [Feb-Sep 2021][92] Two doses: **95%** (95% CI, 78-99)[93]. **71%** (95% CI, 12-95; England) [Feb-Sep 2021][92] *Against death:* **98.2%** (95% CI, 95.9-99.2) [2-9 weeks][71]. **90.4%** (95% CI, 85.1-93.8) [≥20 weeks][71].	No available data	Single dose: **76%** (95% CI, 61-85) **3%** (95% CI, -38 – 39; England) [Feb-Sep 2021][92] Two doses: **86%** (95% CI, 53-96)[93]. **26%** (95% CI, -39 – 73; England) [Feb-Sep 2021][92] *Against death:* **94.1%** (95% CI, 91.8-95.8) [2-9 weeks][71]. **78.7%** (95% CI, 52.1-90.4) [≥20 weeks][71].	***Beta*** **67%** effective at preventing hospitalizations[94]. *Against death:* 96% effective at preventing death[94].	No available data	No available data	No available data	No available data
Gamma	No available data	No available data	No available data	**72.9%** (95% CI, 35.1-91.1)[17] *Against ICU admission:*	No available data	*Against hospitalization:* **95%** (95% CI, 86.9-98.1)[68]	No available data	No available data

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

				92.5% (95% CI, 54.9-99.6)[17] *Against death:* **90.5%** (95% CI, 31.5-99.6)[17]		*Against death:* **94.9%** (95% CI, 76.4-98.9)[68]		
Delta	*Single dose:* **94%** (95% CI, 46-99)[93]. **91%** (95% CI, 90-93)[95] **4%** (95% CI, -21 – 44; England) [Feb-Sep 2021][92] *Two doses*: **96%** (95% CI, 86-99)[93]. **88%** (95% CI, 78.9-93.2)[70]. **75%** (95% CI, 24-93.9)[34]. **84%** (95% CI, 79-89)[96]. **98.4%** (95% CI, 97.9-98.8) [2-9 weeks][71]. **92.7%** (95% CI, 90.3-94.6) [≥20 weeks][71].	*Single dose:* **81%** (95% CI, 81-90.6)[34]. *Two doses:* **84%** (95% CI, 80-87)[95] **95%** (95% CI, 92-97) [Jun-Aug 2021][97] **96.7%** (95% CI, 93.9-98.2)[8] **97.3%** (95% CI, 95.9-98.4; New York) [Aug 2021][99] *Individuals ≥65:* **93.7%** (95% CI, 92.9-94.4; New York) [Aug 2021][99] *Against ICU admission:*	*Single dose*: **71%** (95% CI, 51-83)[93] **88%** (95% CI, 83-91)[95] **2%** (95% CI, -19 – 31; England) [Feb-Sep 2021][92] *Two doses*: **92%** (95% CI, 75-97)[93]. **95.2%** (95% CI, 94.6-95.6) [2-9 weeks][71]. **77.0%** (95% CI, 70.3-82.3) [≥20 weeks][71]. **94%** (95% CI, 92-95)[95] **14%** (95% CI, -5 – 46; England) [Feb-Sep 2021][92]	**71%** [94] **85%** (95% CI, 73-91)[14]. **91%** (95% CI, 88-94)[95] **93.5%** (95% CI, 89.6-96.1; New York) [Aug 2021][99] **85%** effective at preventing severe disease and hospitalization[104]. *Individuals ≥50:* **84% (**95% CI, 81-85)[14] *Individuals ≥65:*	*Single dose:* Does not offer clinically meaningful protection against severe illness [105,lxvi] *Two doses:* **88%** (95% CI, 55-98) adjusted risk reduction in developing severe illness.[105,lxvii]	*Single dose:* Does not offer clinically meaningful protection against severe illness [105,lxviii] *Two doses:* **88%** (95% CI, 55-98) adjusted risk reduction in developing severe illness.[105,lxix]	No available data	No available data

[lxvi] Study does not differentiate between the two inactivated vaccines, BBIBP-CorV and CoronaVac.
[lxvii] Study does not differentiate between the two inactivated vaccines, BBIBP-CorV and CoronaVac.
[lxviii] Study does not differentiate between the two inactivated vaccines, BBIBP-CorV and CoronaVac.
[lxix] Study does not differentiate between the two inactivated vaccines, BBIBP-CorV and CoronaVac.

	96% (95% CI, 95-96)[95] **80%** (95% CI, 73-85) [June-August][97] **93%** (95% CI, 84-96)[98] **96.8%** (95% CI, 93.9-98.3)[2 months after the second dose][4] **93%** (95% CI, 84-96)[35] **91.5%** (95% CI, 89.5-93.2)[8] **24%** (95% CI, -2 – 64; England) [Feb-Sep 2021][92] **95.2%** (95% CI, 93.6-96.5; New York) [Aug 2021][99] *Individuals ≥65:* **88.6%** (95% CI, 87.4-89.6; New York) [Aug 2021][99] *Against death:* **90%** (95% CI, 83-94) [≥2 weeks after second dose][100] *All ages:* **90%** (95% CI, 83-94)[101] *40-59*: **95%** (95% CI, 79-99)[101]	**86%** (95% CI, 79-90)[95] **96%** against severe COVID-19 infection[78]. Estimated risk of SARS-CoV-2 infection is **4.52 events per 1000** persons (95% CI, 4.17-4.84)[102]	**63.1%** (95% CI, 51.5-72.1; India) (Apr – May 2021)[103] *Against moderate to severe disease:* **81.5%** (95% CI, 9.9-99.0; India) (Apr – May 2021)[103] *Against ICU admission:* *Single dose:* **92%** (95% CI, 84-96)[95] *Two doses*: **96%** (95% CI, 94-98)[95] *Against death:* **91%** (95% CI, 86-94) [≥2 weeks after second dose][100] *All ages:* **91%** (95% CI, 86-94)[101] *40-59*: **88%** (95% CI, 76-93)[101] *60+:* **90%** (95% CI, 84-94)[101]	**81.8%** (95% CI, 77.8-85.3; New York) [Aug 2021][99] *Against ICU admission:* **94%** (95% CI, 88-98)[95]				

	60+: **87%** (95% CI, 77-93)[101] Estimated risk of SARS-CoV-2 infection is **5.75 events per 1000** persons (95% CI, 5.39-6.23)[102]								
Omicron	Estimated VE against hospitalization **4 to 5-fold increased** compared to Delta[106]* **84.9%** (95% CI, 83.0-86.6) against Omicron variant for recently vaccinated Pfizer[106] *No differention between mRNA vaccines VE against hospitalization was 70% (95% CI, 62.0-76.0; South Africa)[November 2021 to December 2021][74]	Estimated VE against hospitalization **4 to 5-fold increased** compared to Delta[106]* *No differention between mRNA vaccines							

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	BBIBP-CorV,	CoronaVac	COVAXIN / BBV152	Novavax/ NVX-CoV2373
Duration of protection (antibodies)	Median time between second dose and infection: **146 days (IQR, 121-167)**[107] *Anti-SARS-CoV-2 Antibodies:* 1 month after 2nd dose: **1762 KU/L (IQR: 933-3761)** 3 months after 2nd dose: **1086 KU/L (IQR: 629-2155)** 6 months after 2nd dose: **802 KU/L (IQR, 447-1487)**[108] No health worker had antibodies BELOW method-dependent cut-off (0.8 KU/L) *Neutralizing antibodies:* At peak immunity, NAb titre was	*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[113] *Neutralizing antibodies:* At peak immunity, NAb titre was **5,848**, after 8 months titre was **133**[109] *Pseudovirus neutralizing antibodies:* At peak immunity, pseudovirus NAb titre was **1,569**, after 8 months titre was **273**[109]	*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). Antibody levels after **day 320**: 0.30 GMR (CI, 0.24-0.39)[114] *Cellular Immune Response:* **Day 182** after first dose: median of **237 SFUx10^6 PBMC (IQR, 109-520)**[114] **6 months** after second dose: **(median 1240,**	*Neutralizing antibodies:* Remained largely stable for **8-9 months**[116] Remained **stable for 8 months**; At 4 weeks after immunization NAb titre was **146**, after 8 months titre was **629**[109] *Pseudovirus neutralizing antibodies:* Remained **stable for 8 months**; At 4 weeks after immunization pseudovirus NAb titre was **391**, after 8 months titre was **185**[109] *Binding antibodies:*	*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** (95% CI: 88.2-178.4)[118] **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**	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[120]. **80-90%** of anti-S IgG and Nab titers against wild type waned **6 months** after second vaccination[121] *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)[110]	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; January to July 2021] [115]	No available data

