Literature screening report

COVID-19 vaccines in the WHO's Emergency Use Listing (EUL): report (3)

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Abstract

This report focuses on the World Health Organization's (WHO) Emergency Use Listing (EUL) of authorized vaccines as of 27 August, 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 vaccine effectiveness and vaccine efficacy and effectiveness against variants.

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, only 39.7% of the world populations had received at least one dose of a marketed COVID-19 vaccine as of 30 August 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 August 19, 2021. Articles regarding vaccine effectiveness, vaccine efficacy and effectiveness against variants of concern (VOC), viral transmission, vaccine duration of protection, and rare adverse events 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 regarding these highlighted topics was summarized and can be found in the synoptic table below.

Methodology

We screened the data for the EUL-accepted vaccines as of 27 August, 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.

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 slowly increase across countries, it is important to assess vaccine effectiveness in real-world conditions, especially in relation to evolving variants of concern (VOC). Estimates of vaccine effectiveness concerning Pfizer/ BioNTech BNT162b2 and Moderna's mRNA-1273 from January to May 2021 demonstrated to have 94.6% (95% CI, 61.0-99.2%) and 100% effectiveness against confirmed SARS-CoV-2 infection, respectively, among a cohort of ~8,000 healthcare workers two weeks after the second dose[2]. Another interim study conducted from December 2020 to March 2021 confirmed that two doses of either mRNA vaccines

[1] https://ourworldindata.org/covid-vaccinations (accessed on 30.08.2021).

[2] Effectiveness of mRNA-BNT162b2, mRNA-1273, and ChAdOx1 nCoV-19 vaccines against COVID-19 in healthcare workers: an observational study using surveillance data. *Clinical Microbiology and Infection.* https://www.clinicalmicrobiologyandinfection.com/article/S1198-743X(21)00379-7/fulltext

were 90% (95% CI,68-97%) effective at preventing SARS-CoV-2 infection[3], consistent with phase III trials[4,5]. However, a prospective cohort study (15,000 participants) in the United Kingdom demonstrated BNT162b2 to be only 86% effective after two doses against both asymptomatic and symptomatic infection[6]. This observational study was conducted when the dominant variant of circulation was B.1.1.7 (alpha), and although the vaccine's neutralization capacity was not specifically tested against the B.1.1.7 variant, it could explain BNT162b2's reduced effectiveness in this cohort study compared to prior reported data. Regarding the non-Swiss authorized vaccines, effectiveness estimates for AstraZeneca's ChAdOx1 nCoV-19/ AZD1222/ Covishield [85%; 0.15 (0.08-0.26)] and Janssen's Johnson & Johnson COVID-19 vaccine [76.7%; 95% CI, 30.3-95.3][7] are also comparable to their efficacy estimates in phase III trials (see synoptic table below). In a mass-vaccination Chilean setting (approximately 10.2 million persons), Sinovac/ CoronaVac's effectiveness [65.9%; 65.2-66.6] proved higher than its efficacy estimates[8]. To our knowledge few studies have been published on Sinopharm's BBIBP-CorV real-world effectiveness. Further information on vaccine effectiveness for the six WHO authorized vaccines are summarised in the table below.

Most phase III clinical trials were conducted prior to the evolving VOC[9], and vaccine efficacy and effectiveness against these variants have been unclear. Ongoing clinical trials and test-negative case-control studies have demonstrated reduced vaccine neutralization capacity against COVID-19 variants compared to wild type. Pfizer/ BioNTech's BNT162b2 vaccine had an effectiveness of 93.7% with the alpha variant and 88% with the delta variant[10]. The Centers for Disease Control and Prevention (CDC) reported a decline in mRNA vaccine effectiveness from 91% (95% CI, 81-96), during the months preceding the Delta predominance, to 66% (95% CI, 26-84) in August[11]. Moderna mRNA-1273/ Spikevax titres were reduced 1.5-fold against B.1.1.7 and B.1.617.2 strains and demonstrated 2.4 to

