COVID-19 vaccines in the WHO's Emergency Use Listing (EUL) Report (6) - 15.10.2021

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Literature screening report

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Abstract

This report focuses on the World Health Organization's (WHO) Emergency Use Listing (EUL) of authorized vaccines as of 15 October 2021. Currently six vaccines are authorised for emergency use: 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), and Sinovac/CoronaVac (China). This report provides a condensed summary concerning vaccine efficacy, safety, protection against variants, and further important information for each vaccine, in the form of a synoptic table. The information and data in this synoptic table was extracted from phase III clinical trials and from observational studies. This report particularly focuses on the latest data on vaccine effectiveness, duration of protection and waning immunity, booster doses, efficacy and safety of NVX-CoV2372, and myocarditis.

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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, 48% of the world populations, of which only 2.5% of people in low-income countries, have received at least one dose of a marketed COVID-19 vaccine as of 15 October 2021[1]. Currently, six vaccines [namely, 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), and Sinovac/CoronaVac (China)] were assessed and granted an authorization by WHO as of 29 September 2021. **Articles regarding the latest data on vaccine effectiveness, vaccine effectiveness against hospitalization, booster doses protection across different age groups, new data on the duration of protection and waning immunity, the efficacy and safety of NVX-CoV2373 in adults in the United States and Mexico, and data on myocarditis were prioritized during the literature search and are the latest additions to the table. Data from clinical trials and observational studies for the six EUL-accepted vaccines and the vaccine candidate Novavax regarding these highlighted topics were summarized and can be found in the synoptic table below.**

[1] https://ourworldindata.org/covid-vaccinations (accessed on 15.10.2021).

Methodology

We screened the data for the EUL-accepted vaccines and the vaccine candidate Novavax as of 15 October 2021 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[2].

Results

As phase III COVID-19 vaccine trials confirmed vaccine efficacy and safety for all six 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).

Latest Data on Vaccine Effectiveness

There have not been substantial updates on vaccine effectiveness studies since the previous synoptic table's (30 September 2021) publication. Recently published studies continue to report waning mRNA vaccine protection over time[3] (i.e. **BNT162b2**: VE declined from **93.6%** in May to **65.8%** in July[4]; **mRNA-1273**: VE declined from to **94.1%** 14-60 days after vaccination to **80.0%** 151-180 days after vaccination[5]) and

[2] 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

[3] mRNA vaccine effectiveness against asymptomatic SARS-CoV-2 infections over a seven-month period. *Infection Control & Hospital Epidemiology.* https://www.cambridge.org/core/journals/infection-control-and-hospital-epidemiology/article/mrna-vaccine-effectiveness-against-asymptomatic-sarscov2-infection-over-a-sevenmonth-period/0B67BE1950C88E93B73C15F75E2FC497

[4] COVID-19 vaccine effectiveness by product and timing in New York State. *medRxiv.* https://www.medrxiv.org/content/10.1101/2021.10.08.21264595v1.full-text

[5] Effectiveness of mRNA-1273 against Delta, Mu, and other emerging variants. *medRxiv.* https://www.medrxiv.org/content/10.1101/2021.09.29.21264199v1.full.pdf+html

against the Delta variant[6,7]. See summary paragraph and the synoptic table below for more in-depth information on waning vaccine immunity[8,9,10,11,12]. While both mRNA vaccines demonstrate reduced effectiveness levels, Moderna's mRNA-1273 vaccine has continued to demonstrate higher effectiveness levels[13] and reduced number of breakthrough infections[14] than Pfizer-BioNTech's BNT162b2 vaccine. However, one Belgian study demonstrated that the BNT162b2 vaccine had higher vaccine effectiveness against onwards transmission (**62%; 95% CI, 57-67**) than the mRNA-1273 vaccine (**52%; 95% CI, 33-69**)[15].

A pre-print reported the mRNA-1273 vaccine demonstrated higher effectiveness levels against the Mu (B.1.621) variant of concern (**90.4%** (95% CI, 73.9-96.5) than the Delta variant (**86.7%** (95% CI, 84.3-88.7).[16]

The latest vaccine effectiveness data on AstraZeneca's ChadOx1 nCoV-19/Vaxzevria (VE of **53%** (95% CI, 12-84) in June)[17] or Ad26.COV2.S Janssen vaccines (VE

[6] Transmission event of SARS-CoV-2 delta variant reveals multiple vaccine breakthrough infections. *BMC Medicine.* https://bmcmedicine.biomedcentral.com/articles/10.1186/s12916-021-02103-4

[7] The impact of SARS-CoV-2 vaccination on Alpha & Delta variant transmission. medRxiv. https://www.medrxiv.org/content/10.1101/2021.09.28.21264260v1

[8] Waning of BNT162b2 vaccine protection against SARS-CoV-2 infection in Qatar. New England Journal of Medicine. https://www.nejm.org/doi/full/10.1056/NEJMoa2114114?query=featured_home

[9] Effectiveness of mRNA-1273 against Delta, Mu, and other emerging variants. *medRxiv.* https://www.medrxiv.org/content/10.1101/2021.09.29.21264199v1

[10] Effectiveness of mRNA BNT162b2 COVID-19 vaccine up to 6 months in a large integrated health system in the USA: A retrospective cohort study. *The Lancet.* https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)02183-8/fulltext

[11] mRNA vaccine effectiveness against asymptomatic SARS-CoV-2 infections over a seven-month period. *Infection Control & Hospital Epidemiology.* https://www.cambridge.org/core/journals/infection-control-and-hospital-epidemiology/article/mrna-vaccine-effectiveness-against-asymptomatic-sarscov2-infection-over-a-sevenmonth-period/0B67BE1950C88E93B73C15F75E2FC497

[12] COVID-19 vaccine effectiveness by product and timing in New York State. *medRxiv.* https://www.medrxiv.org/content/10.1101/2021.10.08.21264595v1

[13] Effectiveness of mRNA BNT162b2 COVID-19 vaccine up to 6 months in a large integrated health system in the USA: A retrospective cohort study. *The Lancet.* https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)02183-8/fulltext

[14] A retrospective analysis of COVID-19 mRNA vaccine breakthrough infections – Risk factors and vaccine effectiveness. *medRxiv.* https://www.medrxiv.org/content/10.1101/2021.10.05.21264583v1

[15] Vaccine effectiveness against infection and onwards transmission of COVID-19: Analysis of Belgian contact tracing data, January-June 2021. *Vaccine.* https://www.sciencedirect.com/science/article/pii/S0264410X21011087?via%3Dihub

[16] Effectiveness of mRNA-1273 against Delta, Mu, and other emerging variants. *medRxiv.* https://www.medrxiv.org/content/10.1101/2021.09.29.21264199v1

[17] Vaccine effectiveness against infection and onwards transmission of COVID-19: Analysis of Belgian contact tracing data, January-June 2021. *Vaccine.* https://www.sciencedirect.com/science/article/pii/S0264410X21011087?via%3Dihub

decreased from **89.4%** [1 May] to **51.7%** [10 July])[18] corroborate previously reported data on waning vaccine protection.

Effectiveness data on Sinopharm's BBIBP-CorV and Sinovac's CoronaVac remains scarce. A recent study highlighted that the BBIBP-CorV vaccine induced high levels of IgG anti-spike antibodies (GMC: **377.0 IU/ml**; 95% CI, 324.3-438.3) in SARS-CoV-2 naïve individuals, however antibody (GMC) concentrations reduced to **125.4 IU/ml** (95% CI, 88.2-178.4) three months after receiving the second dose (most individuals received their second dose 54 days after their first dose and not the suggested 21 days apart)[19]. The authors did not specify which SARS-CoV-2 lineage was utilised. Another neutralizing antibody titre (NAb) quantification study demonstrated that the CoronaVac vaccine could not effectively neutralise variants of concern, particularly the delta variant, advocating for the administration of a third CoronaVac or heterologous vaccine dose to maintain long-term immunity against SARS-CoV-2[20]. Although both inactivated virus studies only analysed neutralization level data and not vaccine effectiveness, neutralization levels against SARS-CoV-2 assays have been shown to be highly predictive of immune protection against symptomatic SARS-CoV-2 infection[21].

Despite reports of reduced effectiveness against SARS-Cov-2 infection, vaccine effectiveness remains high against severe infection, hospitalization, and death for all vaccines. Further vaccine effectiveness data can be found in the synoptic table below.