	1,789, after 8 months titre was **53**[109] *Pseudovirus neutralizing antibodies:* At peak immunity, pseudovirus NAb titre was **700**, after 8 months titre was **160**[109] *Anti-spike Protein RBD IgG Antibodies:* At peak immunity, RBD titre was **21,564**, after 8 months titre was **755**[109] **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)[110] **Older age groups (≥60)**: 1 month after 2nd dose: 100%	*Anti-spike Protein RBD IgG Antibodies:* At peak immunity, RBD titre was **25,677**, after 8 months titre was **1,546**[109] *Humoral & Cellular Immune Response:* CD8+ T cell response was **0.017%** 8 months after full vaccination[109]	**IQR 432-2002**) in groups with 15-25 week interval between doses[114] *Anti-spike Protein RBD IgG Antibodies:* **Younger age groups (<60):** 1 month after 2nd dose: 100% seropositivity, **17.1** (IQR, 9.9-23.6) 3 months after 2nd dose: 97% seropositivity, **6.5** (IQR, 3.5-9.3)[110] **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)[110] Median anti-S IgG was **1,299.5 AU/mL (IQ: 517.9-5,019.07)** which is approximately **4-fold higher than**	Remained stable **6 months** irrespective of age group[116] *Humoral & Cellular Immune Response:* Antibody responses were detected in all vaccine recipients on **day 239** (stable response for at least 8 months)[117] CD8+ T cell response was **0.12%** 8 months after vaccination[109] *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**[109]	(95% CI: 147.3-1593)[118] *Anti-RBD IgG*: Decreased up to **41.8%** 2 months after second dose and dropped to **42.9%** decrease after 7 months[119] *Binding Antibodies:* Decreased **82.1%** 7 months after second dose[119]	**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)[110] *Neutralizing Antibody:* Decay from **95.08%** 42 days after 2nd dose to **19.7%**160 days after 2nd dose[122] *Anti-RBD Antibody:* Decay from **100%** 42 days after 2nd dose to **54.10%** 160 days after 2nd dose[122] *Anti-spike IgG:* Decay from **100.0%** 42 days after 2nd dose to **50.82%** 160 days after 2nd dose[122] *Anti-spike IgM:*		

	seropositivity, **29.4** (IQR, 22.5-33.3) 3 months after 2nd dose: 100% seropositivity, **14.8** (IQR, 7.4-18.7)[110] *Sub-populations:* **Older age (≥65): 38%** to **42%** decrease of humoral antibodies compared to 18- to 45-year-old[111] **Older age (≥65) AND men: 37%** to **46%** decrease compared to 18- to 45-year-old women[111] **Immunosuppression: 65% to 70%** decrease compared to non-immunosuppressed[111] **Obesity (BMI ≥30): 31%** increase in neutralizing antibody		**the Covaxin**-induced antibody concentration of 342.7 AU/mL (IQ: 76.1-892.8). [India; January to July 2021] [115]			Decay from **59.02%** 42 days after 2nd dose to **3.28%** 160 days after 2nd dose[122] *Anti-spike IgA:* Decay **31.15%** 42 days after 2nd dose to **0.00%** 160 days after 2nd dose[122] 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][123]		

	compared with nonobese[111] While the mean values of anti-RBD-IgG showed a marked decline at 6 months, high neutralizing bioactivity was maintained at least 6 months after vaccination in almost all study participants (N=57 HCWs)[112] *Humoral & Cellular Immune Response:* CD8+ T cell response was **0.016%** 8 months after full vaccination[109]							
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**	**36.4** (95% CI, 17.1-51.5) reduction of observed incidence rate (SARS-CoV-2 infection) if vaccinated from Dec 2020 – Apr	VE reduced by 7% (95% CI, -18 - 2) for every 30 days from the second dose for those aged 18 to 64 years[60].	A study observed sustained and stable vaccine effectiveness starting 14 days post vaccination to a maximum of **152** days after vaccination[14].	No available data	No available data	No available data	No available data

	5-7 after 2nd dose[124] VE reduced from **87%** (95% CI, 85-89) to **56%** (95% CI, 53-59) after 4 months.[36] VE reduced from **91%** (95% CI, 91-92) in March to **50%** (95% CI, 47-52) in August[73] 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][125lxx] VE decreased by **18.5% points** (95% CI 8.4-33.4) among all ages and **19.9% points** among older individuals (95%	2021 than Jul 2021 – Dec 2020.[133] **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.[133] 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.[62] **91%** [January-March]	VE reduced from **58%** (95% CI, 51-65) to **27%** (95% CI, 17-37) after 4 months.[36] VE reduced from **88%** (95% CI, 87-89) in March to **3%** (95% CI, -7-12) in August[73] 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][126lxxxvi] 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)	VE decreased from **89.4%** in May to **51.7%** in July[50] 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[131] 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][126xcii] VE reduced from **86.6%** (range, 77.8-89.7) for the week of 1 May				

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

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

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

	CI; 9.2-36.7) [Overall average from Systematic Review and Meta-Regression][126][lxxi] 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[99]. **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][127]	**71%** (95% CI, 53-83) [April-May] **63%** (95% CI, 44-76)[50] VE reduced from **90%** (95% CI, 88-91) to **71%** (95% CI, 68-74) after 4 months[36] 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[50] VE reduced from **92%** (95% CI, 92-93) in March to **64%** (95% CI, 62-66) in August[73] VE against infection was **82%** (95% CI, 79-85) 14-90 days after the second dose and appeared to	by the week of August 28 2021[99] Estimated results show that vaccine effectiveness significantly wanes from 60 days after the second dose [Japan; February 2020 to December 2021] [lxxxvii] 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.[129][lxxxviii] VE decreased to 44.3% (95% CI,	2021 to **69.4%** (range, 63.4-77.3) by the week of August 28 2021[99]. 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][75] 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				

[lxxi] Study does not differentiate between Pfizer/BioNTech-Comirnaty, Moderna-mRNA-1273, Janssen-Ad26.COV2.S and AstraZeneca-Vaxrevria.
[lxxxvii] Study does not differentiate between Pfizer Moderna, and AstraZeneca.
[lxxxviii] Study does not differentiate between BNT162b2, mRNA-1273, and ChAdOX-S.

	VE was **94.5% (95% CI, 94.1 to 94.9)** 2 months after the first dose and **decreased to 66.6% (95% CI 65.2-67.8)** at 7 months. [United States; December 2020 to September 2021] [75] 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] [128] Estimated results show that vaccine	**wane over time** and was **63%** (95% CI, 55-68) 91-180 days after the second dose [27 Dec 2020 – 26 Oct 2021; Finland][130lxxviii] 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[131] 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][125lxxix] VE decreased by **18.5% points** (95% CI 8.4-33.4) among all ages	43.2-45.4) by 20 weeks after the second dose. Protection against hospitalization 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] [127] *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][126lxxxix] **50%** (95% CI, 16-69)14-73 days after second dose.	September 2021][128] There was no evidence of 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] [128] *Against symptomatic COVID-19:* VE decreased by **25.4%** (95% CI, 13.7-42.5) among				

[lxxviii] Study does not differentiate between COMIRNATY/BNT162b2 and SPIKEVAX/ mRNA-1273.

[lxxix] Study does not differentiate between the two mRNA vaccines, Pfizer and Moderna.

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

	effectiveness significantly wanes from 60 days after the second dose [Japan; February 2020 to December 2021] [lxxii] 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. [129] [lxxiii] *Against symptomatic COVID-19:*	and **19.9% points** among older individuals (95% CI; 9.2-36.7) [Overall average from Systematic Review and Meta-Regression][126lxxx] 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[99]. 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	Effectiveness did not fall significantly after longer intervals, however this could be influenced by the study's small number of participants[132] *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][126xc] *Against variants:* Among individuals who received 2	all ages and **32.0%** (95% CI, 11.0-69.0) among older individuals [Overall average from Systematic Review and Meta-Regression][126xciii] *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][126xciv]				

[lxxii] Study does not differentiate between Pfizer Moderna, and AstraZeneca.
[lxxiii] Study does not differentiate between BNT162b2, mRNA-1273, and ChAdOX-S.
[lxxx] Study does not differentiate between Pfizer/BioNTech-Comirnaty, Moderna-mRNA-1273, Janssen-Ad26.COV2.S and AstraZeneca-Vaxrevria.
[xc] Study does not differentiate between Pfizer/BioNTech-Comirnaty, Moderna-mRNA-1273, Janssen-Ad26.COV2.S and AstraZeneca-Vaxrevria.
[xciii] Study does not differentiate between Pfizer/BioNTech-Comirnaty, Moderna-mRNA-1273, Janssen-Ad26.COV2.S and AstraZeneca-Vaxrevria.
[xciv] Study does not differentiate between Pfizer/BioNTech-Comirnaty, Moderna-mRNA-1273, Janssen-Ad26.COV2.S and AstraZeneca-Vaxrevria.

	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[126lxxiv] VE reduced by 22% (95% CI, 6-41) for every 30 days from the second dose for those aged 18 to 64 years[60]. 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	September 2021][75] Waning protection against infections started in month 2 for mRNA-1273 (OR [95% CI] in month 6+, 2.76 [2.51, 3.04]). No waning of protection was observed at any time for ICU admissions. [United States, January 2021 to September 2021][128] 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	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] [76] [xci]						

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

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

	Oct 2021; Finland][130][lxxv] VE decreased from **86.9%** (95% CI, 86.5-87.3) in March 2021 to **43.3%** (95% CI, 41.9-44.6) in September 2021[131] 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].[132] VE declined from **86%** (95% CI, 73-93) 14-73 days	September 2021] [128] Estimated results show that vaccine effectiveness significantly wanes from 60 days after the second dose [Japan; February 2020 to December 2021][lxxxi] 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. [129] [lxxxii]							

[lxxv] Study does not differentiate between COMIRNATY/BNT162b2 and SPIKEVAX/ mRNA-1273.
[lxxxi] Study does not differentiate between Pfizer Moderna, and AstraZeneca.
[lxxxii] Study does not differentiate between BNT162b2, mRNA-1273, and ChAdOX-S.