[3] Interim Estimates of Vaccine Effectiveness of BNT162b2 and mRNA-1273 COVID-19 Vaccines in Preventing SARS-CoV-2 Infection Among Health Care Personnel, First Responders, and Other Essential and Frontline Workers — Eight U.S. Locations, December 2020–March 202. Morbidity and Mortality Weekly Report. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8022879/pdf/mm7013e3.pdf

[4] Safety and efficacy of the BNT162b2 mRNA Covid-19 vaccine. *New England Journal of Medicine*. https://www.nejm.org/doi/full/10.1056/nejmoa2034577

[5] Efficacy and safety of the mRNA-123 SARS-CoV-2 vaccine. *New England Journal of Medicine.* https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7787219/

[6] Effectiveness of BNT162b2 mRNA Vaccine Against Infection and COVID-19 Vaccine Coverage in Healthcare Workers in England, Multicentre Prospective Cohort Study (the SIREN Study). *SSRN – Preprint*. https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3790399

[7] Real-world effectiveness of Ad26.COV2.S Adenoviral Vector Vaccine for COVID-19. SSRN – Preprint. https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3835737

[8] Effectiveness of an Inactivated SARS-CoV-2 Vaccine in Chile. *New England Journal of Medicine.* https://www.nejm.org/doi/full/10.1056/NEJMoa2107715

[9] See previous report: COVID-19 vaccines in the WHO's Emergency Use Listing (EUL): report (2).

[10] Effectiveness of COVID-19 vaccines against the B.1.617.2 (Delta) Variant. *New England Journal of Medicine.* https://www.nejm.org/doi/full/10.1056/NEJMoa2108891

[11] Effectiveness of COVID-19 Vaccines in Preventing SARS-CoV-2 Infection Among Frontline Workers Before and During B.1.617.2 (Delta) Variant Predominance — Eight U.S. Locations, December 2020–August 2021. *Morbidity and Mortality Weekly Report.* https://www.cdc.gov/mmwr/volumes/70/wr/mm7034e4.htm#suggestedcitation

3.0-fold reduced binding to the P.1 and B.1.351 strains[12]. While AstraZeneca's ChAdOx1-nCoV effectively neutralizes the B.1.1.7[13] and P.1[14,15] strains and has an effectiveness of 60% (95% CI, 53-66) against the delta variant[16], the vaccine demonstrated a significantly reduced neutralization capacity against the B.1.351 strain[17]. The Ad26.COV2.S COVID-19 vaccine neutralizes the Delta variant at greater capacities than the B.1.351 and P.1 strains[18]. With the ever-changing situation, more clinical and observational studies are needed to confirm vaccine efficacy and effectiveness against VOCs.

Since the approval for emergency use and administration of COVID-19 vaccines, limited data on the duration of protection of the WHO EUL approved vaccines has become available. Studies on the persistence of antibodies, humoral and cellular immune response, and time-to-breakthrough-infection in vaccinated populations provide us with a general idea of the possible duration of protection against COVID-19. Overall, most studies analysing the persistence of antibodies, humoral, and cellular immune responses demonstrated that the mRNA vaccines (BNT162b2 & mRNA-1273), ChAdOx1, and Ad26.COV2.S had a duration of protection ranging from 6 to 8 months[19] [20] [21].

With the emergence of new variants of concern, few breakthrough infections have been reported in fully vaccinated individuals such as 39 SARS-CoV-2 breakthrough infections documented in Health Care Workers in Israel[22]. To better understand the role of vaccines in their prevention against transmission, virus loads, and shedding in breakthrough infections, various studies have tried to infer infectiousness

[12] Durability of mRNA-1273 vaccine–induced antibodies against SARS-CoV-2 variants. *Science.* https://science.sciencemag.org/content/early/2021/08/11/science.abj4176?_ga=2.235822593.145620917.1628696888-1399774036.1602427045

[13] Efficacy of ChAdOx1 nCoV-19 (AZD1222) vaccine against SARS-CoV-2 variant of concern 202012/01 (B.1.1.7): an exploratory analysis of a randomised controlled trial. *The Lancet.* *https://pubmed.ncbi.nlm.nih.gov/33798499/*