Duration of Protection and Waning Immunity

The waning immunity of vaccine protection against SARS-CoV-2 infection and COVID-19 disease remains a concern, especially when trying to control and contain

[18] COVID-19 vaccine effectiveness by product and timing in New York State. *medRxiv.* https://www.medrxiv.org/content/10.1101/2021.10.08.21264595v1

[19] Humoral response to the BBIBP-CoRV vaccine over time in healthcare workers with or without exposure to SARS-CoV-2. *medRxiv*. https://www.medrxiv.org/content/10.1101/2021.10.02.21264432v1.full.pdf

[20] CoronaVac induces lower neutralising activity against variants of concern than natural infection. *The Lancet Infectious Diseases.* https://www.sciencedirect.com/science/article/pii/S1473309921005685?via%3Dihub

[21] Neutralizing antibody levels are highly predictive of immune protection from symptomatic SARS-CoV-2 infection. *Nature.* https://www.nature.com/articles/s41591-021-01377-8#citeas

the ongoing COVID-19 pandemic. Two longitudinal studies examining the waning immunity of the BNT162b2 vaccine provide insightful data on the longitudinal dynamics of the immune response to the vaccine. The first study was conducted over a period of 6 months in which vaccinated health care workers were tested monthly for the presence of anti-spike IgG and neutralizing antibodies[22]. Based on the results, six months after receipt of the second dose of the BNT162b2 vaccine, humoral response substantially decreased, especially among men, among persons 65 years of age or older, and among persons with immunosuppression. Similar results were reported in the second study in which a test-negative, case-control study design was used to estimate the vaccine effectiveness against any SARS-CoV-2 infection and Covid-19 disease in Qatar[23]. The results demonstrated that the BNT162b2-induced protection against SARS-CoV-2 infection appeared to wane rapidly following its peak after second dose, but protection against hospitalization and death persisted at robust level for 6 months after the second dose.

Since the roll-out of COVID-19 vaccines such as mRNA (BNT162b2, mRNA-1273), adenoviral virus (ChAdOx1 nCoV-19), and inactivated virus vaccines (CoronaVac, Sinopharm), concerns regarding the duration of protection and waning immunity have emerged, especially when aiming to compare vaccine platforms. A study seeking to address the duration of protection and waning immunity of BNT162b2, ChAdOx1 nCoV-19, and CoronaVac in younger and older age groups, comparatively analysed the spike RBD IgG antibody titers in those three vaccine platforms[24]. When comparing the three different vaccine types, the BNT162b2 induced the highest overall seropositivity and anti-spike RBD IgG antibody levels in both younger and older age groups, followed by ChAdOx1, and then by CoronaVac vaccine. In regards of the rate

[22] Waning Immune Humoral Response to BNT162b2 Covid-19 Vaccine over 6 Months. *NEJM.* https://www.nejm.org/doi/full/10.1056/NEJMoa2114583?query=featured_home

[23] Waning of BNT162b2 Vaccine Protection against SARS-CoV-2 Infection in Qatar. *NEJM.* https://www.nejm.org/doi/full/10.1056/NEJMoa2114114

[24] Longitudinal comparison of SARS-CoV-2 anti-Spike RBD IgG antibody response after CoronaVac, BNT162b2, ChAdOx1 nCoV-19 vaccines and evaluation of a single booster dose of BNT162b2 or CoronaVac after a primary CoronaVac regimen. *SSRN – Preprint.* https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3929973

of declining antibodies, the CoronaVac group had the fastest decline followed by ChAdOx1, and then by BNT162b2.

Another study aiming to understand the duration of protection and waning immunity, analysed the humoral response to the BBIBP-CorV (Sinopharm) vaccine over time in healthcare workers with or without exposure to SARS-CoV-2[25]. Based on those results, three months after the second dose individuals with SARS-CoV-2 exposure prior to vaccination and individuals without prior exposure showed a decline in antibody levels, being more abrupt in unexposed subjects. Overall, the results showed a trend towards lower antibody concentrations over time following BBIBP-CorV vaccination.

Protection of Booster Doses across age groups

Earlier this month of October, the European Medicines Agency (EMA) released their recommendations on extra doses and boosters[26]. Regarding the administration of extra doses, the EMA concluded that an extra dose of the COVID-19 vaccines Comirnaty (BioNTech/Pfizer) and Spikevax (Moderna) may be given to people with severely weakened immune systems, at least 28 days after their second dose. This conclusion was based on the multiple studies demonstrating the benefits of a third dose in immunocompromised individuals[27,28]. In terms of their recommendation for booster doses in populations with normal immune systems, the EMA concluded that booster doses of the Comirnaty vaccine may be considered at least 6 months after the second dose for people aged 18 years and older. Their decision only applies for the BioNTech/Pfizer COVID-19 vaccine, as the EMA is currently evaluating data to support a booster for Spikevax. Many of the decision regarding the administration of

[25] Humoral response to the BBiBP-CorV vaccine over time in healthcare workers with or without exposure to SARS-CoV-2. *medRxiv.* https://www.medrxiv.org/content/10.1101/2021.10.02.21264432v1

[26] Comirnaty and Spikevax: EMA recommendations on extra doses and boosters. *EMA.* https://www.ema.europa.eu/en/news/comirnaty-spikevax-ema-recommendations-extra-doses-boosters#_ftnref1

[27] Three Doses of an mRNA Covid-19 Vaccine in Solid-Organ Transplant Recipients. *NEJM.* https://www.nejm.org/doi/full/10.1056/NEJMc2108861

[28] Randomized Trial of a Third Dose of mRNA-1273 Vaccine in Transplant Recipients. *NEJM.* https://www.nejm.org/doi/full/10.1056/NEJMc2111462

booster doses rely on data from Israel where boosters started being offered to the whole population early on. One of the first studies to provide data on the protection of BNT162b2 against COVID-19 infections and severe illnesses was their study on the protection of the BNT162b2 vaccine booster against COVID-19 in 60-years-old and over[29]. The study demonstrated that a booster dose lowered the rate of confirmed infection and severe illness in older populations[21], and their newest preprint on the protection of BNT162b2 vaccine booster against COVID-19 across age groups shows that the rate of confirmed infection and severe illness were substantially lowered among those who received a booster dose across all age groups[30]. Overall, the newest results on the protection of BNT162b2 vaccine booster show that confirmed infection rates were approximately **10-fold lower** in the booster group compared to the non-booster group (ranging from **8.8-17.6** for ≥12 days post booster administration and **4.8-11.2** for 3-7 days post booster administration across the five different age groups), while the severe illness rates were **18.7 fold** (95% CI, 15.7-22.4) ≥12 days post booster administration and **6.5-fold** (95% CI, 5.1-8.3) **lower** 3-7 days post booster administration for ages 60 and over, and **22-fold** (95% CI, 10.3-47.0) ≥12 days post booster administration and **3.2-fold** (95% CI, 1.1-9.6) **lower** 3-7 days post booster administration for ages 40-60[10]. In terms of COVID-19 associated death rates, for ages 60 and over, the rates were **14.7-fold** (95% CI, 9.4-23.1) ≥12 days post booster administration and **4.8-fold** (95% CI, 2.8-8.2) **lower** 3-7 days post booster administration[10].

New Data on Efficacy and Safety of Novavax Vaccine

The Novavax COVID-19 vaccine candidate is an adjuvant, recombinant S protein nanoparticle vaccine that has previously demonstrated clinical efficacy for prevention of COVID-19 in phase 2b/3 trials in the United Kingdom and South Africa. New results

[29] Protection of BNT162b2 Vaccine Booster against Covid-19 in Israel. *NEJM.* https://www.nejm.org/doi/full/10.1056/NEJMoa2114255

[30] Protection Across Age Groups of BNT162b2 Vaccine Booster against Covid-19. *medRxiv.* https://www.medrxiv.org/content/10.1101/2021.10.07.21264626v1

from a phase 3, randomized, observer-blinded, placebo-controlled trial performed in the United States and Mexico evaluated the efficacy and safety of NVX-CoV2373 in adults over 18-years of age[31]. Based on the results, a vaccine efficacy of **90.4%** (95% CI: 82.9-94.6) and a vaccine efficacy against any variant of concern/interest (i.e., Alpha, Delta, Kappa) of **92.6%** (95% CI: 83.6-96.7) were reported. In terms of reactogenicity, most reported side effects or adverse events were mild-to-moderate and transient and mainly occurring in the NVX-CoV-2373 recipients and after the second dose. Overall, the Novavax COVID-19 vaccine candidate was well tolerated and demonstrated a high overall VE for prevention of COVID-19 where the most sequenced viral genomes were classified as variants of concern or interest.