	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][132] *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][126lxxvi] *Against Hospitalization and Death:* After reaching peak VE (96.8%) 2 months after 2nd dose, **VE did not decline over**	*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)[126lxxxiii] *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 individuals [Overall average from Systematic Review and Meta-Regression][126lxxxiv] *Against variants:*						

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

	time, except for 7th months (VE 55.6%) with very few cases[124] Evidence of waning protection against hospitalization started in month 2 for BNT162b2 (OR [95% CI], 3.97 [3.26, 4.83] in month 6+) [United States, January 2021 to September 2021] [128] *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	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] [76] [lxxxv]							

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

	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] [76] [lxxvii]							
Transmission prevention	*Prior Delta Variant:* Vaccine effectiveness against infectiousness given infections **41.3%**[134] VE against transmission **88.5%**[134] VE against onwards transmission of Alpha **57% (95% CI, 5-85)**[92] VE against onwards	VE against onwards transmission: **52%** (95% CI, 33-69)[16] 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. [139xcvi] VE against transmissibility was **31%** (95% CI, 26-36) when the	**48%** (limited data) May not be able to block the transmission of the alpha variant as efficiently as the wild type[142]. 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. [139xcvii]	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[140] Estimated SAR to fully vaccinated household contact was **42.7%** (95% CI, 13.6-77.9)[141]	Unknown	Unknown	No available data	No available data

[lxxvii] Study does not differentiate between Pfizer, Moderna, or AstraZeneca.
[xcvi] Study does not differentiate between Comirnaty/BNT162b2, Spikevax/ mRNA-1273, and Vaxzevria/ ChAdOz1 nCOV-19.
[xcvii] Study does not differentiate between Comirnaty/BNT162b2, Spikevax/ mRNA-1273, and Vaxzevria/ ChAdOz1 nCOV-19.

	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)[135] Proportion of the total effect (mediated by Ct values) of two vaccinations on transmission of the Alpha variant was **18%** (95% CI, 9-64)[135] *During Delta Variant:* Similar Ct values (<25) were found in both vaccinated and unvaccinated groups[136] VE against onwards transmission (VET) of Delta two weeks after full vaccination was **50%** (95% CI, 35-61); at 12 weeks	secondary case was not vaccinated and **10%** (95% CI, 0-18) when secondary case was fully vaccinated[140] Estimated SAR to fully vaccinated household contact was **6.2%** (95% CI, 2.8-13.0)[141]	Evidence of fully vaccinated individuals infecting other fully vaccinated individuals[143] 81 breakthrough infections among 1100 HCWs; 32 breakthrough infections among 4000 HCWs[143] VE against onwards transmission of Alpha **35% (95% CI, -26 – 74**)[92] Proportion of the total effect (mediated by Ct values) of two vaccinations on transmission of the Alpha variant was **16%** (95% CI, 1-80)[135] VE against onwards transmission (VET) of Alpha two weeks after full vaccination						

	VET was **24%** (95% CI, 20-28)[135] Proportion of the total effect (mediated by Ct values) of two vaccinations on transmission of the Delta variant was **23%** (95% CI, 17-33)[135] Studies from Scotland and England demonstrated reductions in secondary infections among families of vaccinated individuals compared to families of unvaccinated individuals[137,138]. VE against onwards transmission: **62%** (95% CI, 57-67)[16] VE against transmission from vaccinated index case to		was **24%** (95% CI, 18-30); at 12 weeks VET was **2%** (95% CI, -2-6)[135] 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)[135] Proportion of the total effect (mediated by Ct values) of two vaccinations on transmission of the Delta variant was **7%** (95% CI, 5-10)[135] VE against onwards transmission of Delta **42% (95% CI, 14-69**)[92] VE against transmissibility was **31%** (95% CI,						

	unvaccinated contact is **63%** (95% CI, 46-75) and **40%** (95% CI, 20-54) to a vaccinated contact. [139xcv] VE against onwards transmission of Delta **31% (95% CI, -3 – 61**)[92] VE against infection [within a ten-day window] when having a confirmed household exposure **80.4%** (95% CI, 73.6-85.5)[69] 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		26-36) when the secondary case was not vaccinated and **10%** (95% CI, 0-18) when secondary case was fully vaccinated[140]						

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

	homogenously vaccinated household members [within a ten-day window][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[140] 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[141] Estimated SAR to fully vaccinated household contact was **15.8%** (95% CI, 15.0-16.7)[141]									

Transmission prevention: Omicron	Secondary attack rate was **31%** in households infected with the Omicron VOC and **21%** in households with the Delta VOC[144]. 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[144]. Among individuals who had received a third (booster) shot, secondary attack rate was **25%** for Omicron and **11%** for Delta[144]. 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[144]. 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[144].						
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 Delta variant). Of the 1,120 cases, 126 (12%) were hospitalized. Of the 126 breakthrough admissions, 59	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 Delta variant). Of the 1,120 cases, 126 (12%) were hospitalized. Of the 126 breakthrough	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 after having received two doses of Covishield) were identified. Of these, 199 (83.3%) were	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 Delta variant). Of the 1,120 cases, 126 (12%) were hospitalized. Of the 126 breakthrough	No available data	No available data	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-CoV-2 positive after having received two doses of Covishield) were identified. Of these, 29 (82.9%)	No available data

	were vaccinated with BNT162b2[145]. 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[146] Breakthrough infections remained under 1% for fully vaccinated individuals (no difference between Pfizer or Moderna recipients between May and August 2021.[125] In a study of 10,412 participants, of which 8,554 were	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.[125] 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	symptomatic, 24 (10.0%) were hospitalized - 59 individuals had comorbidities[153] Median antibody titer: 647.5 AU/ml[153] 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 asymptomatic cases (IQR: 16.5 log10/mL vs 30.8 log10/mL, respectively). NAbs were measured for 10 breakthrough cases, all 10	admissions, 10 were vaccinated with Ad26.COV2.S[145]. **4.2%** of fully vaccinated HCWs developed breakthrough infections – all cases were symptomatic but mild, only one case required hospitalization[ciii] [155] Rate of breakthrough infections was comparable to Pfizer and Moderna recipients during the initial stages of the study, but increased to 1.96% (2 times the breakthrough rate of mRNA vaccines).[125]			were symptomatic, 3 (8.6%) were hospitalized. 5 individuals had comorbidities[153] Median antibody titer: 213.5 AU/ml[153] **4.2%** of fully vaccinated HCWs developed breakthrough infections – all cases were symptomatic but mild, only one case required hospitalization [cvi] [155] In a study of 614 of HCW, 13% (81 of 614) had breakthrough infections – within breakthrough infections, 63% (51 of 81**)** were Covaxin recipients. [India;	

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

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

	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] [147] [xcviii] In a case series of 20 HCWs, 90% (18 of 20) had confirmed infection after the 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	September 2021] ([147] [c] 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. [Switzerland; December 2021 to October 2021][ci] Of 23,697 vaccinated HCPs, 0.58% tested positive for COVID (138 of 23,697 cases that	cases had lower NAbs at day 14 and 90 post second vaccination compared to controls[154] 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. [Switzerland; December 2021 to	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] [147] [civ] 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			January to July 2021] [115]	

[xcviii] Study does not differentiate between Pfizer, Moderna, or Johnson & Johnson.
[c] Study does not differentiate between Pfizer, Moderna, or Johnson & Johnson.
[ci] Study does not differentiate between Pfizer, Moderna, AstraZeneca, or Janssen.
[civ] Study does not differentiate between Pfizer, Moderna, or Johnson & Johnson.

	dose. [Saudi Arabia; December 2020 to March 2021] [148] 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. [Switzerland; December 2021 to October 2021] [149]xcix Of 23,697 vaccinated HCPs, 0.58% tested positive for COVID (138 of 23,697	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. [150] 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	October 2021] [149] cii 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] [115]	cases (478 of 492) were asymptomatic or mild and 2.8% (14 of 492) required hospitalization. [Switzerland; December 2021 to October 2021] [149] cv 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 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				

[xcix] Study does not differentiate between Pfizer, Moderna, AstraZeneca, or Janssen).

[cii] ***Study does not differentiate between Pfizer, Moderna, AstraZeneca, or Janssen.

