Literature screening report

COVID-19 vaccines in the WHO’s Emergency Use Listing (EUL): report (2)

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Abstract

This report focuses on the World Health Organization’s (WHO) Emergency Use Listing (EUL) of authorized vaccines as of August 16, 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, in some cases, from observational studies. This report particularly focuses on heterologous vaccination schedules (e.g., mixing ChAdOx1 and mRNA vaccines), Sinopharm/
BBIBP-CorV and Sinovac/ CoronaVac’s inactivated vaccines, and provides the latest updates and information on children and adolescent vaccinations.

Content

Abstract 1
Content 2
Preamble 2
Background 3
Methodology 3
Results 4
References 14

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 31.2% of the world populations had received at least one dose of a marketed Covid-19 vaccine as of 16 August 2021\(^1\). To further accelerate vaccination coverage worldwide, the World Health Organization (WHO) via COVAX ensures the supply of Covid-19 vaccines to member states. The WHO regularly assesses unlicensed vaccines, therapeutics, and in vitro diagnostics to expedite the availability of these products in emergencies\(^2\). Covid-19 vaccines are not an exception; several are currently under evaluation for an Emergency Use Listing (EUL). Of those, six vaccines [namely, Pfizer-BioNTech, USA], Spikevax/Moderna COVID-19 Vaccine/ mRNA-1273 (Modern, 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 July 15, 2021. Here, data from phase III clinical trials – and observational studies where necessary – for those EUL-accepted vaccines was summarized. Additionally, articles regarding the two Chinese inactivated virus vaccines (Sinopharm and CoronaVac), the immunogenicity and reactogenicity of heterologous vaccination schedules, and children and adolescent vaccination were prioritized during the literature search. Data regarding those highlighted topics can be found in the table below.

Methodology

We screened the data for the EUL-accepted vaccines as of August 16, 2021 from PubMed, Embase, medRxiv, bioRxiv, Cochrane, and clinical trials databases such as ClinicalTrials and WHO Trial Registry. The methods used were reported previously.

\(^1\) https://ourworldindata.org/covid-vaccinations (accessed on 12.08.2021).
Results

Data updated biweekly was synthesized in the synoptic table below. Phase III clinical trials and further literature are cited at the end of this report.

Heterologous prime-boost COVID-19 vaccination has become an international topic of interest as several countries changed their recommendations regarding the ChAdOx1 vaccine due to safety concerns\(^3\). Furthermore, heterologous schedules provide flexibility in vaccination programs in response to supply availability, making them a topic of interest in countries with scarce vaccine access and availability\(^3\). This had led numerous studies to analyse the immunogenicity and reactogenicity of heterologous vaccination schedules with most on-going studies and published articles on the combination of ChAdOx1 and mRNA vaccines (mainly ChAdOx1/BNT162b2 schedules). Based on the preliminary results, the mixing of vaccines triggers a robust immune response similar to – or even stronger than – homologous vaccination\(^4\). Additionally, the majority of adverse events reported after undergoing a heterologous vaccination schedule were mild to moderate with very few severe events reported\(^5\).

For the combination of BNT162b2 and ChAdOx1 as the booster shot (BNT162b2/ChAdOx1), a less robust immune response in terms of IgG antibodies than the homologous vaccination (BNT162b2/BNT162b2) was reported; however, the homologous schedule had a slightly higher T-cell response than the homologous one\(^6\).

Nevertheless, studies reporting real-world effectiveness and safety are still needed.

\(^3\) Heterologous vaccine regimens against COVID-19. The Lancet. [https://www.thelancet.com/journals/lancet/article/PiIS0140-6736(21)01442-2/fulltext#back-bib10](https://www.thelancet.com/journals/lancet/article/PiIS0140-6736(21)01442-2/fulltext#back-bib10)

\(^4\) Mix-and-match COVID vaccines: the case is growing, but questions remain. Nature. [https://www.nature.com/articles/d41586-021-01805-9](https://www.nature.com/articles/d41586-021-01805-9)

\(^5\) Immunogenicity and reactogenicity of BNT162b2 booster in ChAdOx1-S-primed participants (CombiVacS): a multicentre, open-label, randomised, controlled, phase 2 trial. The Lancet. [https://www.thelancet.com/journals/lancet/article/PiIS0140-6736(21)01420-3/fulltext](https://www.thelancet.com/journals/lancet/article/PiIS0140-6736(21)01420-3/fulltext)