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

[31] Efficacy and Safety of NVX-CoV2373 in the United States and Mexico. *medRxiv.* https://www.medrxiv.org/content/10.1101/2021.10.05.21264567v1

Synoptic Table

Synoptic table about SARS-CoV-2 vaccines accepted in the WHO's Emergency Use Listing and Novavax Vaccine (as of 15 October 2021)

							AWAITING APPROVAL FROM WHO EUL
	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**	**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)	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-	2 doses, 21 days apart	2 doses, 14 days apart	2 doses, 21 days apart

				dose regime, 56 days apart][i]			
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
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 to 8 °C
Approving authorities	FDA (11.12.20)[ii]; 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)	Waiting on approval (Not-yet-approved by countries or WHO for emergency use)
Booster shot approving authorities	EMA approves booster for those aged 18 and above, 6 months after the 2nd dose[1]	EMA authorises booster dose for immunocompromised individuals[iv] FDA approves a third booster dose					

[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

[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

[iv] 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

	FDA approves booster for those ages 16 and above, 6 months after the 2nd dose[iii]	for individuals older than 65 and high-risk individuals, 6 months after the 2nd dose[v]					
EFFECTIVENESS AGAINST ANY SARS-COV-2 INFECTION							
Effectiveness single dose	*General population:* Against 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] *Individuals ≥70:* Symptomatic disease: **58%**[5].	*General population:* Symptomatic disease: **60%** (95% CI, 57-64; >2 weeks after dose)[7].[vii] **88.9%** (95% CI, 78.7-94.2)[3] *Individuals ≥70:* Symptomatic disease: **64%** (95% CI, 46-78;	*General population:* Asymptomatic or symptomatic disease: **64%;** Symptomatic disease: **67%**[8]. *Individuals ≥70:* Symptomatic disease: **58%**[5]. Hospitalization risk reduced by **35-45%**[5].	**50.6%** (95% CI, 14.0-74.0) in preventing SARS-CoV-2 infection (<2 weeks after dose); **76.7%** (95% CI, 30.3-95.3) in preventing SARS-CoV-2 infection (>2 weeks after dose)[9]. **79%** (95% CI, 77-80) (when corrected for	Partial protection[14].[x]	**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[15]. **18.6%** (95% CI, 17.6-19.6) against SARS-CoV-2	Ongoing studies in South Africa[17] and United Kingdom[18]

[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] 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

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

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

	Hospitalization risk reduced by 35-**45%**[5]. Risk of death reduced by **54%**[5]. *Individuals ≥50:* ≥14 days after first dose: **54%** (95% CI, 47-61) effectiveness against hospitalization [1 January-22 June[6].[vi]	>2 weeks after dose)[7].[viii] *Individuals ≥50:* ≥14 days after first dose: **54%** (95% CI, 47-61) effectiveness against hospitalization [1 January-22 June[6].[ix]		under-recording, VE was estimated to be **69%** (95% CI, 67-71)[10]. **81%** (95% CI, 79-84) for preventing hospitalization when corrected for under-recording, VE was estimated to be **73%** (95% CI, 69-76)[10]. **75%** (95% CI, 65-82) against severe critical COVID-19[11]. **71%** (95% CI, 56-81) [11 March – 15 August][12]. **61%** (95% CI, 29-84) [January-June][13] *Individuals ≥50:*		infection, **28.1%** (95% CI, 26.3-29.9) against hospitalization, **28.5%** (95% CI, 25.4-31.4) against ICU admission, and **29.4%** (95% CI, 26.7.3-31.9) against death [January-April][16]	

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

				68% (95% CI, 50-79)[6].			
Effectiveness of two doses	*SARS-Cov-2 infection:* **85%**[2]. **94.6%**[19]. **94.5%**[20]. **76%** (95% CI, 69-81) [January-July][21]. **88.8%** (95% CI, 84.6-91.8) [December-May][3] **74%** (95% CI, 72-76) [January-June][13] **77.5%** (95% CI, 76.4-78.6) [first month after second dose][4]	*SARS-Cov-2 infection:* **100%**[19]. **86%** (95% CI, 81-90.6) [January-July][21]. **96.3%** (95% CI, 91.3-98.4) [December-May][3] **85%** (95% CI, 80-90) [January-June][13] *Symptomatic disease*: **91%** (95% CI, 89-93; >2 weeks after dose)[7].[xiii]	*SARS-CoV-2 infection*: **85%**; **53%** (95% CI, 12-84) [January-June][13] *Symptomatic disease*: **90%**[8].	Not Applicable (one dose schedule)	Partial protection[14].[xvi]	**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[15].[xvii] **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,	Ongoing studies in South Africa[17] and United Kingdom[18]

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

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

[xvii] 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

	Asymptomatic SARS-CoV-2 infection: **90.6%**[22].[xi] **73.1** (95% CI, 70.3-75.5)[4] *Hospitalization:* **85%** (95% CI, 73-93) [January-July][21]. **88%** (95% CI, 85-91) [11 March – 15 August][12]. **89%** (95% CI, 87-91) for individuals ≥50 years [1 January-22 June[6].[xii]	*Asymptomatic SARS-CoV-2 infection:* **90.6%**[22].[xiv] **71%** (95% CI, 61-78) [January-August][23] *Hospitalization:* **91.6%** (95% CI, 81-97) [January-July][21]. **93%** (95% CI, 91-95) [11 March – 15 August)[12]. **89%** (95% CI, 87-91) for individuals ≥50 years [1 January-22 June[6].[xv]				and **73.7%** (95% CI, 72.3-75.0) against death [January-April][16]	
EFFECTIVENESS AGAINST VARIANTS[xviii]							

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

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

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

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

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

Alpha (B.1.1.7)	*Single dose:* **48.7%** (95% CI, 45.5 to 51.7)[24] **66%** (95% CI,64-68)[25]. **54.5%** (95 CI, 50.4-58.3)[26] *Two doses:* **93.7%** (95% CI, 91.6 to 95.3)[24] **92%** (95% CI, 90-93)[27]. **89%** (95% CI, 86-91)[25]. **78%** (95% CI, 68-84)[28] **84.4%** (95 CI, 81.8-86.5)[26]	*Single dose:* **88.1%** (95% CI, 83.7 to 91.5)[29] **83%** (95% CI, 80-86)[25]. *Two doses:* **100%** (95% CI, 91.8 to 100)[29] **92%** (95% CI, 86-96)[25]. **98.4%** (95% CI, 96.9-99.1)[30]	*Single dose:* **48.7%** (95% CI 45.5 to 51.7)[24] 6**4%** (95% CI, 60-68)[25]. *Two doses:* **74.5%** (95% CI, 68.4 to 79.4)[24] **73%** (95% CI, 66-78)[27]. 79% (95% CI, 56-90)[28].	-	No published data	*Two doses:* Equally effective **(~76%**) in neutralizing D614G, B.1.1.7 and B.1.429 as the wild-type strain.	Ongoing studies in South Africa[17] and United Kingdom[18]
Beta (1.351)	*Single dose:* **60%** (95% CI, 52-67)[25]. *Two doses:* **84%** (95% CI, 69-92)[25].	*Single dose:* **61.3%** (95% CI, 56.5 to 65.5)[29] **77%** (95% CI, 69-92)[25]. *Two doses:* **96.4%** (95% CI, 91.9 to 98.7)[29]	*Single dose:* **48%** (95% CI, 28-63)[25].	-	No published data	Neutralization capacity was decreased by factor **5.27**[31].	No available data

Gamma (P.1)	Neutralization activity reduced by **3.3-fold**[32].	-	-	-	No published data	Demonstrated **42%** vaccine effectiveness in a setting with high P.1 transmission, in individuals aged 70 and above[33]. **50.2%** against P.1 (>14 days after 2nd dose)[34]. Neutralization was decreased by factor **3.92**[31].	No available data
Delta (1.617.2)	*Single dose:* **30.7%** (95% CI, 25.2 to 35.7)[24]; **57%** (95% CI, 50-63)[28] **22.5%** (95 CI, 17.0-27.4)[26] *Two doses:* **88.0%** (95% CI, 85.3 to 90.1)[24]; **80%** (95% CI, 77-83)[28] **79%** (95% CI,75-82)[27]. **80%** (95% CI, 77-83)[28]	*Single dose:* **72%** effective against symptomatic SARS-Cov-2 infection[39]. *≥14 days after second dose:* **76%** (95% CI, 58-87)[21]. **94.5%** (95% CI, 94.1-95) [2-9 weeks after second dose][36]. **50.6%** (95% CI, 45.0-55.7) [among	*Single dose:* **30.7%** (95% CI 25.2 to 35.7)[24] *Two doses:* **67.0%** (95% CI, 61.3 to 71.8)[24] **67%** (95% CI, 62-71)[28]. **60%** (95% CI, 53-66)[27]. **66.7%** (95% CI, 45-49.6) [2-9 weeks after second dose][36]. **47.3%** (95% CI, 66.3-67.0) [≥20	**78%** (95% CI, 73-82) against SARS-CoV-2 infection[10]. *Individuals ≥50:* **83% (**95% CI, 81-85)[10]		*Single dose:* **13.8%** (95% CI, -60.2-54.8)[41]. *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[41].	No available data