[14] AstraZeneca's COVID-19 vaccine shows effectiveness against Indian variants of SARS-CoV-2 virus. *AstraZeneca.* https://www.astrazeneca.com/media-centre/articles/2021/astrazenecas-covid-19-vaccine-shows-effectiveness-against-indian-variants-of-sars-cov-2-virus.html

[15] Antibody evasion by the Brazilian P.1 strain of SARS-CoV-2. *bioRxiv.* http://biorxiv.org/content/early/2021/03/15/2021.03.12.435194.abstract

[16] SARS-CoV-2 Delta VOC in Scotland: demographics, risk of hospital admission, and vaccine effectiveness. *The Lancet.* https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)01358-1/fulltext

[17] Efficacy of the ChAdOx1 nCoV-19 Covid-19 Vaccine against the B.1.351 Variant. *New England Journal of Medicine.* https://www.nejm.org/doi/full/10.1056/nejmoa2102214#:~:text=A%20pooled%20analysis%20of%20the,%5D%2C%2057.4%20to%2074.0).

[18] Ad26.COV2.S elicited neutralizing activity against Delta and other SARS-CoV-2 variants of concern. bioRxiv. https://www.biorxiv.org/content/10.1101/2021.07.01.450707v1

[19] mRNA Vaccination Induces Durable Immune Memory to SARS-CoV-2 with Continued Evolution to Variants of Concern. *bioRxiv.* http://biorxiv.org/content/early/2021/08/23/2021.08.23.457229.abstract

[20] Tolerability and Immunogenicity After a Late Second Dose or Third Dose of ChAdOx1 nCoV-19 (AZD1222). *SSRN Preprint*. https://ssrn.com/abstract=3873839

[21] Humoral and Cellular Immune Responses 8 Months after Ad26.COV2.S Vaccination. *New England Journal of Medicine*. https://www.nejm.org/doi/full/10.1056/NEJMc2108829

[22] Covid-19 Breakthrough Infections in Vaccinated Health Care Workers. *New England Journal of Medicine.* https://www.nejm.org/doi/full/10.1056/NEJMoa2109072

using the SARS-CoV-2 PCR cycle threshold (Ct) value as an indicator. A Ct value lower than 25-30 has become an indicator of the presence of infectious SARS-CoV-2 and, therefore, allowed scientists to infer the infectiousness, transmissibility, and virus shedding in infected individuals[23]. Before the prevalence of the Delta variant, studies demonstrated that infectivity and transmission was significantly reduced in cases vaccinated with BNT162b2 and ChAdOx1 as inoculated individuals were 40% to 78% less likely to spread the virus to other household members[24] [25] [26]. Nevertheless, as the Delta variant became the predominant variant in many countries worldwide, studies comparing Ct values between vaccinated and unvaccinated individuals detected no significant difference in Ct values by vaccination status[27]. However, two studies reported that although the Ct values were similar, the viral loads decreased faster[28], and lower probability of infectious virus detection were detected in vaccinated individuals[29]. Overall, further studies are needed to better understand viral dynamics in breakthrough infections, especially in cases with the B.1.617.2 (Delta) variant.

Further (biweekly) updated data on the six WHO EUL vaccines are synthesized in the synoptic table.

[23] One number could help reveal how infectious a COVID-19 patient is. Should test results include it?. *Science.* https://www.sciencemag.org/news/2020/09/one-number-could-help-reveal-how-infectious-covid-19-patient-should-test-results

[24] Effect of Vaccination on Household Transmission of SARS-CoV-2 in England. *New England Journal of Medicine*. https://www.nejm.org/doi/10.1056/NEJMc2107717

[25] Impact of BNT162b2 vaccination and isolation on SARS-CoV-2 transmission in Israeli households: an observational study. *medRxiv.* https://www.medrxiv.org/content/10.1101/2021.07.12.21260377v1.full-text

[26] Vaccination with BNT162b2 reduces transmission of SARS-CoV-2 to household contacts. *medRxiv.* *https://www.medrxiv.org/content/10.1101/2021.07.13.21260393v1.full-text*

[27] Shedding of Infectious SARS-CoV-2 Despite Vaccination when the Delta Variant is Prevalent – Wisconsin, July 2021. *medRxiv.* https://www.medrxiv.org/content/10.1101/2021.07.31.21261387v3.full