Both inactivated virus vaccines, Sinopharm/ BBIBP-CorV and CoronaVac, have recently received emergency use approval by the WHO\(^7\). Both vaccines pass the WHO’s minimum vaccine efficacy threshold of 50% and provide upwards than 90% protection against severe COVID-19 infections\(^8,9\). Phase III clinical trials demonstrated that Sinopharm/ BBIBP-CorV and the Sinovac/ CoronaVac vaccine provided 72.8\(^{\circ}\) - 79\(^{\circ}\)\(^{10}\) and 50.7\(^{\circ}\)\(^{12}\) efficacy respectively, against symptomatic COVID-19 infection. These trials were conducted between July and December of 2020, a period prior to the delta (B.1.617.2) variant transmission. Further case control studies in Brazil (a setting of high P.1-variant transmission) confirm CoronaVac’s effectiveness outside a clinical setting, which ranged from 49.4\(^{\circ}\)\(^{13}\) to 51.8\(^{\circ}\) between February and March 2021\(^{14}\). In a real-world study including 10.2 million participants in Chile, CoronaVac had an adjusted vaccine effectiveness of 65.9\(^{\circ}\)\(^{15}\). Follow-up studies demonstrated that antibody production after BBIBP-CorV or CoronaVac vaccination decreases with older age of the vaccinated person over time\(^{16,17}\). Although no studies have been released thus far concerning the safety and immunogenicity of booster shots for BBIBP-CorV, a CoronaVac booster dose was found to be safe and rapidly re-establish robust immune responses in individuals over the age of 60 years\(^{18}\).

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\(^{7}\) Immunogenicity and safety of the CoronaVac inactivated vaccine in patients with autoimmune rheumatic diseases: A phase 4 trial. *Nature Medicine.* [https://www.nature.com/articles/s41591-021-01469-5](https://www.nature.com/articles/s41591-021-01469-5)

\(^{8}\) Effect of 2 Inactivated SARS-CoV-2 Vaccines on Symptomatic COVID-19 Infection in Adults: A Randomized Clinical Trial. *JAMA.* [https://jamanetwork.com/journals/jama/fullarticle/2780562](https://jamanetwork.com/journals/jama/fullarticle/2780562)


\(^{10}\) Effect of 2 Inactivated SARS-CoV-2 Vaccines on Symptomatic COVID-19 Infection in Adults: A Randomized Clinical Trial. *JAMA.* [https://jamanetwork.com/journals/jama/fullarticle/2780562](https://jamanetwork.com/journals/jama/fullarticle/2780562)

\(^{11}\) WHO approval of Chinese CoronaVac COVID vaccine will be crucial to curbing pandemic. *Nature.* [https://www.nature.com/articles/d41586-021-01497-8](https://www.nature.com/articles/d41586-021-01497-8)


\(^{13}\) Effectiveness of CoronaVac in the setting of high SARS-CoV-2 P.1 variant transmission in Brazil: A test-negative case-control study. *medRxiv.* [https://www.medrxiv.org/content/10.1101/2021.04.07.21255081v1](https://www.medrxiv.org/content/10.1101/2021.04.07.21255081v1)


\(^{16}\) Virus neutralizing antibody responses after two doses of BBIBP-CorV (Sinopharm, Beijing CNBG) vaccine. *medRxiv.* [https://www.medrxiv.org/content/10.1101/2021.07.15.21260382v1](https://www.medrxiv.org/content/10.1101/2021.07.15.21260382v1)

\(^{17}\) Effectiveness of the CoronaVac vaccine in the elderly population during a P.1 variant-associated epidemic of COVID-19 in Brazil: A test-negative case-control study. *medRxiv.* [https://www.medrxiv.org/content/10.1101/2021.05.19.21257472v1](https://www.medrxiv.org/content/10.1101/2021.05.19.21257472v1)

\(^{18}\) A booster dose is immunogenic and will be needed for older adults who have completed two doses vaccination with CoronaVac: a randomised, double-blind, placebo-controlled, phase 1/2 clinical trial. *medRxiv.* [https://www.medrxiv.org/content/10.1101/2021.08.03.21261544v1](https://www.medrxiv.org/content/10.1101/2021.08.03.21261544v1)
Clinical trials and studies are currently focusing on the safety and efficacy of vaccines on children and adolescents. WHO’s Strategic Advisory Group of Experts (SAGE) has deemed the Pfizer/ BioNTech vaccine to be suitable for children aged 12 years and above and recommends children of high risk to be vaccinated. The U.S. Food and Drug Administration (FDA) has authorized the administration of Pfizer/ BioNTech in children and adolescents aged from 12 through to 15 years of age in the United States and is currently assessing Moderna’s emergency use application to vaccinate people under the age of 15. Swissmedic authorised the use of Pfizer/ BioNTech vaccine in young individuals (12 to 15 years) in June, and has recently approved Moderna’s Spikevax vaccine to be extended towards children and adolescents aged 12 to 17. Both Pfizer/ BioNTech and Moderna’s clinical trials demonstrated comparable safety and immune responses in children to those in young adults aged 18 to 25 years. Additionally, the Chinese vaccine CoronaVac showed, in its phase1/2 report, that the vaccine was well tolerated, safe and induced a humoral response in children aged 3 to 17 years of age. Further vaccine trials concerning children and adolescents are ongoing.