	40.5% (95% CI, 8.7-61.2)[35]. **42%** (95% CI, 13-62)[21]. **89.8%** (95% CI, 89.6-90.0) [2-9 weeks after second dose][36]. **69.7%** (95% CI, 68.7-70.5) [≥20 weeks after second dose][36]. **64.6%** (95 CI, 60.6-68.2)[26] **52.4%** (95% CI, 48.0-56.4) [among nursing home residents][37]. **53%** (95% CI, 39-65) [4 months after second dose][38]	nursing home residents][37]. **86.7%** (95% CI, 84.3-88.7)[30] *10-14 weeks after second dose:* **90.3%** (95% CI, 67.2-97.1)[36].	weeks after second dose][36]. 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 [40].				
Mu (B.1.621)	No available data	*Two doses:* **90.4%** (95% CI, 73.9-96.5)[30] (demonstrated similar protective measures as against the Alpha variant)	No available data	No available data	No available data	No available data	No available data

EFFECTIVENESS AGAINST HOSPITALIZATION							
Alpha	Single dose: **83%** (95% CI, 62-93) Two doses: **95%** (95% CI, 78-99)[42]. ***Delta*** *Against severe COVID-19*: **91.4%** (95% CI, 82.5-95.7)[35]. *Against death:* **98.2%** (95% CI, 95.9-99.2) [2-9 weeks][36]. **90.4%** (95% CI, 85.1-93.8) [≥20 weeks][36].		Single dose: **76%** (95% CI, 61-85) Two doses: **86%** (95% CI, 53-96)[42]. *Against death:* **94.1%** (95% CI, 91.8-95.8) [2-9 weeks][36]. **78.7%** (95% CI, 52.1-90.4) [≥20 weeks][36].	***Beta*** **67%** effective at preventing hospitalizations[43]. *Against death:* 96% effective at preventing death[43].	-	-	No available data
Delta	*Single dose:* **94%** (95% CI, 46-99)[42]. **91%** (95% CI, 90-93)[44]	*Single dose:* **81%** (95% CI, 81-90.6)[21]. *Two doses:*	*Single dose*: **71%** (95% CI, 51-83)[42] **88%** (95% CI, 83-91)[44]	**71%** [43] **85%** (95% CI, 73-91)[10].	*Single dose:* Does not offer clinically meaningful protection against severe illness [47,xix]	*Single dose:* Does not offer clinically meaningful protection against severe illness [47,xxi]	

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

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

	Two doses: **96%** (95% CI, 86-99)[42]. **88%** (95% CI, 78.9-93.2)[35]. **75%** (95% CI, 24-93.9)[21]. **84%** (95% CI, 79-89)[45]. **98.4%** (95% CI, 97.9-98.8) [2-9 weeks][36]. **92.7%** (95% CI, 90.3-94.6) [≥20 weeks][36]. **96%** (95% CI, 95-96)[44] **93%** (95% CI, 84-96)[38] **96.8%** (95% CI, 93.9-98.3)[2 months after the second dose][4]	**84%** (95% CI, 80-87)[44] 90 *Against ICU admission:* **86%** (95% CI, 79-90)[44] **96%** against severe COVID-19 infection[39].	*Two doses:* **92%** (95% CI, 75-97)[42]. **95.2%** (95% CI, 94.6-95.6) [2-9 weeks][36]. **77.0%** (95% CI, 70.3-82.3) [≥20 weeks][36]. **94%** (95% CI, 92-95)[44] *Against ICU admission:* *Single dose:* **92%** (95% CI, 84-96)[44] *Two doses*: **96%** (95% CI, 94-98)[44]	**91%** (95% CI, 88-94)[44] **85%** effective at preventing severe disease and hospitalization[46]. *Individuals ≥50:* **84% (**95% CI, 81-85)[10] *Against ICU admission:* **94%** (95% CI, 88-98)[44]	*Two doses:* **88%** (95% CI, 55-98) adjusted risk reduction in developing severe illness.[47,xx]	*Two doses:* **88%** (95% CI, 55-98) adjusted risk reduction in developing severe illness.[47,xxii]	
SAFETY AND ADVERSE EVENTS							

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

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

Common side effects	Pain at the injection site, fatigue, headache, myalgia, chills and fever.[48] Optimal safety for asthma patients[49]. The vaccine is considered safe for cancer patients undergoing treatments[50].	Pain at injection site, headache, fatigue, myalgia, arthralgia[51], Covid arm (cutaneous hypersensitivity)[52]. The vaccine is considered safe for cancer patients undergoing treatments[50].	Fatigue, myalgia, arthralgia, headache[53], lethargy, fever, & nausea[54].	Headache, fever, chills, fatigue, myalgia, and nausea[55].	Pain at the injection site, dizziness, fever, headache, fatigue, nausea, vomiting, & allergic dermatitis[54,56].	Pain at injection site, headache, fatigue, tremors, & flushing[57], inflammatory reaction, urticaria[58].	Pain at injection-site, headache, muscle pain, fatigue[59]
Rare adverse events	Myocarditis & myopericarditis[60-62], anaphylaxis and swelling of the lips, face, and tongue related to anaphylaxis[63] (11 anaphylaxis cases per million doses administered)[64], axillary lymphadenopathy, paroxysmal ventricular arrhythmia, leg paresthesia[65], pityriasis rosea[66] (lesions improved completely after	Myocarditis & myopericarditis [60-62], orofacial swelling & anaphylaxis[63]. Potential risk factor for Bell's palsy[83] (most improve upon follow-up)[91], herpes zoster reactivation[70], varicella zoster reactivation[70], herpes zoster ophtalmicus[92], eczema & urticaria[93], transverse	Transverse myelitis, high fever[53,100], cutaneous hypersensitivity[100], vasculitis[101], cerebral venous sinus thrombosis[102] (higher risk for women)[103], thromboembolism[104], vaccine induced immune thrombotic thrombocytopenia[105,106-108],	Thrombosis, thrombocytopenia, cerebral venous sinus thrombosis[124], increased risk of developing Guillain-Barré syndrome post vaccination[125], herpes zoster ophtalmicus[92]. 97% of reported reactions after vaccine administration were non-serious[55].	Rare adverse events were similar among the vaccine groups and control group within 7 days[126]. Pityriasis rosea[127]	Myalgia, fever[57], pityriasis rosea (lesions improved completely after ~8 weeks)[67], reactivation of herpes zoster and herpes simplex[58]. Most reactions improved without treatment within a few weeks[58], Guillain-Barré syndrome[128], subacute thyroiditis[129]	Myocarditis was reported in one vaccine recipient, occurring 3 days after second dose[59]

	~8 weeks)[67], lymphocytic vasculitis[68], varicella-zoster reactivation [69-71], Kikuchi-Fujimoto disease[72], thrombotic thrombocytopenic purpura[73,74], IgA nephropathy flare-up[75], Guillain-Barré syndrome [76,77], pustural psoriasis[78], immunoglobulin A vasculitis[79], immune complex vasculitis[80], Rhabdomyolysis[81], subacute thyroiditis[82], Bell's Palsy[83], erythema multiforme[84], vaccine induced interstitial lung disease[85], macular neuroretinopathy[86], brachial neuritis[87], thyroid eye disease[88],	myelitis[94], Guillain-Barré syndrome[95,96], acute generalized exanthematous pustulosis[97], rhabdomyolysis[98,99]	intracerebral haemorrhage[109], small vessel vasculitis[101,110], psoriasis[111], rosacea, raynaud's phenomenon[93], Ischaemic stroke[112], anaphylaxis[113], recurrent herpes zoster[114,xxiii], generalized bullous fixed drug eruption[115], Guillain-Barré syndrome[77,116], pityriasis rosea[117,118]. Vaccination in individuals with adrenal insufficiency can lead to adrenal crises[119], Dariers				

[xxiii] All cases occurred in patients with chornic urticaria and were being treated with cyclosporine.

	exacerbation of subclinical hyperthyroidism[89], rhabdomyolysis[90]		disease[120], vaccine induced acute localized exanthematous pustulosis[121], Henoch-Schönlein Purpura[122], rhabdomyolysis[123]				
Potential associated adverse events (causal links not yet proven)	Cerebral venous sinus thrombosis and intracranial haemorrhage[130], aseptic meningitis[131], autoimmune hepatitis[132,133], multiple sclerosis relapse[134], myeloperoxidase anti-neutrophil cytoplasmic antibody-positive optic perineuritis[135], central retinal vein occlusion[136], paracentral acute middle maculopathy &	Autoimmune hepatitis[132], myocardial infarction[140], autoimmune haemolytic anaemia[141], hypophysitis & panhypopituitarism[142] One case developed IgA Nephropathy after receiving the second dose of mRNA-1273 (causal link not yet proven)[143].	Autoimmune hepatitis[132], Acute hyperglycaemic crisis[144], Facial nerve palsy, cervical myelitis[112], alopecia areata[145]	Facial Diplegia[146]	-	-	No available data

	acute macular neurotinopathy[137], Stevens-Johnson syndrome/ toxic epidermal necrolysis[138,139]					
Myocarditis data	Mainly reported in young adults and adolescents [147] Israeli study: Estimated incidence within 42 days after receipt of first dose per 100,000 vaccinated persons was **2.13** cases (95% CI, 1.56-2.7)[148] Male patients Incidence of **4.12** (95% CI, 2.99-5.26) per 100,000 vaccinated[148] Male patients (16-29 years)	Mainly reported in young adults and adolescents [147]	No available data	No available data	No available data	No available data	Myocarditis was reported as viral myocarditis. Participant fully recovered after 2 days of hospitalisation. No episode of anaphylaxis or vaccine-associated enhanced COVID-19 was reported[59]