[28] Virological and serological kinetics of SARS-CoV-2 Delta variants vaccine-breakthrough infections: a multi-center cohort study. *medRxiv.* https://www.medrxiv.org/content/10.1101/2021.07.28.21261295v1

[29] Virological characteristics of SARS-CoV-2 vaccine breakthrough infections in health care workers. *medRxiv.* https://www.medrxiv.org/content/10.1101/2021.08.20.21262158v1.full.pdf+html

Synoptic table about SARS-CoV-2 vaccines accepted in the WHO's Emergency Use Listing (as of 27 August, 2021)

	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
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)
Dose and frequency	2 doses, 21 days apart	2 doses, 28 days apart	2 doses, 4-12 weeks apart	1 dose, once	2 doses, 21 days apart	2 doses, 14 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
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
Approving authorities	FDA, EMA, WHO EUL, and list of countries (including Switzerland)	FDA, EMA, WHO EUL, and list of countries (including Switzerland)	FDA (ongoing), EMA, WHO EUL, and list of countries (Switzerland is ongoing too)	FDA, EMA, WHO EUL, and list of countries (including Switzerland)	WHO EUL, and list of 55 countries (e.g., Argentina, Bahrain, Brazil, China, Indonesia, United Arab Emirates, Zimbabwe)	WHO EUL, and list of 33 countries (e.g., Albania, Chile, Egypt, Hong Kong, Malaysia, Tunisia, Turkey, Ukraine)

PHASE III TRIALS RESULTS						
Number of participants (vaccine/ placebo)	43,448 (21,720/ 21,728)[1]	30,420 (15,210/15,210)[2]	17,178 (8597/8581)[3]	39,321 (19,630/19,691)[4]	26,917 (13,459/13458); or 26,914 (13,465/13,458)[5]	9,823 (4,953/4,870)[6]
Total COVID-19 cases (vaccine/ control)	170(8/162)[1]	196 (11/185)[2]	332 (84/248)[3]	464 (116/348)[4]	121(26/95) or 116(21/95)[5]	253(85/168)[6]
Efficacy estimates in Phase III trials[i]	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).[1]	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).[2]	14 days and more, participants with two standard doses: efficacy was **63·1%** (95% CI 51.8 to 71.7) 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-	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%**	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).[5]	After 14 days, efficacy against symptomatic cases was **50.7%** (95% CI 35.9 to 0-62.0).[6]

[i] 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, and 21 July and 16 December 2020 for the Sinovac/ CoronaVac 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. This will be covered in the next synoptic table report.

			positive swab: efficacy was 54.1% (95% CI 44.7 to 61.9)[3].	(95% CI 54.2 to 96.9) after 28 days.[4]		
EFFICACY						
Efficacy of single doses	52% (95% CI, 29.5 to 68.4; starting at 12 days) or 82.2% (75.1 to 87.3; starting at ≥14 days)[7]. Another phase III trial: 91% (95% CI, 85-94)[8].[ii]	95.2% (95% CI, 91.2.8 to 97.4; starting at >14 days)[2].	72.8% (starting at 22 days up to 60 days)[3]. Another phase III trial: 88% (95% CI, 75-94)[8].[ii]	Single dose vaccine	Unknown	35.1% (95% CI, -6.6 to -60.5) [conducted in a setting with high P.1 transmission][9].
Efficacy against variants	Two doses of the vaccine effectively neutralize the B.1.1.7 variant and the D614G substitution. Neutralization of the B.1.351 was diminished by a factor of 5. Despite this, the BNT162b2 mRNA vaccine	NAbs remained high and consistent with titres of the wildtype for the B.1.1.7 variant. For the B.1.351 variant NAbs were 6-fold lower. The NAbs against the B.1.351 variant were still found to be protective[11].	Two doses of the vaccine had no efficacy against the B.1.351 (VE = 21.9%; 95% CI, -49.9 to 59.8)[12]. 70.4% (95% CI, 43.6-84.5) against symptomatic infection with alpha variant (B.1.1.7);	Efficacy against moderate-severe-critical Covid-19 due to the 20H/501Y.V2 variant was 52.0% (>14 days) and 64.0% (>28 days). Efficacy against severe-critical COVID-19 was 73.1% (>14 days)	Sinopharm has a reduced neutralizing capacity to B.1.617.2 and B.1.351. However, there were no differences in the NAbs titres against B.1.617.2 and B.1.351. in vaccinated individuals vs. those naturally infected,	49.6% against P.1 (>14 days after 1st dose)[9].