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

	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.[150] Among 1,128 cluster-associated cases of COVID, 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 &	across Pfizer, Moderna, and Johnson & Johnson vaccines.[151]			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][156] Among 1,128 cluster-associated cases of COVID, 918 (81%) were identified as breakthrough infections. Of these, 121 (13%) received the Johnson & Johnson vaccine. Characteristics of breakthrough infection cases were similar				

	Johnson vaccines.[151] Overall test positivity rate was 6.4% during the period of Delta dominance and 24.4% during a proxy Omicron period.[South Africa] [74] *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[152]			across Pfizer, Moderna, and Johnson & Johnson vaccines.[151]				
	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**	**BBIBP-CorV,**	**CoronaVac**	**COVAXIN / BBV152**	**Novavax/ NVX-CoV2373** (Awaiting approval from WHO EUL)

Common side effects	Pain at the injection site, fatigue, headache, myalgia, chills and fever, arthralgia Optimal safety for asthma patients. The vaccine is considered safe for cancer patients undergoing treatments.	Pain at injection site, headache, fatigue, myalgia, arthralgia, Covid arm (cutaneous hypersensitivity). The vaccine is considered safe for cancer patients undergoing treatments.	Fatigue, myalgia, arthralgia, headache, lethargy, fever, & nausea.	Headache, fever, chills, fatigue, myalgia, and nausea.	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
Rare adverse events	Myocarditis & myopericarditis, anaphylaxis and swelling of the lips, face, and tongue related to anaphylaxis (11 anaphylaxis cases per million doses administered), axillary aadenopathy, paroxysmal ventricular arrhythmia, leg paresthesia, pityriasis rosea (lesions improved completely after ~8 weeks), lymphocytic vasculitis,	Myocarditis & myopericarditis, 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	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,	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[163] 97% of reported reactions after	Cutaneous reactions, herpes zoster[169], CNS demyelination[163] 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,	Subacute thyroiditis, herpes zoster[170]	Cutaneous reactions Myocarditis was reported in one vaccine recipient, occurring 3 days after second dose

	varicella-zoster reactivation, Kikuchi-Fujimoto disease, thrombotic thrombocytopenic purpura, IgA nephropathy flare-up, Guillain-Barré syndrome, pustural psoriasis, immunoglobulin A vasculitis, immune complex vasculitis, 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,	pustulosis, rhabdomyolysis, 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 reactions, Löfgren's syndrome, erythema multiforme, pemphigus vulgaris, graft rejection (corneal), thrombotic thrombocytopenic purpura, reactivation of BCG scars[162],	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 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[165], acute-onset polyradiculoneuro	vaccine administration were non-serious.		serum sickness-like reaction, cutaneous reactions, neuromyelitis optica spectrum disorders (transverse myelitis or optic neuritis), bullous pemphigoid, CNS demyelination[163]		

	glomerulonephritis, Ramsay-Hunt syndrome, Sweet's syndrome, neurological autoimmune disease, axillary adenopathy, multiple sclerosis, meningoencephalitis, intracerebral haemorrhage due to vasculitis, cutaneous reactions, pigmented purpuric dermatosis, graft rejection (corneal), flexural exanthema, severe non-anaphylatic allergic reaction, uveitis, erythroderma, Behçet's disease [157], brachial plexus neuritis[158], systemic capillary leak syndrome [159], chronic graft-versus-host-disease flare up[160], vaccine-induced	urticarial vasculitis[164], CNS demyelination[163]	pathy[166], cutaneous reactions, leukocytoclastic vasculitis, Löfgren's syndrome, acute eosinophilic pneumonia, bullous sweet syndrome, neuralgic amyotrophy of the lumbosacral plexus, sudden sensorineural hearing loss, graft rejection (corneal), erythema annulare centrfugum, graft rejection (stromal)[167], leukocytoclastic vasculitis[168]						

	pneumonitis[161], reactivation of BCG scars[162], CNS demyelination[163] Systemic allergic symptoms were more common in BNT162b2 than 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	Cerebral venous sinus, Autoimmune hepatitis, myocardial infarction, autoimmune haemolytic	Autoimmune hepatitis, Acute hyperglycaemic crisis, Facial nerve palsy, cervical myelitis, alopecia areata, takotsubo (stress)	Facial Diplegia, acute macular neurotinopathy, cerebral venous sinus thrombosis, oral lichen planus	Longitudinally extensive transverse myelitis	Likely vaccine associated disease enhancement (VADE), autoimmune hepatitis	No available data	No available data

	sclerosis relapse, myeloperoxidase anti-neutrophil cytoplasmic antibody-positive optic perineuritis, central retinal vein occlusion, paracentral acute middle 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	anaemia, hypophysitis & panhypopituitarism, erythema nodosum-like rash, pulmonary embolism, minimal change disease, encephalomyelitis, lupus nephritis, retinal vein occlusion, takotsubo syndrome[175] One case developed IgA Nephropathy after receiving the second dose of mRNA-1273.	cardiomyopathy, acute disseminated encephalomyelitis, cerebral venous sinus thrombosis (higher risk for women), ophthalmic vein thrombosis, retinal vein occlusion, Still's disease, autoimmune encephalitis, acute abducens palsy, lichenoid eruption					

	disease, miller fisher syndrome, unilateral acute foveolitis, encephalomyelitis, acute posterior multifocal placoid pigment epitheliopathy, trigeminal neuralgia, vestibular neuritis[171], autoimmune acquired factor XIII/13 deficiency[172], Still's disease[173], [171], autoimmune acquired factor XIII/13 deficiency[172], Still's disease[173], cranial nerve palsy [174]							
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)[176]	Mainly reported in young adults and adolescents *First dose (1-28 days post vaccination):* No association[176] *Second dose:*	*First dose (1-28 days post vaccination):* Incidence rate ratio of **1.27** (95% CI, 1.05-1.55)[176] *Second dose:* No association[176] *Third dose:*	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

	Second dose: Incidence rate ratio of **1.60** (95% CI, 1.31-1.97)[176] *Third dose:* Incidence rate ratio of **2.02** (95% CI, 1.40-2.91)[176] *Males <40 years:* *First dose [1-28 days post vaccination]:* Incidence rate ratio of **1.66** (95% CI, 1.14-2.41)[176] *Second dose [1-28 days post vaccination]:* Incidence rate ratio of **3.41** (95% CI, 2.44-4.78)[176] *Third dose [1-28 days post vaccination]:* Incidence rate ratio of **7.60** (95% CI, 2.44-4.78)[176] Israeli study: Estimated incidence within 42 days after receipt of first	Incidence rate ratio of **13.71** (95% CI, 8.46-22.20)[176] *Third dose:* No association[176] (small sample size) *Males <40 years:* *First dose [1-28 days post vaccination]:* Incidence rate ratio of **2.34** (95% CI, 1.03-5.34)[176] *Second dose [1-28 days post vaccination]:* Incidence rate ratio of **16.52** (95% CI, 9.10-30.0)[176] *Females <40 years* *Second dose [1-28 days post vaccination]:* Incidence rate ratio of **7.55** (95% CI, 1.67-34.12)[176]	No association[176] (small sample size) *Males <40 years:* *Second dose [1-28 days post vaccination]:* Incidence rate ratio of **2.57** (95% CI, 1.52-4.35)[176]						enhanced COVID-19 was reported

	dose per 100,000 vaccinated persons was **2.13** cases (95% CI, 1.56-2.7) <u>Male patients</u> 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[177] **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	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 patients aged 12-39[178] *<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[179] <u>Male patients</u> **6.3** (95% CI, 3.6-10.2) per 100,000 vaccinated[179]							

	95.4 (95% CI, 52.1-160.0) **cases** per 1 million second dose administrations in patients aged 12-39[178] **5.07** cases per 100,000 Disease severity 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) Risk per 100,000 persons 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**								

	12–39-year-olds (within 28 days of vaccination: Female patients **1.3** (95% CI, 0.8-1.9) per 100,000 vaccinated[179] Male patients **1.5** (95% CI, 1.0-2.2) per 100,000 vaccinated[179]							
	CHILDREN VACCINATION							
	BNT162b2/ COMIRNATY	**Spikevax/ Moderna COVID-19 Vaccine/ mRNA-1273**	**Vaxzevria/ ChAdOx1 nCoV-19/ AZD1222/ Covishield**	**Janssen COVID-19 vaccine/Johnson & Johnson**	**BBIBP-CorV,**	**CoronaVac**	**COVAXIN / BBV152**	**Novavax/ NVX-CoV2373**
Efficacy	*Adolescents (12-15):* After one dose had efficacy of **75% (CI, 7.6-95.5)** After second dose efficacy of **100% (CI, 78.1-100)**[180]. *Children (5-11):*	*Adolescents (12-17):* 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)**[183] ***Against SARS-CoV-2 Infection:***	No available data Paused ongoing trials in children aged 6-17 due to concerns over rare blood clots reported in adult population[185].	No available data Announced at beginning of April ongoing study in adolescents but paused to investigate blood clots in adult population[185].	*Children (3-17):* Unknown. Ongoing clinical trial only looked at safety, tolerability, and immunogenicity[cvii] *	*Children (3-17):* Unknown. Clinical trial only looked at safety, tolerability and immunogenicity[186].	No available data	*Adolescents (16-17):* PREVENT-19 clinical trial[cviii] expanded to assess efficacy, safety, and immunogenicity in 12–17-year-old adolescents[187]

[cvii] 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

[cviii] 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

	After second dose efficacy of **90.7% (CI, 67.7-98.3)**[181] *Children (Under 5 years):* Ongoing trials[182]	14 days after first dose efficacy of **68.9% (95% CI, 49.9-82.1)** 14 days after second dose efficacy of **55.7% (95% CI, 16.8,82.1)**[183] ***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)**[183] *Children (6month-11):* Ongoing trials[184]			* The study design administered **three doses** of 2 µg, 4 µg, or 8 µg of vaccine			
Effectiveness	*Adolescents Against SARS-CoV-2 infection:* **91.5%** (95% CI, 88.2-93.9)[188] **91%** (95% CI, 88-93)[189] *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)[189]
93% (95% CI,83-97)[190]
94% (95% CI, 91 to 97)
Adolescents against ICU care:
98% (95% CI, 93 to 99)191