	Incidence of **10.69** (95% CI, 6.93-14.46) per 100,00 vaccinated[148] <u>Female patients</u> Incidence of **0.23** (95% CI, 0-0.49) per 100,000 vaccinated[148] <u>16-29 years</u> Incidence of **5.49** (95% CI, 3.59-7.39) per 100,00 vaccinated[148] <u>≥30 years</u> Incidence of **1.13** (95% CI, 0.66-1.60) per 100,00 vaccinated[148] <u>Disease severity</u> Mild: **1.62** (95% CI, 1.12-2.11) Intermediate: **0.47** (95% CI, 0.21-0.74) Fulminant: **0.04** (95% CI, 0-0.12)[148]							

	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**[149]						
TRANSMISSION, PREVENTION & PROTECTION							
Immunogenicity	*7-14 days after second dose:* *18-55 years*: GMT ranged from **1.7 to 4.6** times the GMT of the convalescent serum[150]. *65-85 years*: GMT ranged from **1.1 to 2.2** times the GMT of the convalescent serum[150].	*14 days after second dose:* *18-55 years*: $PRNT_{80}$ GMT **654.3 (95% CI, 460.1-930.5)**[151]. *56-70 years:* $PRNT_{80}$ GMT **878 (95% CI, 516-1494)**[152]. *≥71 years*: $PRNT_{80}$ GMT **317**	*28 days after second dose median antibody titres:* *18–55 years*: **20,713 AU/mL [IQR 13,898 - 33,550]**[153] *56–69 years*: 1**6,170 AU/mL [IQR 10,233 - 40,353]**[153].	*29 days after vaccination:* *18-55 years:* GMC **586 (95% CI, 445-771**); GMT **224 (95% CI, 168-298)**[154]. *≥65 years*: GMC **312 (95% CI, 246-396);** GMT **212 (95% CI, 163-266)**[154].	*14 days after second dose:* *18-55 years:* GMT ***211.2*** **(95% CI, 158.9-280.6)**[155]. *≥60 years: GMT* ***131.5*** **(95% CI, 108.2-159.7)**[155].	*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) *Two doses (≥4 weeks)*: **194.61±174.88 IU/ml (min: 0, max: 677.82);**	*14 days after second dose (18-84 years):* 5-ug: IgG GMT **44,421 EU/ ml (95% CI, 37,929-52,024)**[157]. 25-ug: IgG GMT **46,459 EU/ml (95% CI, 40,839-52,853)**[157].

		(95% CI, 181-557)[152].	≥*70 years*: **17,561 AU/mL [IQR 9,705 - 37,796]**[153].	*<u>57 days after vaccination:</u>* *18-55 years*: **754 (95% CI, 592-961)**; GMT **288 (95% CI, 221-376)**[154].		11.48% of participants did not develop sufficient antibody titres (<25.6 IU ml)[156].	
Transmission prevention	*<u>Prior Delta Variant:</u>* Vaccine effectiveness against infectiousness given infections **41.3%**[158] Vaccine effectiveness against transmission **88.5%**[158] *<u>During Delta Variant:</u>* Similar Ct values (<25) were found in both vaccinated and unvaccinated groups[159] Studies from Scotland and England	VE against onwards transmission: **52%** (95% CI, 33-69)[13]	**48%** (limited data) May not be able to block the transmission of the alpha variant as efficiently as the wild type[162].	Limited data	Unknown	Unknown	Unknown

	demonstrated reductions in secondary infections among families of vaccinated individuals compared to families of unvaccinated individuals[160,161]. VE against onwards transmission: **62%** (95% CI, 57-67)[13]						
Duration of protection	Median time between second dose and infection: **146 days (IQR, 121-167)**[163] *Anti-SARS-CoV-2 Antibodies:* 1 month after 2nd dose: **1762 KU/L (IQR: 933-3761)**	*Preliminary phase I results:* Antibody activity remained high in all age groups at **day 209** (approximately 6 months) GMT were lower in ≥56 years old[168] **36.4** (95% CI, 17.1-51.5) reduction of	*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**:	*Neutralizing antibodies:* Remained largely stable for **8-9 months**[171] *Binding antibodies:* Remained stable **6 months** irrespective of age group[171]	*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)[173]	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[174]. **80-90%** of anti-S IgG and Nab titers against wild type waned **6 months**	Unknown

	3 months after 2nd dose: **1086 KU/L (IQR: 629-2155)** 6 months after 2nd dose: **802 KU/L (IQR, 447-1487)**[164] No health worker had antibodies BELOW method-dependent cut-off (0.8 KU/L) VE reduced by 22% (95% CI, 6-41) for every 30 days from the second dose for those aged 18 to 64 years[28]. *Effectiveness against any SARS-CoV-2 Infection:* After reaching peak VE (77.5%) 1 month after 2nd dose, VE dropped to **20%** in **months 5-7** after 2nd dose[165]	observed incidence rate (SARS-CoV-2 infection) if vaccinated from Dec 2020 – Apr 2021 than Jul 2021 – Dec 2020.[169] **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.[169] 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-	0.30 GMR (CI, 0.24-0.39)[170] *Cellular Immune Response:* **Day 182** after first dose: median of **237 SFUx10^6 PBMC (IQR, 109-520)**[170] **6 months** after second dose: **(median 1240, IQR 432-2002**) in groups with 15-25 week interval between doses[170] VE reduced by 7% (95% CI, -18 - 2) for every 30 days from the second dose for those aged 18 to 64 years[28]. *Anti-spike Protein RBD IgG Antibodies:* **Younger age groups (<60):**	*Humoral & Cellular Immune Response:* Antibody responses were detected in all vaccine recipients on **day 239** (stable response for at least 8 months)[172] A study observed sustained and stable vaccine effectiveness starting 14 days post vaccination to a maximum of **152** days after vaccination[10]. VE decreased from **89.4%** in May to **51.7%** in July[23]	**Exposed subjects:** Before 1st dose: **203.2 UI/mL** (95% CI: 42.9-962.4) After 1st dose: **761.7 UI/mL** (95% CI: 381.1-1522) After 2nd dose: **719.9 UI/mL** (95% CI : 264.6-1959) 3 months after 2nd dose: **484.4 IU/mL** (95% CI: 147.3-1593)[173]	after second vaccination[175] *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)[166] **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)[166]	

	Effectiveness against Hospitalization and Death: After reaching peak VE (96.8%) 2 months after 2nd dose, **VE did not decline over time**, except for 7th months (VE 55.6%) with very few cases[165] *Anti-spike Protein RBD IgG Antibodies:* **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)[166] **Older age groups (≥60)**: 1 month after 2nd dose: 100%	180 days after vaccination.[30] **91%** [January-March] **71%** (95% CI, 53-83) [April-May] **63%** (95% CI, 44-76)[23]	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)[166] **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)[166]				

	seropositivity, **29.4** (IQR, 22.5-33.3) 3 months after 2nd dose: 100% seropositivity, **14.8** (IQR, 7.4-18.7)[166] *Sub-populations:* **Older age (≥65): 38%** to **42%** decrease of humoral antibodies compared to 18- to 45-year-old[167] **Older age (≥65) AND men: 37%** to **46%** decrease compared to 18- to 45-year-old women[167] **Immunosuppression: 65% to 70%** decrease compared to non-immunosuppressed[167]							

	Obesity (BMI ≥30): **31%** increase in neutralizing antibody compared with nonobese[167]						
CHILDREN VACCINATION							
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)**[176]. *Children (5-11):* Ongoing trials[177] *Children (Under 5 years):* Ongoing trials[177]	*Adolescents (12-17):* 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)**[178]. *Children (6month-11):* Ongoing trials[179]	No available data Paused ongoing trials in children aged 6-17 due to concerns over rare blood clots reported in adult population[180].	No available data Announced at begging of April ongoing study in adolescents but paused to investigate blood clots in adult population[180].	*Children (3-17):* Unknown. Ongoing clinical trial only looked at safety, tolerability, and immunogenicity[xxiv] * * The study design administered **three doses** of 2 µg, 4 µg, or 8 µg of vaccine	*Children (3-17):* Unknown. Clinical trial only looked at safety, tolerability and immunogenicity[181].	*Adolescents (16-17):* PREVENT-19 clinical trial[xxv] expanded to assess efficacy, safety, and immunogenicity in 12–17-year-old adolescents[182]