### Synoptic table about SARS-CoV-2 vaccines accepted in the WHO’s Emergency Use Listing (as of August 16th, 2021)

<table>
<thead>
<tr>
<th>Vaccine Name</th>
<th>Platform</th>
<th>Dose and frequency</th>
<th>Target population</th>
<th>Storage conditions</th>
<th>Approving authorities</th>
</tr>
</thead>
<tbody>
<tr>
<td>BNT162b2/COMIRNATY (Pfizer-BioNTech, USA)</td>
<td>mRNA-based vaccine</td>
<td>2 doses, 21 days apart</td>
<td>12 years old and over</td>
<td>2°C to 8 °C (for 1 month)</td>
<td>FDA, EMA, WHO EUL, and list of countries (including Switzerland)</td>
</tr>
<tr>
<td>Spikevax/Moderna COVID-19 Vaccine/mRNA-1273 (Moderna, USA)</td>
<td>mRNA-based vaccine</td>
<td>2 doses, 28 days apart</td>
<td>12 years old and over</td>
<td>2°C to 8 °C (for 1 month)</td>
<td>FDA, EMA, WHO EUL, and list of countries (including Switzerland)</td>
</tr>
<tr>
<td>Vaxzevria/ChAdOx1 nCoV-19/AZD1222/Covishield (AstraZeneca/Oxford, UK, India)</td>
<td>Non-replicating vector-based vaccine</td>
<td>2 doses, 4-12 weeks apart</td>
<td>18 years old and over</td>
<td>2°C until 8 °C</td>
<td>FDA (ongoing), EMA, WHO EUL, and list of countries (Switzerland is ongoing too)</td>
</tr>
<tr>
<td>Janssen COVID-19 vaccine/Johnson &amp; Johnson (Janssen, USA)</td>
<td>Non-replicating vector-based vaccine</td>
<td>1 dose, once</td>
<td>18 years old and over</td>
<td>2°C to 8 °C (for 3 months)</td>
<td>FDA, EMA, WHO EUL, and list of countries (including Switzerland)</td>
</tr>
<tr>
<td>Sinopharm/BBIBP-CorV, China</td>
<td>Inactivated virus (Vero cell)</td>
<td>2 doses, 21 days apart</td>
<td>18 years old and over</td>
<td>2°C until 8 °C</td>
<td>WHO EUL, and list of 55 countries (e.g., Argentina, Bahrain, Brazil, China, Indonesia, United Arab Emirates, Zimbabwe)</td>
</tr>
<tr>
<td>Sinovac CoronaVac, China</td>
<td>Inactivated virus (Vero cell)</td>
<td>2 doses, 14 days apart</td>
<td>18 years old and over</td>
<td>2°C until 8 °C</td>
<td>WHO EUL, and list of 33 countries (e.g., Albania, Chile, Egypt, Hong Kong, Malaysia, Tunisia, Turkey, Ukraine)</td>
</tr>
</tbody>
</table>

**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) | 30,420 (15,210/15,210) | 17,178 (8597/8581) | 39,321 (19,630/19,691) | 26,917 (13,459/13,458); or 26,914 (13,465/13,458) | 9,823 (4,953/4,870) |
| Total COVID-19 cases (vaccine/control) | 170 (8/162) | 196 (11/185) | 332 (84/248) | 464 (116/348) | 121 (26/95) or 116 (21/95) | 253 (85/168) |
| Efficacy estimates in Phase III trials | Starting from 7 days after 2nd dose: 95.0% (95% CI, 90.3 to 97.6) in population without prior SARS-CoV-2 infection. Efficacy of 94.6% (95% CI, 89.9 to 97.3) in population with or without prior infection. 100% among adolescents (12-15 years old). After a median follow-up of less than 63 days: Efficacy of 94.1% (95% CI, 89.3 to 96.8; P<0.001). 100% among adolescents (12 to <18 years old). 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). After 14 days, efficacy against symptomatic cases was 50.7% (95% CI 35.9 to 62.0). |