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 days192

Immunogenicity	*Adolescents (12-15) serum-neutralizing titer:* 1 month after 2nd dose had **1283.0 GMN_{50} (CI, 1095.5-1402.5)**[180]. *Adolescents/young adult (16-25) serum-neutralizing titer:* 1 month after 2nd dose had **705.1 GMN_{50} (CI, 621.4-800.2)**[180]. *Children (5-11):* 1 month after 2nd dose had **1,197.6 GMT (95% CI, 1106.1-1296.6)** SARS-CoV-2-neutralizing antibody[181] *Children (Under 5):* Ongoing trials[182]	*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)**[183] *Children (6-11):* Seroreponse of **99.3%**[193] *Children (6month-11):* Ongoing trials[184]	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[194] GMC of anti-RBD antibody in adolescent cohort aged 12-17 was **102.9 BAU/mL (95%CI; 91.0-116.4)** after 4 weeks since 2nd dose[195]	*Children (3-17):* Neutralizing antibody response after 2nd dose **(100%)** with GMT ranging from **45.9-212.6**[186]	Ongoing clinical trial[196] 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[197]	Ongoing clinical trial[198]

Safety and Adverse events	Rare possibility of developing multisystem inflammatory syndrome[199] *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%)** Severe adverse events **(0.6%)**[180]. *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%)**[180]. *Children (5-11):*	Rare possibility of developing multisystem inflammatory syndrome[199] *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%)** Fatigue **(67.8%)** Grade 3 adverse events **(6.8%)**)[202] 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**[183] *Children (6-11):*	No available data	Rare possibility of developing multisystem inflammatory syndrome[199]	*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** Adverse events were mostly mild to moderate in severity[194] **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[195]	*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%)**[186]	Ongoing clinical trial[196] 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 group197	Ongoing clinical trial[198]

	Pain at injection site, fatigue, headache, chills were reported. Overall, the vaccine is safe and tolerable[181] *Children (Under 5):* Ongoing trials[182] Multisystem inflammatory syndrome (causal link not yet proven)[200] Additional reports of rare cases of multisystem inflammatory syndrome[199] *Adverse events cases:* 15-year old boy developed nephrotic syndrome[201]	Vaccine was generally well tolerated[193] *Children (6month-11):* Ongoing trials[184]						
Myocarditis Data	Few reported cases of acute myocarditis and pericarditis in 16-	Few reported cases of acute myocarditis and pericarditis	No available data	No available data	No available data	No available data	No available data	No available data

	25 year olds (mainly in males)[202] Male patients 12-17 years **97 cases per million** (1 in 10,000 males)[203] Female patients 12-17 years **16 cases per million** (1 in 63,000 females)[203] 16-29 years Incidence of **5.49** (95% CI, 3.59-7.39) per 100,00 vaccinated[177] Male patients (16-29 years) Incidence of **10.69** (95% CI, 6.93-14.46) per 100,000 vaccinated[177] Incidence of **13.6 cases** (95% CI, 9.30-19.20) per 100,000 vaccinated[204]	(mainly in males)[202] *16-17 year old boys in US*: *Second dose*: 31.2 cases per million doses administered[205]							

	12-15 year old boys in US: *First dose*: 4.8 cases per million doses administered[205] *Second dose*: 42.6 cases per million doses administered[205] *12-15 year old girls in US*: *First dose*: 0.5 cases per million doses administered[205] *Second dose*: 4.3 cases per million doses administered[205] *16-17 year old boys in US*: *First dose*: 5.2 cases per million doses administered[205] *Second dose*: 71.5 cases per million doses administered[205] *16-17 year old girls in US*: *First dose*: 0.0 cases per million								

	doses administered[205] *Second dose*: 8.1 cases per million doses administered[205]							
	HETEROLOGOUS VACCINATION							
Vaccine Schedule	**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 first dose was Sinovac[cix] **CoronaVac/Convidecia**	**ChAdOx1/BBV152** Administration of Covaxin as second/booster dose	Ongoing trial[206] (Com-Cov2)[cx]
Immunogenicity	*GMCs of SARS-CoV-2 anti-spike IgG at 28 days post booster:*	**Spike-specific IgG antibodies:* Heterologous **(3602 BAU/mL)** vs.	*RBD antibody titres:* Heterologous **(7756.68 BAU/mL, CI**	Not Applicable (one dose schedule)	Unknown (on-going clinical trial)[49]	**CoronaVac/ChAdOx1 :** *Anti-S Antibodies:*	*RBD antibody titres:* Heterologous **(1866 GMT; 95% CI, 1003-3472)**	No available data Ongoing trial[206]

[cix] 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/

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

	Heterologous **(7133 ELU/mL, CI 6415-7932)** vs. Homologous **(14080 ELU/mL, CI 12491-15871)**[207]. *SFC frequency (T0cell ELISpot):* Heterologous **(99 SFC/10^6 PBMCs)** vs. Homologous **(80 SFC/10^6 PBMCs)**[207]**.** ***Heterologous mRNA:*** **84.7%** effectiveness (95% CI, 83.1-86.1)[8]	Homologous **(4189 BAU/mL)**[48] **Neutralizing antibodies:* Heterologous **(100%)** vs. Homologous **(100%)**[208]. ***Heterologous mRNA:*** **84.7%** effectiveness (95% CI, 83.1-86.1)[8] *Results based on immunosuppressed population	**7371.53-8161.96)** vs. Homologous **(99.84 BAU/mL, CI 76.93-129.59)** at day 14[209]. *IgG antibody titres:* Heterologous **(3684 BAU/mL)** vs. Homologous **(101.2 BAU/mL)** at day 14[209]. *Neutralizing antibodies:* Heterologous **(100%)** at day 14 vs. Homologous **(30%)** at day 14[209]. Heterologous **(median 99%)** vs. Homologous (BNT162b2/BNT162b2) **(median 62%)**[210]	For more information refer to booster section		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)**[211] **CoronaVac/Convidecia** *Neutralizing antibodies :* Heterologous **54.4 GMT** (95% CI, 37.9-78) vs. Homologous CoronaVac **12.8 GMT** (95% CI, 9.3-17.5)[212]	vs. Homologous Covishield **(2260 GMT; 95% CI, 1881-2716)** vs. Homologous Covaxin **(710 GMT, 95% CI, 461-1092)**[213] *N-protein IgG:* Heterologous **(1145 GMT; 95% CI, 520.7-2520)** vs. Homologous Covishield **(353.7 GMT; 95% CI, 219.9-568.9)** vs. Homologous Covaxin **(742.4 GMT; 95% CI, 485.8-1134)**[213] *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)**[213]	
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[210] *Omicron (B.1.1.529):* **13/20 seropositive** against Omicron[214]	No available data	No available data	No available data	*Neutralizing antibody titres **B.1**:* **539.4 GMT (95% CI, 263.9-1103)**[213] *Neutralizing antibody titres **Alpha**:* **396.1 GMT (95% CI, 199.1-788)**[213] *Neutralizing antibody titres **Beta**:* **151 GMT (95% CI, 80.21-284.3)**[213] *Neutralizing antibody titres **Delta**:* **241.2 GMT (95% CI, 74.99-775.9)**[213]	No available data
Reactogenicity	Observed increase in systemic reactogenicity after boost in heterologous schedules in	*Adverse events in heterologous and homologous vaccination groups were very similar[208].	*Adverse events in heterologous:* Headache **(44%)**, Myalgia **(43%)**, Malaise **(42%)**, Fever **(2%)**, Injection site pain	Not Applicable (one dose schedule) For more information refer to booster section	Unknown (on-going clinical trial)[215]	**CoronaVac/ChAdOx1:** Unknown **CoronaVac/Convidecia:**	*Most common local adverse events:* Pain at injection site **(11.1%)**[213]	No available data Ongoing trial[206]

	comparison with homologous schedules[207] *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[207]. *Adverse events in homologous:* Adverse events **(81)** Grade 1 **(59.3%)** Grade 2 **(39.5%)** Grade 3 **(1.2%)** Grade 4 **(0%)**[207].	*Majority of adverse events self-reported were Pain at injection site, Swelling at injection site, Fever, Headaches, Fatigue, Chills, GI effects, Myalgia, Arthralgia[208]. *Results based on immunosuppressed population	**(88%)**, Induration **(35%)**, Erythema **(31%)**[209]. *Severity of adverse events in heterologous:* Mild **(68%)**, Moderate **(30%)**, Severe **(2%)**[209].			Convidecia recipients reported more adverse reactions and reported higher occurrence of solicited injection-site pain)[212]	*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[213]	
	BOOSTER DOSES							
Vaccine Schedule	**BNT162b2/BNT162b2**	**mRNA-1273/mRNA-1273**	**ChAdOx1/ChAdOX1**	**Ad26.CoV.2.S/ Ad26.CoV.2.S**	**SinoPharm/SinoPharm**	**CoronaVac/CoronaVac**	**Covaxin/Covaxin**	**NVX-CoV2373/NVX-CoV2373**
Approved Administration	*Israel:* 12-year-old and over can received homologous booster shot 5	Phase II booster trial of three booster doses are ongoing[216]	Preliminary results on tolerability and immunogenicity of third dose of ChAdOx1 vaccines showed	Johnson & Johnson has said it will submit all of their new data to the FDA for potential	*UAE:* Offering booster doses of Pfizer and Sinopharm to people who received full	**Turkey** and the **United Arab Emirates** began homologous booster shots	**India** has started administering homologous booster doses	Ongoing phase II trials[218]

	months after full jab[cxi] *United States:* Starting September, adults who received mRNA vaccine 8 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[cxii]	Moderna sought FDA approval of its COVID-19 vaccine booster[cxiii] *United States:* Starting September, adults who received mRNA vaccine 8 months ago are eligible for booster.	strong boost to the immune response[217]	consideration for adding a booster dose and consideration to authorize two-dose regimen[cxiv]	Sinopharm jab ≥6 months ago	**Indonesia** and **Thailand** are considering giving homologous booster shot to HCW[cxv]		Results below are based on ongoing phase II trial