[xxiv] 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

[xxv] 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

Immunogenicity	*Adolescents (12-15) serum-neutralizing titer:* 1 month after 2nd dose had **1283.0 GMN_{50} (CI, 1095.5-1402.5)**[176]. *Adolescents/young adult (16-25) serum-neutralizing titer:* 1 month after 2nd dose had **705.1 GMN_{50} (CI, 621.4-800.2)**[176]. *Children (5-11):* 1 month after 2nd dose had **1,197.6 GMT (95% CI, 1106.1-1296.6)** SARS-CoV-2-neutralizing antibody[183] *Children (Under 5):* Ongoing trials[177]	*Adolescents (12-17):* Neutralizing antibody titer after 2nd dose was **1401.7 GMN_{50} (CI, 1276.3-1539.4)** Serological response was **98.8% (CI, 97.0-99.7)** *Children (6month-11):* Ongoing trials[179]	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[184]	*Children (3-17):* Neutralizing antibody response after 2nd dose **(100%)** with GMT ranging from **45.9-212.6**[181]	Ongoing clinical trial[185]

Safety and Adverse events	*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%)**[176]. *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%)**[176]. *Children (5-11):* Preliminary results on safety profile	*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%)** Few reported cases of acute myocarditis and pericarditis (mainly in males)[186] *Children (6month-11):* Ongoing trials[179]	No available data	No available data	*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[184]	*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%)**[181]	Ongoing clinical trial[185]

	are consistent with those observed in older populations [183] *Children (Under 5):* Ongoing trials[177]						
Myocarditis Data	Few reported cases of acute myocarditis and pericarditis in 16-25 year olds (mainly in males)[186]	Few reported cases of acute myocarditis in adolescents and young adults	No available data	No available data	No available data	No available data	No available data
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	Ongoing trial[187] (Com-Cov2)[xxvii]

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

						second dose for individuals whose first dose was Sinovac[xxvi] **CoronaVac/Convidecia**	
Vaccine Immunogenicity	*GMCs of SARS-CoV-2 anti-spike IgG at 28 days post booster:* Heterologous **(7133 ELU/mL, CI 6415-7932)** vs. Homologous **(14080 ELU/mL, CI 12491-15871)**[188]. *SFC frequency (T0cell ELISpot):* Heterologous **(99 SFC/10^6 PBMCs)** vs. Homologous **(80 SFC/10^6 PBMCs)**[188]**.**	**Spike-specific IgG antibodies:* Heterologous **(3602 BAU/mL)** vs. Homologous **(4189 BAU/mL)**[48] **Neutralizing antibodies:* Heterlogous **(100%)** vs. Homologous **(100%)**[189].	*RBD antibody titres:* Heterologous **(7756.68 BAU/mL, CI 7371.53-8161.96)** vs. Homologous **(99.84 BAU/mL, CI 76.93-129.59)** at day 14[190]. *IgG antibody titres:* Heterologous **(3684 BAU/mL)** vs. Homologous **(101.2 BAU/mL)** at day 14[190].	Not Applicable (one dose schedule) For more information refer to booster section	Unknown (on-going clinical trial)[49]	**CoronaVac/ChAdOx1 :** *Anti-S Antibodies:* Heterologous **(797 U/mL; 95% CI, 598.7-1062)** vs. Homologous CoronaVac **(94.4 U/mL; 95% CI : 76.1-122.1)** vs. Homologous ChAdOx1 **(818 U/mL; 95% CI: 662.5-1010)**[191] **CoronaVac/Convidecia** *Neutralizing antibodies :* Heterologous	No available data Ongoing trial[187]

[xxvi] 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/

		*Results based on immunosuppressed population	*Neutralizing antibodies:* Heterologous **(100%)** at day 14 vs. Homologous **(30%)** at day 14[190].			**54.4 GMT** (95% CI, 37.9-78) vs. Homologous CoronaVac **12.8 GMT** (95% CI, 9.3-17.5)[192]	
Vaccines Reactogenicity	Observed increase in systemic reactogenicity after boost in heterologous schedules in comparison with homologous schedules[188] *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[188]. *Adverse events in homologous:*	*Adverse events in heterologous and homologous vaccination groups were very similar[189]. *Majority of adverse events self-reported were Pain at injection site, Swelling at injection site, Fever, Headaches, Fatigue, Chills, GI effects, Myalgia, Arthralgia[189]. *Results based on immunosuppressed population	*Adverse events in heterologous:* Headache **(44%)**, Myalgia **(43%)**, Malaise **(42%)**, Fever **(2%)**, Injection site pain **(88%)**, Induration **(35%)**, Erythema **(31%)**[190]. *Severity of adverse events in heterologous:* Mild **(68%)**, Moderate **(30%)**, Severe **(2%)**[190].	Not Applicable (one dose schedule) For more information refer to booster section	Unknown (on-going clinical trial)[193]	**CoronaVac/ChAdOx1:** Unknown **CoronaVac/Convidecia:** Convidecia recipients reported more adverse reactions and reported higher occurrence of solicited injection-site pain)[192]	No available data Ongoing trial[187]

	Adverse events **(81)** Grade 1 **(59.3%)** Grade 2 **(39.5%)** Grade 3 **(1.2%)** Grade 4 **(0%)**[188].						
BOOSTER DOSES							
Vaccine Schedule	*Homologous:* **BNT162b2/BNT162b2**	*Homologous:* **mRNA-1273/mRNA-1273**	*Homologous:* **ChAdOx1/ChAdOX1**	*Homologous:* **Ad26.CoV.2.S/ Ad26.CoV.2.S** *Heterologous:* **BNT162b2/Ad26.CoV.2.S**	*Homologous:* **SinoPharm/SinoPharm** *Heterologous:* **SinoPharm/BNT162b2**	*Homologous:* **CoronaVac/CoronaVac** *Heterologous 1:* **CoronaVac/ChAdOx1** *Heterologous 2 :* **CoronaVac/BNT162b2**	*Homologous:* **NVX-CoV2373/NVX-CoV2373** *Heterologous:* Ongoing trial of heterologous booster shot using NVX-CoV2373[xxviii]
Approved Administration	*Israel:* 12-year-old and over can received homologous booster shot 5 months after full jab[xxix]	Phase II booster trial of three booster doses are ongoing[194] Moderna sought FDA approval of	Preliminary results on tolerability and immunogenicity of third dose of ChAdOx1 vaccines showed strong boost to the	Johnson & Johnson has said it will submit all of their new data to the FDA for potential consideration for	*UAE:* Offering booster doses of Pfizer and Sinopharm to people who received full	**Turkey** and the **United Arab Emirates** began homologous booster shots	Ongoing phase II trials[196] Results below are based on

[xxviii] COV-Boost Evaluating COVID-19 Vaccine Boosters. *University of Southampton & NHS.* https://www.covboost.org.uk/home

[xxix] 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/

	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[xxx]	its COVID-19 vaccine booster[xxxi] *United States:* Starting September, adults who received mRNA vaccine 8 months ago are eligible for booster.	immune response[195]	adding a booster dose and consideration to authorize two-dose regimen[xxxii]	Sinopharm jab ≥6 months ago	**Indonesia** and **Thailand** are considering giving homologous booster shot to HCW[xxxiii]	ongoing phase II trial
Time-to-booster dose	**6 months to 8 months** after	**6 months to 8 months** after	**6-9 months** after initial two-dose regimen	*Homologous:*	**6 months** after initial two-dose regimen	*Homologous:* **6 months to 12 months**	**6 months** after initial two-dose

[xxx] 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/

[xxxi] 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/

[xxxii] 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

[xxxiii] 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/

	initial two-dose regimen Israel offers up to **5 months** after initial two-dose regimen	initial two-dose regimen		**6 months** after one dose regimen[171] *Heterologous:* **4 months** after initial two-dose BNT162b2 regimen[197]		After primary vaccination **8 months** after the primary vaccination to healthy adults ≥60 years *Heterologous 1:* **21 to 26 days** after full jab of CoronaVac *Heterologous 2:* **6 months** after primary vaccination of CoronaVac	regimen (**189 days**)[196]
Immunogenicity	*Neutralizing titers:* Elicits **>5-8 more** for wild type after 6 months after 2nd dose[198]	Booster doses (mRNA1273 or mRNA1273.351) increased neutralizing antibody titers against wild-type[199]	*Antibody Levels:* Higher levels after third dose (tIgG EU **3746**; IQR: 2047-6420) [195] *Spike Cellular Immune Response:* Increased from **200 SFUx10^6 PBMC (IQR, 127-389)** after the second dose to	*Homologous:* 5X10^{10} vp booster dose elicited **9-fold** increase at day 7 compared to first dose after 29 days in 18-55-year-olds[171] 1.25X10^{10} vp booster dose elicited **6-7.7-fold** increase at day 28 compared to first	Ongoing trial[193]	*Homologous:* Neutralizing Antibodies: **60%** higher NAbs activity against wild-type compared to 2-doses[175] Anti-S IgG and NAbs: **20-fold** increase 4 weeks post	*Anti-spike IgG:* Increase of **4.6-fold** compared to peak response after 2nd dose (**Day 217 GMEU = 200408**; 95% CI: 159796-251342)[196] *Wild-type Neutralizing Response:*