1 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.
<table>
<thead>
<tr>
<th>Efficacy of single doses</th>
<th>Efficacy against variants</th>
</tr>
</thead>
<tbody>
<tr>
<td>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)</td>
<td>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</td>
</tr>
<tr>
<td>92.1% (95% CI 68.8 to 99.1; starting at ≥14 days) - Statistically non-significant reduction before 14 days</td>
<td>NAbs remained high and consistent with titres of the wildtype for the B.1.1.7 variant. For the B.1.351 variant NAds were 6-fold lower. The NAds against the B.1.351</td>
</tr>
<tr>
<td>72.8% (starting at 22 days up to 60 days)(^3)</td>
<td>Two doses of the vaccine had no efficacy against the B.1.351 (VE = 21.9%; 95% CI, -49.9 to 59.8).(^{11})</td>
</tr>
<tr>
<td>Single dose vaccine</td>
<td>Efficacy against moderate-severe-critical Covid-19 due to the 20H/501Y.V2 variant was 52.0% (&gt;14 days) and 64.0% (&gt;28 days). Efficacy against severe-critical</td>
</tr>
<tr>
<td>Unknown</td>
<td>Sinopharm has a reduced neutralizing capacity to B.1.617.2 and B.1.351. However, there were no differences in the NAds titres against B.1.617.2 and B.1.351. in</td>
</tr>
<tr>
<td>(95% CI 54.2 to 96.9) after 28 days.(^4)</td>
<td>49.6% against P.1 (&gt;14 days after 1st dose)(^8)</td>
</tr>
<tr>
<td>35.1% (95% CI, -6.6 to -60.5) [conducted in a setting with high P.1 transmission](^8)</td>
<td>Demonstrated 42% effectiveness in a setting with high P.1 transmission, in</td>
</tr>
</tbody>
</table>

Positive swab: efficacy was 54.1% (95% CI 44.7 to 61.9).\(^3\)
factor of 5. Despite this, the BNT162b2 mRNA vaccine provides some protection against B.1.351.\(^9\)

variant were still found to be protective.\(^{10}\)

COVID-19 was 73.1\% (>14 days) and 81.7\% (>28 days).\(^4\)

vaccinated individuals vs. those naturally infected, suggesting the vaccines have a similar level of protection against infection as natural infections.\(^{12}\)

individuals aged 70 and above.\(^{13}\)

## SAFETY AND ADVERSE EVENTS

| Safety (adverse events) | Common side effects: pain at the injection site, fatigue, headache, myalgia, chills and fever.\(^{14}\) Rare adverse events: axillary lymphadenopathy, paroxysmal ventricular arrhythmia, leg paresthesia.\(^1\) Myocarditis\(^{15,16}\), anaphylaxis and swelling of the lips, face, and tongue related to anaphylaxis\(^{17}\) (11 anaphylaxis cases per million doses) | Common side effects: fatigue, myalgia, arthralgia, headache\(^{23}\), lethargy, fever, & nausea\(^{24}\). Rare adverse events: Myocarditis\(^{15,16}\), orofacial swelling & anaphylaxis.\(^{17}\). | Common adverse events: headache, fever, chills, fatigue, myalgia, and nausea.\(^{31}\) Common adverse events: headache, fever, chills, fatigue, myalgia, and nausea.\(^{31}\) Common adverse events: pain at the injection site, dizziness, headache, fatigue, nausea, & allergic dermatitis.\(^{33}\). Common adverse events: pain at the injection site and fever.\(^{33}\) Common adverse events: thrombosis, thrombocytopenia, cerebral venous sinus thrombosis.\(^{32}\) 97\% of reported reactions after vaccine. | Common side effects: pain at the injection site, headache, fatigue, myalgia, arthralgia, and swelling of the lips, face, and tongue related to anaphylaxis.\(^{17}\) | Common adverse events: headache, fever, chills, fatigue, myalgia, and nausea.\(^{31}\) | Common adverse events: transverse myelitis, high fever\(^{23}\), vasculitis\(^{25}\), cerebral venous sinus thrombosis\(^{26}\), thromboembolism\(^{27}\), vaccine induced immune thrombotic thrombocytopenia\(^{28}\), small vessel vasculitis\(^{29}\). Vaccination in individuals with \(\geq 70\) years of age. | Common side effects: headache, fever, chills, fatigue, myalgia, and swelling of the lips, face, and tongue related to anaphylaxis.\(^{17}\) | Common adverse events: headache, swelling & allergic dermatitis.\(^{33}\). | Common adverse events: myalgia & fever.\(^6\) | Rare adverse events: myalgia & fever.\(^6\) | Serious adverse events were similar in number in the vaccine and placebo groups (judged unrelated to the vaccine).\(^6\) |
Potential association: cerebral venous sinus thrombosis and intracranial haemorrhage (causal link not yet proven). 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. Adrenal insufficiency can lead to adrenal crises. Administration were non-serious.