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

	provides some protection against B.1.351[10].		28.9% (95% CI, -77.1 to 71.4) against asymptomatic infection with B.1.1.7[13].	and 81.7% (>28 days)[4]. 1.6-fold reduction in neutralization sensitivity for B.1.167, 3.6-fold for B.1.351, and 3.4 for P.1[14].	suggesting the vaccines have a similar level of protection against infection as natural infections[15].	
EFFECTIVENESS						
Effectiveness of single dose	*Individuals ≥70:* Symptomatic disease: 58%[16]. Hospitalization risk reduced by 35-45%[16]. Risk of death reduced by 54%[16]. *General population:* Against infection: 70%[17].	*Individuals ≥70:* Symptomatic disease: 64% (95% CI, 46-78; >2 weeks after dose)[18].[iii] *General population:* Symptomatic disease: 60% (95% CI, 57-64; >2 weeks after dose)[18].[iv] No further data has been published on the mRNA-1273 vaccine[19].	*Individuals ≥70:* Symptomatic disease: 58%[16]. Hospitalization risk reduced by 35-45%[16]. *General population:* Asymptomatic or symptomatic disease: 64%; Symptomatic disease: 67%[20].	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)[21].	Partial protection[22].[v]	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[23].

[iii] mRNA-aggregated data (results do not disaggregate between BNT162b2 and mRNA-1273).
[iv] mRNA-aggregated data (results do not disaggregate between BNT162b2 and mRNA-1273).
[v] Study did not report numerical data on vaccine effectiveness. Further studies are required to validate results.

Effectiveness two doses	*General population:* Against infection: 85%[17]. 94.6%[24].	*General population:* 100%[24]. Symptomatic disease: 91% (95% CI, 89-93; >2 weeks after dose)[18].[vi] No further data has been published on the mRNA-1273 vaccine[19].	*General population:* Asymptomatic or symptomatic disease: 85%; Symptomatic disease: 90%[20].	Not Applicable (one dose schedule)	Partial protection[22].[vii]	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[23].
Effectiveness against variants	*Single dose:* Delta: 30.7% (95% CI, 25.2 to 35.7)[25] Alpha: 48.7% (95% CI, 45.5 to 51.7)[25] *Two doses:* Delta (B.1.617): 88.0% (95% CI, 85.3 to 90.1)[25] Alpha (B.1.1.7): 93.7 (95% CI, 91.6 to 95.3)[25]	*Single dose:* Alpha: 88.1% (95% CI, 83.7 to 91.5)[27] Beta: 61.3% (95% CI, 56.5 to 65.5)[27] *Two doses:* Alpha: 100% (95% CI, 91.8 to 100)[27] Beta: 96.4% (95% CI, 91.9 to 98.7)[27]	*Single dose:* Delta: 30.7% (95% CI 25.2 to 35.7)[25] Alpha: 48.7% (95% CI 45.5 to 51.7)[25] *Two doses:* Delta: 67.0% (95% CI, 61.3 to 71.8)[25] Alpha: 74.5 (95% CI, 68.4 to 79.4)[25] Odds ratio of 5.45 (95% CI, 1.39-21.4) to become infected	No published data.	No published data.	Demonstrated 42% vaccine effectiveness in a setting with high P.1 transmission, in individuals aged 70 and above[29]. *Two doses:* Equally effective (~76%) in neutralizing D614G, B.1.1.7 and B.1.429 as the wild type strain. Neutralization was decreased by factor 4.03 for