			399 SFUx10^6 PBMC (IQR, 314-662) after the third one[195]	dose after 29 days in 18-55 and ≥65-year-old[171] *Heterologous:* **14.8 to 32.4-fold** increase in neutralization titers against wild-type virus[197]		booster vaccination NAbs were maintained **60** to **180 days** post booster[175] *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[200] *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	Increase of **4.3-fold** compared to peak response after 2nd dose **(IC50 = 6231; 95% CI: 4738-8195)** [196] *Older Participants (60-84):* **5.4-fold** increase in antibody response[196] *Younger Participants (18-59):* **3.7-fold** increase in antibody response[196]

						factor of 46.6 but IgG-N titers decreased by **factor of 6.5**[201] Single booster dose of BNT162b2 induced higher anti-spike RBD IgG antibody levels, compared to single booster dose of CoronaVac[166]	
Immunogenicity against variants	*Beta (B.1.351):* Elicits **15-21** more neutralizing titers for Beta variant after 6 months after 2nd dose[198] *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	Preliminary results of booster doses of mRNA-1273 vaccine show robust antibody response against Delta variant[194]	Third dose provided higher antibody titers against Alpha, Beta, and Delta variants[195]	*Homologous:* No available data *Heterologous:* **10.9 to 21.2-fold** increase in pseudovirus neutralization assay (one volunteer did not have any against fB.1.351) [197]	Ongoing trial[193]	*Homologous:* **Beta (B.1.351):** **3.0-fold** decrease in neutralizing antibodies compared to wild type[175] **Gamma (P.1):** **3.1-fold** decrease in neutralizing antibodies compared to wild type[175] **Delta (B.1.671.2):**	High levels of functional antibodies against Alpha (B.1.1.7), Beta (B.1.351), and Delta (B.1.671.2)[196] *Delta (B.1.671.2):* Increase of **6.6-fold** in antibody response compared to Delta response observed with

	compared to dose 2 titers in 65–85-year-olds[198]					**2.3-fold** decrease in neutralizing antibodies compared to wild type **2.5-fold** higher neutralizing potency than 2-dose vaccination[175] *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**[200]	primary vaccination[196]
Reactogenicity	Preliminary results show consistent tolerability[198]	Similar safety and tolerability compared to second dose[194] *Common solicited local adverse events:*	Lower reactogenicity after third dose compared to first dose[170]	No available data	Ongoing trial[193]	The third shot is considered to be safe[174]. *Common side effects:* Pain at the injection site.	Booster dose was **well tolerated** Local and systemic **reactogenicity increased** between Dose

		Injection-site pain **(68.4% for mRNA-1273.351, 90% for mRNA-1273)** fatigue **(36.8% for mRNA-1273.351, 70% for mRNA-1273)** headache **(36.8% for mRNA1273.351, 55.0% for mRNA-1273)** myalgia **(31.6% for mRNA-1273.351, 45.0% for mRNA-1273)** arthralgia **(21.1% for mRNA-1273, 50.0% for mRNA-1273)**[199]				*Adverse events:* Unrelated to the vaccination	1, Dose 2, and Dose 3 **90%** of symptoms were rated as mild or moderate[196]
Protection against COVID-19	***Confirmed Infection:*** Youngest age group (16-29): **17.6 (95% CI, 15.6-19.9) lower rate** in booster group[202] 30-39 age group:	No available information	No available information	No available information	No available information	No available information	No available information

	8.8 (95% CI, 8.2-9.5) lower rate in booster group[202] <u>40-49 age group:</u> **9.7 (95% CI, 9.2-10.4) lower rate** in booster group[202] <u>50-59 age group:</u> **12.2 (95% CI, 11.4-13.1) lower rate** in booster group[202] <u>Oldest age group (≥60):</u> **11.3 (95% CI, 10.4-12.3) lower rate** in booster group [203] **12.4 (95% CI, 11.9-12.9) lower rate** in booster group[202] ***<u>Severe Illness:</u>*** <u>40-59 age group:</u> **22.0 (95% CI, 10.3-47.0) lower**							

	rate in booster group[202] Older population (≥60): **19.5 (95% CI, 12.9-29.5) lower rate** in booster group[203] **18.7 (95% CI, 15.7-22.4) lower rate** in booster group[202]							
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%**[204]					For more detailed information regarding immunogenicity of third dose refer to study[xxxiv] Ongoing clinical trial examining the immunogenicity and safety of a third dose vaccination with ChAdOx1 or BNT162b2		

[xxxiv] 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*

						vaccine among adults who received full jab of CoronaVac[xxxv]	

[xxxv] 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	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 to 8 °C
Approving authorities	FDA (11.12.20)[xxxvi]; EMA (21.12.20); WHO EUL (31.12.20); and list of countries (including Switzerland –	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	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)	Waiting on approval (Not-yet-approved by countries or WHO for emergency use)

[xxxvi] 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

	approved on 20.12.20)		awaiting on approval)				
				EFFICACY			
Single dose[xxxvii]	**52%** (95% CI, 29.5 to 68.4; starting at 12 days) or 82.2% (75.1 to 87.3; starting at ≥14 days)[205]. **91%** (95% CI, 85-94)[206].	**95.2%** (95% CI, 91.2.8 to 97.4; starting at >14 days)[51].	**72.8%** (starting at 22 days up to 60 days)[207]. **88%** (95% CI, 75-94)[206].[xxxviii]	Single dose vaccine	Unknown	**35.1%** (95% CI, -6.6 to -60.5) [conducted in a setting with high P.1 transmission][208].	**83.4%** (95% CI, 73.6-89.5) starting at ≥14 days[59]
Two doses[xxxix]	**95.0%** (95% CI, 90.3-97.6) starting at ≥7 days in population without prior SARS-CoV-2 infection[65] **94.6%** (95% CI, 89.9-97.3) starting at ≥7 days in	**94.1%** (95% CI, 89.3-96.8) after median follow-up of less than 63 days[51] **93.2%** (95% CI, 91.0-94.8)[209]	**63.1% (**95% CI, 51.8-71.7) starting at ≥14 days for two standard doses[207] **80.7%** (95% CI, 62.1-90.2) starting at ≥14 days for first low dose and	**66.9%** (95% CI 59.0-73.4) after 14 days and **66.1%** (95% CI 55.0-89.1) after 28 days for VE against moderate-severe-critical COVID-19[210]	After 14 days, efficacy against symptomatic cases was **72.8%** (95% CI 58.1-82.4; in WIV04 vaccine) or **78.1%** (95% CI 64.8 to 86.3; in HBO2 vaccine).[126]	After 14 days, efficacy against symptomatic cases was **50.7%** (95% CI 35.9 to 0-62.0).[57] 99.17% of NAb titres were above or equal to the	**89.7%** (95% CI, 80.2-94.6) starting at ≥7 days[59] **90.4%** (95% CI, 82.9-94.6)[212] **100%** (95% CI, 87-100) against moderate-to-

[xxxvii] Against SARS-COV-2 infection

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

[xxxix] Against SARS-CoV-2 infection.