[cxi] 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/

[cxii] 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/

[cxiii] 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/

[cxiv] 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

[cxv] 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/

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 new Omicron variant[cxvi]	**6 months to 8 months** after initial two-dose regimen	**6-9 months** after initial two-dose regimen	**6 months** after one dose regimen[116]	**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**)[218]
Efficacy	*Symptomatic COVID-19:* **95.6%** during Delta prevalent period[219] **95.3% (**95% CI, 89.5-98.3)[220] **96.5%** (95% CI, 89.3-99.3) in *16-55 year old*[220] **93.1%** (95% CI, 78.4-98.6) in *≥55 year old*[220]	No available data	No available data	No available data	No available data	No available data	Ongoing clinical trials[xxxvii]	No available data

[cxvi] 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	*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[221] *Effectiveness against symptomatic infection:* **92%** (95% CI, 91-92)[222] **85.6%** (95% CI, 79.2-90.1) relative to two doses[223] **88%** (95% CI, 87-88)[223] **82%** (95% CI, 79-85)[223] *Effectiveness in ≥50:* **84.4%** (95% CI, 82.8-85.8) against symptomatic COVID-19[224] **94.0%** (93.4-94.6) against symptomatic	*Effectiveness against infection:* **94%** (95% CI, 91-95)[222] **91%** (95% CI, 90-92)[223] **87%** (95% CI, 83-91)[223] *Effectiveness against hospitalization:* **86%** (95% CI, 82-89)[223]	No available data	No available data	No available data	*Effectiveness against symptomatic infection:* **78.8%** (95% CI, 76.8-80.6)[225] *Effectiveness against hospitalization:* **86.3%[225]** *Effectiveness against ICU admission:* **92.2%[225]** *Effectiveness against COVID-19 related death:* **86.7%[225]**	No available data	No available data

	COVID-19 compared with unvaccinated[224] *Effectiveness against hospitalization:* **87%** 0-6 days after receiving booster dose **92% to 97% lower** than those who received 2 doses[221] **88%** (95% CI, 86-90)							
Effectiveness against Variants	***Omicron (B.1.1.529):*** **75.5%** (95% CI, 56.1-86.3) effectiveness against symptomatic infection[83] If assuming 25-fold decrease compared to wild-type, **81%** (95% CI, 59-95) **54.6%** (95% CI, 30.4-70.4) effectiveness	**Delta (1.617.2):** 95.2% (93.4%-96.4%)[86] **Omicron (B1.1.529):** 62.5% (95% CI 56.2-67.9%)[86]		***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				

	against symptomatic infection in ≥60-year-old[85]			months post booster[226]				
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[223] *IgG Antibodies:* **1.7-fold increase** (95% CI, 1.6-1.9) following booster compared to 2-initial doses[223] ***≥ 60 years:*** *Neutralizing antibody:* **9.34 times higher** than second dose *IgG Antibodies in* **97%** seroconversion with increase in IgG antibody titers[227]	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[228] *IgG Seroconversion:* **175/176** vaccinees were seropositive for IgG 14 days after receiving third dose 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[228]	Neutralizing Antibodies: **60%** higher NAbs activity against wild-type compared to 2-doses Anti-S IgG and NAbs: **20-fold** increase 4 weeks post booster vaccination NAbs were maintained **60** to **180 days** post booster	*Neutralizing Antibodies ($PRNT_{50}$):* **30-fold increase** with **746 GMT** (95% CI, 515-1081) 4 weeks after booster[229] *S-protein IgG:* Increase of IgG to **11,119 GMT** (95% CI, 8,689-14,229) 4 weeks after booster dose[229] *Anti-RBD & Anti-nucleocapsid IgG:* **Increase** in IgG antibodies 4 weeks after booster dose[229]	*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; 95% CI: 4738-8195)** [218] *Serum IgG:* **4.7-fold increase** from **43,905 EU** following primary vaccination to **204,367 EU** following booster[230] *Older Participants (60-84):*

	33-fold increase in IgG after booster dose				*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%)**			**5.4-fold** increase in antibody response[218] **5.1-fold increase** in serum IgG[230] *Younger Participants (18-59):* **3.7-fold** increase in antibody response **4.1-fold increase** in serum IgG[230]
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	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[232] **Omicron (B.1.1.529):** **12-fold increase** in neutralization titer (GMT) against Omicron	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 **Delta (B.1.671.2):** **83.4%%** plasma inhibitions against Delta variant **Lambda:** **89.0%** plasma inhibitions against Lambda variant **Omicron:** **4-fold increase** in neutralization titer against Omicron compared to 2-	**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	**Alpha (B.1.1.7):** **161-fold increase** with **338 GMT** (95% CI, 188-607) 4 weeks after booster dose[229] **Beta (B.1.351):** **265-fold increase** with **147.3 GMT** (95% CI, 75-289) 4 weeks after booster dose[229] **Delta (B.1.671.2):** **32.6-fold increase** with **252 GMT** (95% CI, 133-482) 4 weeks after booster dose[229]	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[230] **Beta (B.1.351):** **40.6-fold increase** in serum IgG[230] **24.5-fold increase** in anti-S IgG compared to 2-initial doses[230]

	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 **17-fold increase** in neutralization titer compared to 2-initial doses[231]	compared to 2-initial doses[232]			dose vaccination[232] **11-fold decrease** in neutralization titer 14 days after booster dose compared to wild type[232] **3.3-fold increase** in neutralizing activity 28 days after booster compared to 2-initial doses against Omicron[228]	**2.5-fold** higher neutralizing potency than 2-dose vaccination	**Delta Plus:** **174-fold increase** with **174 GMT** (95% CI, 64-474) 4 weeks after booster dose[229]	**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 IgG compared to 2-initial doses[230] **Omicron (B.1.1.529):** **20.1-fold increase** in anti-S IgG compared to 2-initial doses[230]
Reactogenicity	Preliminary results show consistent tolerability **25%** reported at least one adverse event[220] *Common solicited AE:* Injection site pain, injection site redness, injection	Similar safety and tolerability compared to second dose *Common solicited local adverse events:* Injection-site pain **(68.4% for mRNA-1273.351, 90% for mRNA-1273)**	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:* Pain at the injection site. *Adverse events:* Unrelated to the vaccination	Most reported adverse events were **mild and resolved within 24 hours**[229] *Solicited Adverse Events:* **8** solicited adverse events were reported **5.4%** care of pain, **2.1%** itching **1%** redness[229]	Booster dose was **well tolerated** Local and systemic **reactogenicity increased** between Dose 1, Dose 2, and Dose 3 **90%** of symptoms were rated as mild or moderate

	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	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)**						
Protection against COVID-19	***Confirmed Infection:*** 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	No available information	No available information	No available information	No available information	No available information	Ongoing clinical trials[xxxvii]	No available information

	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 [233] **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[233] **17.9 (95% CI, 15.1-21.2) lower rate** in booster group[234]									

	Mortality: ≥60 years old: **14.7 (95% CI, 10.0-21.4) lower rate** in booster group[234] ≥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[235]							
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)**[236] *Viral Load:* **52% decrease** in Ct-reduction post the booster shot	No available data	No available data	No available data	No available data	No available data	No available data	No available data

	over time (decline in reducing viral loads over time)[237]							
Other	Detailed report from Pfizer regarding booster doses can be found here: https://www.fda.gov/media/152161/download 14-20 days after booster, marginal effectiveness increases to **70-84%** ***Incidence Rate:*** Infection in individuals <60: **0.22 (95% CI, 0.22-0.23) incidence rate** in booster compared to non-booster[238] Infection in individuals ≥60: **0.16 (95% CI, 0.15-0.17)**					For more detailed information regarding immunogenicity of third dose refer to study[cxvii]		

[cxvii] 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*

	incidence rate in booster compared to non-booster[238] Severe illness in individuals <60: **0.33 (95% CI, 0.21-0.52) incidence rate** in booster compared to non-booster[238] Severe illness in individuals ≥60: **0.12 (95% CI, 0.10-0.14) incidence rate** in booster compared to non-booster[238]							
	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:* **SinoPharm/BNT162b2**	*Heterologous 1:* **CoronaVac/ChAdOx1** *Heterologous 2 :* **CoronaVac/BNT162b2** *Heterologous 3 :* **CoronaVac/SinoPharm** *Heterologous 4:*	No available data	*Heterologous 1:* **BNT162b2/NVX-CoV2373** *Heterologous 2:* **ChAdOx1/NVX-CoV2373** *****Received NVX-CoV2373 as booster dose

							CoronaVac/mRNA1273 *Received CoronaVac as initial regimen		
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[239] 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:* **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	No available data	**6 months** after initial two-dose regimen
Effectiveness	*Heterologous 1:* **94%** (95% CI, 91-96) effectiveness against infection[222] *Heterologous 2 – Effectiveness in ≥50:*	*Heterologous 1:* **92%** (95% CI, 88-95) effectiveness against infection[222] *Heterologous 3:*	No available data	No available data	No available data	*Heterologous 1:* **93.2%** (95% CI, 92.9-93.6) against symptomatic infections[225] **97.7%** against hospitalization[225]	No available data	No available data