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

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

	Gamma (P.1): Neutralization activity reduced by 3.3 fold[26].		with B.1.167 compared to non-B.1.167[28].			B.1.526, factor 3.92 for P.1, and factor 5.27 for B.1.351[30]. *Delta variant:* Single dose: 13.8% (95% CI, -60.2-54.8) Two doses: 59% (95% CI, 16-81.6) against SARS-CoV-2 infection and 70.2% (95% CI, 29.6-89.3) against moderate COVID-19 infection[31].
SAFETY AND ADVERSE EVENTS						
Safety (adverse events)	Common side effects: pain at the injection site, fatigue, headache, myalgia, chills and fever.[32] Optimal safety for asthma patients[33]. Rare adverse events: axillary lymphadenopathy, paroxysmal	Common side effects: pain at injection site, headache, fatigue, myalgia, arthralgia[2], Covid arm (cutaneous hypersensitivity)[45]. Rare adverse events: Myocarditis[34,35], orofacial swelling &	Common side effects: fatigue, myalgia, arthralgia, headache[49], lethargy, fever, & nausea[50]. Rare adverse events: transverse myelitis, high fever[49,51], cutaneous hypersensitivity[51],	Common adverse events: headache, fever, chills, fatigue, myalgia, and nausea[58]. Rare adverse events: thrombosis, thrombocytopenia, cerebral venous sinus thrombosis[59], increased risk of developing Guillain-	Common side effects: pain at the injection site, dizziness, headache, fatigue, nausea, vomiting, & allergic dermatitis[50]. Common adverse events: pain at the injection site and fever[50].	Common side effects: pain at injection site, headache, fatigue, tremors, & flushing[6]. Rare adverse events: myalgia, fever[6], pityriasis rosea (lesions improved completely after ~8 weeks)[38].

	ventricular arrhythmia, leg paresthesia[1]. Myocarditis[34,35], anaphylaxis and swelling of the lips, face, and tongue related to anaphylaxis[36] (11 anaphylaxis cases per million doses administered)[37], pityriasis rosea (lesions improved completely after ~8 weeks)[38], lymphocytic vasculitis[39], reactivation of varicella-zoter virus after second dose (typically occur in individuals with pre-existing conditions)[40], Kikuchi-Fujimoto disease[41]. Potential association: cerebral venous sinus thrombosis and intracranial haemorrhage	anaphylaxis[36]. Potential risk factor for Bell's palsy (most improve upon follow-up)[46], herpes zoster reactivation (very rare)[47] One case developed IgA Nephropathy after receiving the second dose of mRNA-1273 (causal link not yet proven)[48].	vasculitis[52], cerebral venous sinus thrombosis[53] (higher risk for women)[54], thromboembolism[55], vaccine induced immune thrombotic thrombocytopenia[56], small vessel vasculitis[52]. Vaccination in individuals with adrenal insufficiency can lead to adrenal crises[57].	Barré syndrome post vaccination[60]. 97% of reported reactions after vaccine administration were non-serious[58].	Unsolicited adverse reactions were similar among the vaccine groups and control group within 7 days[5].	Serious adverse events were similar in number in the vaccine and placebo groups (judged unrelated to the vaccine)[6].

	(causal link not yet proven)[42], aseptic meningitis (causal link not yet proven)[43]. Serious adverse events were observed in a similar proportion of vaccine (0.6%) and placebo (0.5%) recipients, which also occur at a similar frequency within the general population[32,44].					
TRANSMISSION, PREVENTION, PROTECTION						
Severe disease/death prevention	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)[6]
Transmission prevention	*Prior Delta Variant:* Vaccine effectiveness against infectiousness given infections **41.3%**[61] Vaccine effectiveness against transmission **88.5%**[61]	Limited data	48% (limited data) May not be able to block the transmission of the alpha variant as efficiently as the wild type[13].	Limited data	Unknown	Unknown

	During Delta Variant: Similar Ct values (<25) were found in both vaccinated and unvaccinated groups[62]					
Duration of protection	Limited data[63] Median time between second dose and infection: **146 days (IQR, 121-167)**[64]	Limited data[63] *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[65]	*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)[66] *Cellular Immune Response:* **Day 182** after first dose: median of **237 SFUx10^6 PBMC (IQR, 109-520)**[66] **6 months** after second dose: **(median 1240, IQR**	Limited data[63] *Humoral & Cellular Immune Response:* Antibody responses were detected in all vaccine recipients on **day 239** (stable response for at least 8 months)[67]	Limited data[63]	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[68].