	population with or without prior infection[65]	Against severe disease: **98.2%** (95% CI, 92.8-99.6)[209]	standard second dose[207] **66.7%** (95% CI, 57.4-74.0) starting at ≥14 days for pooled analysis efficacy[207]	**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[210]		Nab positivity cut-off (20 units) against wild-type[211].	severe COVID-19[212] **100%** (95% CI, 34.6-100) against severe COVID-19[212]
Against asymptomatic infection	**90%** (starting at 14 days) regardless of symptom status[213]	**63.0%** (95% CI, 56.6-68.5)[209]	Statistically non-significant **reduction of 22.2%** (95% CI -9.9 to 45.0) for asymptomatic cases	At day 71, vaccine efficacy against asymptomatic infections was **65.5%** (95% CI 39.9 to 81.1)[210].	Efficacy against symptomatic and asymptomatic cases was **64%** (95% CI 48.8 to 74.7; in WIV04 vaccine) or 73.5% (95% CI 60.6 to 82.2; in HBO2 vaccine)[126].	Unknown	Unknown
EFFICACY AGAINST VARIANTS							
Alpha (B.1.1.7)	Two doses of the vaccine **effectively neutralize** the B.1.1.7 variant and the D614G substitution[214].	**NAbs remained high** and consistent with titres of the wildtype for the B.1.1.7 variant[215].	**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[162].	**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.	**10.4-fold** reduction in neutralization capacity when compared to natural infection sera[211]. **85.83%** of NAb titres were above or equal to the	Two dose efficacy against the B.1.1.7 variant **86.3%** (95% CI, 71.3-93.5)[59] **93.6%** (95% CI, 81.7-97.8) against the Alpha variant[212]

					those naturally infected, suggesting the vaccine has a similar level of protection against infection as natural infections[216].	Nab positivity cut-off (20 units) against wild-type[211]. Neutralization decreased by **4.1-fold** when compared to wild-type[217].	
Beta (B.1.351)	Neutralization was **diminished by a factor of 5**. Despite this, the BNT162b2 mRNA vaccine still provides some protection against B.1.351[218] **100%** (95% CI, 53.5-100)[219].	NAbs were **6-fold** lower. Nevertheless, NAbs were still found to be protective[215].	Two doses of the vaccine had no efficacy against the B.1.351 (VE = **21.9%;** 95% CI, -49.9 to 59.8)[220].	Efficacy against moderate-severe-critical Covid-19 due to the variant was **52.0%** (>14 days) and **64.0%** (>28 days). Efficacy against severe-critical COVID-19 was **73.1%** (>14 days) and **81.7%** (>28 days)[210]. Demonstrated **3.6-fold** reduction in neutralization sensitivity[221]. Neutralization titres were decreased by **6.7-fold**[222].	No published data	NT_{GM} **35.03 (95% CI, 27.46-44.68**); **8.75-fold** reduction in neutralization capacity when compared to natural infection sera[211]. **82.5%** of NAb titres were above or equal to the Nab positivity cut-off (20 units) against wild-type[211].	**51.0%** (95% CI, -0.6-76.2) efficacy against B.1.351 variant[223]

Gamma (P.1)	*Single dose:* *≥21 days*: **83%** against hospitalization and death[224]. *Two doses*: *≥14 days*: **98%** against hospitalization and death[224].	**3.2-fold** reduction in neutralization capacity when compared to wild-type[225].	*Single dose:* *≥21 days*: **94%** against hospitalization and death[224]. *Two doses:* **64%** (95% CI, -2-87) [n=18][226] Efficacy against Zeta (P.2) [2 doses]: **69%** (95% CI, 55-78)[226]	Demonstrated **3.4-fold** reduction in neutralization sensitivity[221].	No published data	**49.6%** against P.1 (>14 days after 1st dose)[208]. Neutralization decreased by **7.5-fold** when compared to wild-type[217].	No available data
Delta (1.671.2)	**Reduced NAb activity** relative to B.1.1.7 strain[227].	**2.1-fold** reduction in neutralization capacity when compared to wild-type[225].	*Single dose:* *≥21 days*: **90%** against hospitalization and death[224].	Demonstrated **1.6-fold** reduction in neutralization sensitivity[221]. Neutralization titres were decreased by **5.4-fold[222]**.	Demonstrated **reduced neutralizing capacity**. However, there were no differences in the NAbs titres against B.1.617.2 in vaccinated individuals vs. those naturally infected, suggesting the vaccine has a similar level of protection against infection as	NT_{GM} **24.48** (95% CI,19.2-31.2)[211]. **69.17%** of NAb titres were above or equal to the Nab positivity cut-off (20 units) against wild-type[211].	No available data

					natural infections[216].		
PHASE III TRIALS RESULTS[xl]							
Number of participants (vaccine/ placebo)	43,448 (21,720/ 21,728)[65]	30,420 (15,210/15,210)[51]	17,178 (8597/8581)[207]	39,321 (19,630/19,691)[210]	26,917 (13,459/13458); or 26,914 (13,465/13,458)[126]	9,823 (4,953/4,870)[57]	14,039 (7,020/7,019)[59]
Total COVID-19 cases (vaccine/ control)	170(8/162)[65]	196 (11/185)[51]	332 (84/248)[207]	464 (116/348)[210]	121(26/95) or 116(21/95)[126]	253(85/168)[57]	106(10/96)[59]
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%**	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)[51].	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	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%	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	After 14 days, efficacy against symptomatic cases was **50.7%** (95% CI 35.9 to 0-62.0).[57]	**83.4%** (95% CI, 73.6-89.5) starting at ≥14 days after first dose[59] **89.7%** (95% CI, 80.2-94.6) starting at ≥7 days after second dose[59]

[xl] 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, 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.

	(95% CI, 89.9 to 97.3) in population with or without prior infection. **100%** among adolescents (12-15 years old)[65].		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)[207].	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[210].	86.3; in HBO2 vaccine)[126].		
Efficacy against hospitalization and death	**100%** (after 7 days)[65]	**100%** (≥14 days)[51]	**100%** (after 21 days)[207]	**76.7%** (≥14 days) or **85.4%** (≥28 days)[210]	**100%** (>14 days)[126]	**100%** (>14 days)[57]	**100%** (after 7 days)[59].
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[48,228].	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	Serious adverse events were balanced across the study arms. 79 cases occurred in the vaccine group and 89 cases in the placebo group – 3 cases were considered related to the experimental or control vaccine (out of 11 636 vaccine recipients):	Serious adverse events were reported in 0.4% of vaccine recipients and 0.4% of placebo recipients. Seven of the serious adverse events were considered to be related to the vaccine: Guillain-Barré syndrome (1), pericarditis (1), brachial radiculitis (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[56].	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[57].	<u>Phase II:</u> Nine serious adverse events were reported, only one of which was assessed as related to the vaccine: acute colitis[157].

		case occurred in the placebo group[51].	transverse myelitis, haemolytic anaemia and a case of fever higher than 40°C [53].	hypersensitivity (1), Bell's Palsy (2), & severe generalized weakness, fever & headache (1)[210].			
PHASE III TRIAL OTHER							
Comments	Specific populations were excluded (HIV and immunocompromised patients, and pregnant women).	Calculation of efficacy were not based on the total number of confirmed Covid-19 cases.		**2-DOSE EFFICACY** *Efficacy against symptomatic (moderate to severe/ critical) SARS-CoV-2 infection* **94%** (95% CI, 58-100) in the US. **75%** (95% CI, 55-87) globally.[11] *Efficacy against severe/ critical SARS-CoV-2 infection* **100%** (95% CI, 33-100)[11]	Only 2 severe cases occurred in the control group and none in the vaccine group (very few cases to get a reliable estimate).		Novavax is currently awaiting FDA, EMA, and WHO EUL approval. Upcoming information regarding results of clinical trials or approval will be updated in upcoming reports

VACCINE PRODUCTION SITES							
	BNT162b2/ COMIRNATY (Pfizer-BioNTech, USA)[xli]	**Spikevax/ Moderna COVID-19 Vaccine/ mRNA-1273 (Moderna, USA)[xlii]**	**Vaxzevria/ ChAdOx1 nCoV-19/ AZD1222/ Covishield (AstraZeneca/Oxford, UK, India)[xliii]**	**Janssen COVID-19 vaccine/Johnson & Johnson (Janssen, USA)[xliv]**	**Sinopharm/BBIBP-CorV, China[xlv]**	**Sinovac CoronaVac, China[xlvi]**	**Novavax/ NVX-CoV2373**
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)	Novavax (USA)

[xli] 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

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

2. WHO recommendation Moderna COVID-19 mRNA Vaccine (nucleoside modified). *WHO*. https://extranet.who.int/pqweb/vaccines/covid-19-mrna-vaccine-nucleoside-modified

[xliii] 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

[xliv] 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

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

[xlvi] 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

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) Pfizer Manufacturing Belgium NV	Baxter Pharmaceutical Solutions, LLC. (USA)[1] Catalent Indiana, LLC. (USA)[1] Rovi Pharma Industrial Services, S.A. (Spain)[2]	Catalent Anagni (Italy) CP Pharmaceuticals (United Kingdom) IDT Biologika (Germany) SK Bioscience (Republic of Korea)	Janssen Biologics B.V. (The Netherlands) Janssen Pharmaceutica NV (Belgium) Aspen SVP. (South Africa) Catalent Indiana LLC. (USA)	Beijing Institute of Biological Products Co., Ltd. (China)	Sinovac Life Sciences Co., Ltd. (China)	Novavax (Bohumil, Czech Republic)

	(Belgium) Novartis Pharma Stein AG (Switzerland) Mibe GmbH Arzneimittel (Brehna, Germany)		Universal Farma, S.L. ("Chemo") (Spain) Amylin Ohio 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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