	87.4% (95% CI, 84.9-89.4) against symptomatic COVID-19[224] **93.1%** (95% CI, 91.7-94.3) against symptomatic COVID-19 compared to unvaccinated[224] *Heterologous 3:* **82%** (95% CI, 68-90) effectiveness against infection[222]	**91%** (95% CI, 63-98) effectiveness against infection[222]				**98.9%** against ICU admission[225] **98.1%** against COVID-19 related death[225] *Heterologous 2:* **96.5%** (95% CI, 96.2-96.7) against symptomatic infections[225] **96.1%** against hospitalization[225] **96.2%** against ICU admission[225] **96.8%** against COVID-19 related death[225]		
Effectiveness against Variants	No available data	No available data	***Omicron (B.1.1.529):*** *Heterologous 1:* **71.4%** (95% CI, 41.8-86.0) against symptomatic infection[83]	No available data	No available data	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[240] *Neutralizing Antibody Responses:* **341.3-677.9 IU50/mL** 15 days after booster with BNT162b2[240] Participants who received mRNA-based booster vaccination had four-fold increase compared to Ad26.COV2.S. ***Heterologous 3:*** *Anti-spike IgG:* In individuals <70: **22479 ELU/mL** (95% CI, 18276-27648) Individuals ≥70: **19091 EUL/mL** (95% CI, 15554-23432)	*Binding Antibody Responses:* **2-fold or greater rise** in bAb noted in **96-100%** of mRNA1273 recipients[240] *Neutralizing Antibody Responses:* **676.1-901.8 IU50/mL** 15 days after booster with mRNA1273[240] 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)	***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)[241] *Cellular Response :* In individuals <70 : **105** (95% CI, 67-164) In individuals ≥70: **84** (95% CI, 45-156)[241]	***Heterologous 1:*** **14.8 to 32.4-fold** increase in neutralization titers against wild-type virus[239] *Binding Antibody Responses (bAb):* **2-fold or greater rise** in bAb noted in **98-100%** of Ad26.COV2.S. recipients[240] *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:*	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 highest antibody response, IgA, and neutralizing antibodies than other groups[242] *Anti-RBD Antibody:* **9865 U/mL** 14-days after booster[243] ***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	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)[241] *Cellular Response:* In individuals <70: **69** (95% CI, 45-156) In individuals ≥70: **45** (95% CI, 22-92)[241] ***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:*

	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	*Cellular Response :* In individulas <70 : **143 (95% CI, 82-250)** In individuals ≥70: **88 (95% CI, 46-168)** ***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) *Cellular Response:* In individuals <70: **228** (95% CI, 177-294) In individuals ≥70: **101** (95% CI, 54-187)		In individuals <70: **114** (95% CI, 55-236) In individuals ≥70: **109** (95% CI, 64-187)[241] ***Heterologous 3 :*** *Anti-spike IgG:* 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)		decreased by **factor of 6.5** *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 ***Heterologous 3:*** *Anti-spike RBD:* **1073 U/mL** 14 days after booster ***Heterologous 4:*** *IgG:* **9.3-fold increase** in median IgG titer compared to 2-initial doses **(250 to 2313 BAU/mL)**[244] *Seropositivity:* Increase from **96.4% to 100%**		In individuals <70: **137** (95% CI, 88-213) In individuals ≥70: **55** (95% CI, 35-89)

						after booster dose[244]		
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% lower** 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:*** *Pseudotype virus neutralizing antibody NT_{50}:*	*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:*** *Pseudotype virus neutralizing antibody NT_{50}:*	*AZD1222/ BNT162b2* Demonstrated **80%** response rate against Omicron serum sample & **14.7-fold** decrease in GMT[245] *AZD1222/ mRNA-1273* Demonstrated **82%** response rate against Omicron serum sample & **17.5-fold** decrease in GMT[245] *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}:* **418 GMT** (95% CI, 330-530) against **Delta**	No available data	***Heterologous 1:*** Neutralizing activity against the wild type and variant strains showed higher neutralizing activity in the following order: **wild type > B.1.617.2 > B.1.1.7 > B.1.351** ***Heterologous 2:*** **6.3-fold increase** in neutralization titers against **Delta** 28 days after booster dose compared to 2-initial doses[246] **6.3-fold decrease** in neutralization titers against **Omicron** 28 days after booster dose compared to wild type[246]	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**

	315 GMT (95% CI, 1314–1998) against **Delta**	**508.7 GMT** (95% CI, 408.6-633.4) against **Delta**[241] ***Heterologous 3:*** *Pseudotype virus neutralizing antibody NT_{50}:* **559.7 GMT** (95% CI, 441.3-709.9) against **Delta**		**41-fold increase** against **Omicron** compared to 2-initial doses[231] ***Heterologous 3:*** *Pseudotype virus antibody NT_{50}:* **125 GMT** (95% CI, 99-159) against **Delta**				
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[244]	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[cxviii]		

[cxviii] 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)	Sinopharm/BBIBP-CorV, China	Sinovac CoronaVac, China	COVAXIN/ BBV152 (Bharat Biotech, India)	Novavax/ NVX-CoV2373
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)[cxix]; EMA (21.12.20); WHO EUL (31.12.20); and list of countries (including Switzerland – approved on 20.12.20)	FDA (18.12.20); EMA (06.01.21); WHO EUL (30.04.21); and list of 51 countries (including Switzerland – approved 12.01.21)	FDA (awaiting on approval); EMA (29.01.21); WHO EUL (15.02.21); and list of 121 countries (Switzerland awaiting on approval)	FDA (27.02.21); EMA (11.03.21), WHO EUL (12.03.21), and list of 59 countries (including Switzerland – approved 22.03.21)	WHO EUL (07.05.21); and list of 55 countries (e.g., Argentina, Bahrain, Brazil, China, Indonesia, United Arab Emirates, Zimbabwe)	WHO EUL (01.06.21), and list of 33 countries (e.g., Albania, Chile, Egypt, Hong Kong, Malaysia, Tunisia, Turkey, Ukraine)	WHO EUL (03.11.21) and list of 9 countries (Guyana, Inidia, Iran, Mauritius, Mexico, Nepal, Paraguay, Philippines & Zimbabwe)	Waiting on approval (Not-yet-approved by countries or WHO for emergency use)
IMMUNOGENICITY								

[cxix] 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

Immunogenicity	*Single Dose (≥4 weeks):* **79.4% IgG seropositivity** (95% CI, 75.7-83.1)[247] *Second dose (≥4 weeks):* **96.5% IgG seropositivity** (95% CI, 94.9-98.1) to **92% IgG seropositivity onwards**[247] *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 the GMT of the convalescent serum.	*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**).	*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[115] *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**).	*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)[247] *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 titres (<25.6 IU ml) **94.8 BAU/ mL**	*IgG Antibodies:* **342.7 AU/mL** highest median[115] *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)** for SARS-CoV-2 spike antibody titre	

						77.4% IgG seropositivity (95% CI, 75.5-79.3)[247] *Two doses (8-12 weeks):* 34.7 BAU/ mL		
Immunogenicity against Delta variant	**7.77-fold reduction** in neutralization titres for **Delta (B.1.617.1)** when compared with wild-type[248] **11.30-fold reduction** in neutralization titres for **Delta (B.1.617.2)** when compared with wild-type[248] **157 $PRNT_{50}$** neutralization against **Delta (B.1.617.1)**[249] **355 $PRNT_{50}$** neutralization against **Delta (B.1.617.2)**[249]							

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[250] Boosted (3-dose schedule) **7-fold** decrease in neutralization against Omicron when compared to wild type[250]							
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[251] Plasma specimens one month after full mRNA vaccination, NT_{50} values were 127±66 times lower for Omicron than the wild type (Wuhan) strain. After 5 months, the neutralization	**20-fold decrease** in neutralization 6 months after vaccination compared to Delta[251] **1/10 seropositive** against Omicron[214] Plasma specimens one month after full mRNA vaccination, NT_{50} values were 127±66 times lower for Omicron than the wild type (Wuhan) strain. After 5 months, the neutralization potency was	Mean neutralizing titres drop to below the detectable threshold in all but one participant[251] **0/20 seropositive** against Omicron[214] The mean Omicron titre estimate in the infected + double vaccinated group suggests protection against symptomatic Omicron disease is **80%**[250] Demonstrated **50%** response	Vaccine lacked detectable neutralizing activity against Omicron.[252] Demonstrated **9%** response rate against Omicron serum sample[245]		Not a single serum sample demonstrated neutralizing antibodies against the Omicron VOC among 25 blood samples[257]	Only 5/20 live virus samples exhibited neutralization titres above the lower limit of quantification.[256]	

	potency was 27±17 lower for Omicron.[252] 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[252] A third booster dose increased the neutralization capacity against Omicron by **38** times.[252] **11.4-fold decrease** in neutralization 6 months after vaccination compared to Delta **25-fold decrease** in neutralization titers against Omicron variant	27±17 lower for Omicron.[252] 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[252] A third booster dose increased the neutralization capacity against Omicron by **38** times.[252] The mean Omicron titre estimate in the infected + double vaccinated group suggests protection against symptomatic Omicron disease is **91%**[250] Demonstrated **100%** response	rate against Omicron serum sample & **12.8-fold** decrease in GMT[245] Only 5/20 live virus samples exhibited neutralization titres above the lower limit of quantification.[256] No neutralizing antibodies were observed in serum samples obtained 1 months after the receipt of the second dose[255]						

	compared to wild-type[253] **41-fold decrease** in neutralization level against Omicron[254] **9/20 seropositive** against Omicron [214] Demonstrated **33%** response rate against Omicron serum sample[245] **9/20 participants** neutralized Omicron variant 1 month after 2nd dose[255]	rate against Omicron serum sample & **15.8-fold** decrease in GMT[245] No neutralizing antibodies were observed in serum samples obtained 4-6 months after the receipt of the second dose[255]						
				EFFICACY				
Single dose[cxx]	**52%** (95% CI, 29.5 to 68.4; starting at 12 days) or 82.2% (75.1 to 87.3; starting at ≥14 days).	**95.2%** (95% CI, 91.2.8 to 97.4; starting at >14 days)[258].	**72.8%** (starting at 22 days up to 60 days). **88%** (95% CI, 75-94).[cxxii]	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

[cxx] Against SARS-COV-2 infection

[cxxii] Conducted between 8 December 2020 and 8 February 2021. Study sample = ≤1 million participants.