			432-2002) in groups with 15-25 week interval between doses[66]			
Asymptomatic prevention in/outside clinical trials	90% (starting at 14 days) regardless of symptom status[69].	90% (starting at 14 days)	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)[4].	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)[5].	Unknown
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)**[70]. *Children (6months-11):* Ongoing trials[71]	*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)**[72]. *Children (6month-11):* Ongoing trials[73]	No available data Paused ongoing trials in children aged 6-17 due to concerns over rare blood clots reported in adult population[74].	No available data Announced at begging of April ongoing study in adolescents but paused to investigate blood clots in adult population[74].	*Children (3-17):* Ongoing clinical trial[75]. Countries such as China and UAE have approved its use in children[76].	*Children (3-17):* Unknown. Clinical trial only looked at safety, tolerability and immunogenicity[77].
Immunogenicity	*Adolescents (12-15) serum-neutralizing titer:* 1 month after 2nd dose had **1283.0**	Adolescents (12-17): Neutralizing antibody titer after 2nd dose was **1401.7 GMN_{50}**	No available data	No available data	Ongoing clinical trial[75].	*Children (3-17):* Neutralizing antibody response after 2nd dose **(100%)**

	GMN_{50} (CI, 1095.5-1402.5)[70]. *Adolescents/young adult (16-25) serum-neutralizing titer:* 1 month after 2nd dose had **705.1 GMN_{50} (CI, 621.4-800.2)**[70]. *Children (6months-11):* Ongoing trials[71]	**(CI, 1276.3-1539.4)** Serological response was **98.8% (CI, 97.0-99.7)** *Children (6month-11):* Ongoing trials[73]				with GMT ranging from **45.9-212.6**[77]
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%)**[70]. *Adolescent/young adults (16-25):* Local and systemic events were generally mild to moderate	*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)[78]	No available data	No available data	Ongoing clinical trial[75]	*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%)**[77]

	Severe injection-site pain **(3.4%)** Fever **(17%)** Adverse events **(6%)** Severe adverse events **(1.7%)**[70]. Few reported cases of acute myocarditis and pericarditis (mainly in males)[78] *Children (6months-11):* Ongoing trials[71]	*Children (6month-11):* Ongoing trials[73]				
HETEROLOGOUS VACCINATION						
Heterologous vaccines 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)	BBIBP/BNT162b2	Press releases have confirmed that Thailand will use the AstraZeneca vaccine as the second dose for individuals whose first dose was Sinovac[viii]

[viii] 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/

Heterologous vaccines immunogenicity	*GMCs of SARS-CoV-2 anti-spike IgG at 28 days post booster:* Heterologous **(7133 ELU/mL, CI 6415-7932)** vs. Homologous **(14,080 ELU/mL, CI 12491-15871)**[79]. *SFC frequency (T0cell ELISpot):* Heterologous **(99 SFC/10^6 PBMCs)** vs. Homologous **(80 SFC/10^6 PBMCs)**[79]**.**	*Spike-specific IgG antibodies:* Heterologous **(3602 BAU/mL)** vs. Homologous **(4189 BAU/mL)**[48] *Neutralizing antibodies:* Heterlogous **(100%)** vs. Homologous **(100%)**[80]. *Results based on immunosuppressed population	*RBD antibody titres:* Heterologous **(7756.68 BAU/mL, CI 7371.53-8161.96)** vs. Homologous **(99.84 BAU/mL, CI 76.93-129.59)** at day 14[81]. *IgG antibody titres:* Heterologous **(3684 BAU/mL)** vs. Homologous **(101.2 BAU/mL)** at day 14[81]. *Neutralizing antibodies:* Heterologous **(100%)** at day 14 vs. Homologous **(30%)** at day 14[81].	Not Applicable (one dose schedule)	Unknown (on-going clinical trial)[49]	Unknown
Heterologous vaccines reactogenicity	Observed increase in systemic reactogenicity after boost in heterologous schedules in comparison with homologous schedules[79] *Adverse events in heterologous:*	*Adverse events in heterologous and homologous vaccination groups were very similar[80]. *Majority of adverse events self-reported were Pain at injection site, Swelling at injection site, Fever,	*Adverse events in heterologous:* Headache **(44%)**, Myalgia **(43%)**, Malaise **(42%)**, Fever **(2%)**, Injection site pain **(88%)**, Induration **(35%)**, Erythema **(31%)**[81].	Not Applicable (one dose schedule)	Unknown (on-going clinical trial)[82]	Unknown

	Adverse events **(90)** Grade 1 **(54.4%)** Grade 2 **(37.8%)** Grade 3 **(7.8%)** Grade 4 **(0%)** Arthralgia, Migraine, Back Pain[79]. *Adverse events in homologous:* Adverse events **(81)** Grade 1 **(59.3%)** Grade 2 **(39.5%)** Grade 3 **(1.2%)** Grade 4 **(0%)**[79].	Headaches, Fatigue, Chills, GI effects, Myalgia, Arthralgia[80]. *Results based on immunosuppressed population	*Severity of adverse events in heterologous:* Mild **(68%)**, Moderate **(30%)**, Severe **(2%)**[81].			
OTHER						
Third dose/prime boosters	Booster trial of third dose of current BNT162b2 vaccine are ongoing. Initial data demonstrates that given 6 months after second dose has consistent tolerability and high immunogenicity against wild type and Beta variant[83].	Phase II booster trial of three booster doses are ongoing[83]. Preliminary results of booster doses of mRNA-1273 vaccine show robust antibody response against Delta variant and similar safety and tolerability compared to second dose[84].	Preliminary results on tolerability and immunogenicity of third dose of ChAdOx1 vaccines showed strong boost to the immune response[84]. Preprint reported that antibody levels 28 days after third dose were significantly higher than second dose antibodies after 28	Janssen/ Johnson & Johnson are testing a 2-dose version of their vaccine that provides stronger immunogenicity and duration of protection[85].	No further available data Study using animal model suggests that heterologous prime-boost with two doses of inactivated vaccine followed by either recombinant RBD, adenovirus-vectored or mRNA vaccine improves humoral immune response[86].	A third (booster) dose was administered to healthy adults ≥60 years, 8 months after the primary vaccination. The third dose significantly increased NAbs, which had previously dropped below the seropositive cut-off. The most common side effect was pain at the injection site.

			days and that third dose provided higher antibody titters against Alpha, Beta, and Delta variants[66].			All other adverse events were considered unrelated to the vaccination. The third shot is considered to be safe[68]. Indonesia and Thailand are considering a third booster shot to HCW that were vaccinated with CoronaVac. Turkey and the United Arab Emirates have already began to give booster shots to those vaccinated with Sinovac/ CoronaVac.[ix] Study using animal model suggests that heterologous prime-boost with two doses of inactivated vaccine followed by either recombinant

[ix] Indonesia, 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/

						RBD, adenovirus-vectored or mRNA vaccine improves humoral immune response[86].
Comments /ongoing studies	Specific populations were excluded (HIV and immunocompromised patients, pregnant women, and younger adults) were excluded from the current analysis. No data related to asymptomatic protection or transmission. Risk of myocarditis and pericarditis is added to the vaccine information sheet	Evaluation of the incidence of asymptomatic or subclinical infection and viral shedding would have been interesting. Calculation of efficacy were not based on the total number of confirmed Covid-19 cases. Risk of myocarditis and pericarditis is added to the vaccine information sheet.	Blood clots, thrombotic events and thrombocytopenia were reported in real-world settings, although quite rare.	Blood clots, thrombotic events and thrombocytopenia were reported in real-world settings, although quite rare.	Only 2 severe cases occurred in the control group and none in the vaccine group (very few cases to get a reliable estimate).	Death reports on fully vaccinated doctors (10 cases during June 2021 in Indonesia). It may be related to new variants. [media report][x]

[x] 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

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