	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, 8 Dec 2020 – 15 Mar 2021] [cxxi]		≥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] [cxxiii]					
Two doses[cxxiv]	**95.0%** (95% CI, 90.3-97.6) starting at ≥7 days in population without prior SARS-CoV-2 infection	**94.1%** (95% CI, 89.3-96.8) after median follow-up of less than 63 days	**63.1% (**95% CI, 51.8-71.7) starting at ≥14 days for two standard doses	**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-	After 14 days, efficacy against symptomatic cases was **72.8%** (95% CI 58.1-82.4; in WIV04 vaccine) or **78.1%**	After 14 days, efficacy against symptomatic cases was **50.7%** (95% CI 35.9 to 0-62.0).	*Symptomatic SARS-CoV-2 infection:* **77.8%** (95% CI, 65.2-86.4)	**89.7%** (95% CI, 80.2-94.6) starting at ≥7 days **90.4%** (95% CI, 82.9-94.6)

[cxxi] Does not differentiate between BNT162b2 and ChAdOx1 nCoV-19.
[cxxiii] Does not differentiate between BNT162b2 and ChAdOx1 nCoV-19.
[cxxiv] Against SARS-CoV-2 infection.

	94.6% (95% CI, 89.9-97.3) starting at ≥7 days in population with or without prior infection	**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) [259] *Prevention against severe disease:* **98.2%** (95% CI, 92.8-99.6; United States) [259] *Prevention against asymptomatic infection starting 14 days after second infection:* **63.0%** (95% CI, 56.6-68.5; United States) [259]	**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 June – 09 November 2020][260]	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	(95% CI 64.8 to 86.3; in HBO2 vaccine).	99.17% of NAb titres were above or equal to the Nab positivity cut-off (20 units) against wild-type.	*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	**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)
Against asymptomatic infection	**90%** (starting at 14 days) regardless of symptom status	**63.0%** (95% CI, 56.6-68.5)[259]	Statistically non-significant **reduction of 22.2%** (95% CI -	At day 71, vaccine efficacy against asymptomatic infections was	Efficacy against symptomatic and asymptomatic cases was **64%**	Unknown	**63.6** (95% CI, 29.0-82.4) efficacy against	Unknown

			9.9 to 45.0) for asymptomatic cases **61.9%** efficacy[51]	**65.5%** (95% CI 39.9 to 81.1).	(95% CI 48.8 to 74.7; in WIV04 vaccine) or 73.5% (95% CI 60.6 to 82.2; in HBO2 vaccine).		asymptomatic cases	
	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, suggesting the vaccine has a similar level of protection against infection as natural infections.	**10.4-fold** reduction in neutralization capacity when compared to natural infection sera[261]. **85.83%** of NAb titres were above or equal to the Nab positivity cut-off (20 units) against wild-type. Neutralization decreased by **4.1-fold** when compared to wild-type.	$PRNT_{50}$ **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)[55] **93.6%** (95% CI, 81.7-97.8) against the Alpha variant *Against non-B.1.1.7 variant* **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	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).	Efficacy against moderate-severe-critical Covid-19 due to the variant was **52.0%** (>14 days) and **64.0%**		NT_{GM} **35.03 (95% CI, 27.46-44.68**); **8.75-fold** reduction in neutralization capacity when	GMT **61.57 (95% CI, 36.34-104.3)** against Beta variant with significant	**51.0%** (95% CI, -0.6-76.2) efficacy against B.1.351 variant

	provides some protection against B.1.351 **100%** (95% CI, 53.5-100).		*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]	(>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	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.	reduction in neutralization titre	
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[262]. *Two doses:* **64%** (95% CI, -2-87) [n=18] Efficacy against Zeta (P.2) [2 doses]: **69%** (95% CI, 55-78)[263]	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.	Demonstrated **reduced neutralizing capacity**. However, there	NT_{GM} **24.48** (95% CI,19.2-31.2). **69.17%** of NAb titres were above	**65.2** (95% CI, 33.1-83.0) estimated efficacy	No available data

				Neutralization titres were decreased by **5.4-fold**.	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.	or equal to the Nab positivity cut-off (20 units) against wild-type.	GMT **68.97** (95% CI, 24.72-192.4) against Delta variant with significant reduction in neutralization titre	
Omicron (B.1.1.529)	**22.5%** (95% CI, 8.5-40.7) against symptomatic infection							
PHASE III TRIALS RESULTS [cxxv]								
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)

[cxxv] 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.

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 adolescents (12-15 years old).	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 **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).	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%** (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[264]	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
Efficacy against	**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).

hospitalization and death								
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 one Bell's Palsy case occurred in the placebo group.	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): transverse myelitis, haemolytic anaemia and a case of fever higher than 40°C.	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 (1), hypersensitivity (1), Bell's Palsy (2), & severe generalized weakness, fever & headache (1).	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.
	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.		**<u>2-DOSE EFFICACY</u>** *<u>Efficacy against symptomatic (moderate to severe/ critical) SARS-CoV-2 infection</u>*	Only 2 severe cases occurred in the control group and none in the vaccine group (very few cases to	-	-	Novavax is currently awaiting FDA, EMA, and WHO EUL approval. Upcoming information

				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)	get a reliable estimate).			regarding results of clinical trials or approval will be updated in upcoming reports

	VACCINE PRODUCTION SITES							
	BNT162b2/ COMIRNATY (Pfizer-BioNTech, USA)[cxxvi]	**Spikevax/ Moderna COVID-19 Vaccine/ mRNA-1273 (Moderna, USA)[cxxvii]**	**Vaxzevria/ ChAdOx1 nCoV-19/ AZD1222/ Covishield (AstraZeneca/Oxford, UK, India)[cxxviii]**	**Janssen COVID-19 vaccine/Johnson & Johnson (Janssen, USA)[cxxix]**	**Sinopharm/BBIBP-CorV, China[cxxx]**	**Sinovac CoronaVac, China[cxxxi]**	**COVAXIN / BBV152 (Bharat Biotech, India)**	**Novavax/ NVX-CoV2373**

[cxxvi] 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

[cxxvii] 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
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[cxxviii] 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

[cxxix] 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

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

[cxxxi] 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

EUL holder	BioNTech Manufacturing GmbH (Germany)	ModernaTX, Inc. (USA)[1] Moderna Biotech (Spain)[2]	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 (USA)
Production sites (Drug substance)	BioNTech Manufacturing GmbH (Mainz, Germany) BioNTech Manufacturing Marburg (Marburg, Germany) Rentschler Biopharma SE (Laupheim, Germany) Wyeth BioPharma Division of Wyeth Pharmaceuticals (USA)	Lonza Biologics, Inc., (USA)[1] Moderna TX, Inc. (USA)[1] Lonza AG (Switzerland)[2]	Henogen S.A (Belgium) Catalent Maryland, Inc. (USA) Oxford Biomedica (UK) Ltd. (United Kingdom) SK Bioscience (Republic of Korea) Halix B.V (Netherlands) WuXi Biologics (China)	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)
Production sites (Drug product)	Baxter Oncology GmbH (Halle/ Westfallen, Germany) BioNTech Manufacturing GmbH (Mainz, Germany)	Baxter Pharmaceutical Solutions, LLC. (USA)[1] Catalent Indiana, LLC. (USA)[1] Rovi Pharma Industrial	Catalent Anagni (Italy) CP Pharmaceuticals (United Kingdom) IDT Biologika (Germany)	Janssen Biologics B.V. (The Netherlands) Janssen Pharmaceutica NV (Belgium) Aspen SVP. (South Africa)	Beijing Institute of Biological Products Co., Ltd. (China)	Sinovac Life Sciences Co., Ltd. (China)	-	Novavax (Bohumil, Czech Republic)

	Pfizer Manufacturing Belgium NV (Belgium) Novartis Pharma Stein AG (Switzerland) Mibe GmbH Arzneimittel (Brehna, Germany) Delpharm Saint-Remy (France) Sanofi-Aventis Deutschland GmbH (Germany)	Services, S.A. (Spain)[2]	SK Bioscience (Republic of Korea) Universal Farma, S.L. ("Chemo") (Spain) Amylin Ohio LLC (USA)	Catalent Indiana LLC. (USA) Grand River Aseptic Manufacturing Inc. (USA) Catalent Anagni S.R.L. (Italy)				
Diluent suppliers	Pfizer Perth, Australia Fresenius Kabi, USA	-	-	-	-	-	-	-

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