| 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)

| Transmission prevention | 46% (limited data) | Limited data | 48% (limited data) | Limited data | Unknown | Unknown

TRANSMISSION, PREVENTION, PROTECTION

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### Duration of Protection

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Limited Data&lt;sup&gt;34&lt;/sup&gt;</th>
<th>Limited Data&lt;sup&gt;34&lt;/sup&gt;</th>
<th>Limited Data&lt;sup&gt;34&lt;/sup&gt;</th>
<th>Limited Data&lt;sup&gt;34&lt;/sup&gt;</th>
<th>Limited Data&lt;sup&gt;34&lt;/sup&gt;</th>
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</table>

### Asymptomatic Prevention in/Outside Clinical Trials

| Vaccine  | 90% (Starting at 14 days) Regardless of Symptom Status<sup>36</sup> | 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)<sup>4</sup> | 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)<sup>5</sup> | Unknown |

### Children Vaccination

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Adolescents (12-15): After One Dose Had Efficacy of 75% (CI, 7.6-95.5)&lt;sup&gt;37&lt;/sup&gt; After Second Dose Efficacy of 100% (CI, 78.1-100)&lt;sup&gt;37&lt;/sup&gt;</th>
<th>Adolescents (12-17): After One Dose Had Efficacy of 92.7% (CI, 67.8-99.2)&lt;sup&gt;38&lt;/sup&gt; After Second Dose Efficacy of 93.3% (CI, 47.9-99.9)&lt;sup&gt;39&lt;/sup&gt;</th>
<th>Children (6 Month-11): Ongoing Trials&lt;sup&gt;40&lt;/sup&gt;</th>
<th>No Available Data</th>
<th>No Available Data</th>
<th>Children (3-17): Ongoing Clinical Trial&lt;sup&gt;42&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Ongoing Trials&lt;sup&gt;41&lt;/sup&gt;</td>
<td>Ongoing Trials&lt;sup&gt;41&lt;/sup&gt;</td>
<td>Ongoing Trials&lt;sup&gt;41&lt;/sup&gt;</td>
<td>Paused Ongoing Trials in Children Aged 6-17 Due to Concerns Over Rare Blood Clots Reported in Adult Population&lt;sup&gt;41&lt;/sup&gt;</td>
<td>Announced at Beginning of April Ongoing Study in Adolescents But Paused to Investigate Blood Clots in Adult Population&lt;sup&gt;41&lt;/sup&gt;</td>
<td>Countries Such as China and UAE Have Approved Its Use in Children&lt;sup&gt;43&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

**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<sup>35</sup>.

**Asymptomatic Prevention** in/outside clinical trials 90% (Starting at 14 days) regardless of symptom status<sup>36</sup>.

**Statistical** 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)<sup>4</sup>.

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)<sup>5</sup>.

**Unknown**

**Children Vaccination**

- **Adolescents (12-15):** After one dose had efficacy of 75% (CI, 7.6-95.5)<sup>37</sup> After second dose efficacy of 100% (CI, 78.1-100)<sup>37</sup>
- **Adolescents (12-17):** After one dose had efficacy of 92.7% (CI, 67.8-99.2)<sup>38</sup> After second dose efficacy of 93.3% (CI, 47.9-99.9)<sup>39</sup>
- **Children (6 months-11):** Ongoing trials<sup>40</sup>
- **No available data**
- **No available data**
- **Children (3-17):** Ongoing clinical trial<sup>42</sup>
- **Countries such as China and UAE have approved its use in children**<sup>43</sup>
### Immunogenicity

#### Adolescents (12-15) serum-neutralizing titer:
- 1 month after 2nd dose had 1283.0 GMN$_{50}$ (CI, 1095.5-1402.5)$^{37}$
- Adolescents/young adult (16-25) serum-neutralizing titer: 1 month after 2nd dose had 705.1 GMN$_{50}$ (CI, 621.4-800.2)$^{37}$
- Children (6months-11): Ongoing trials  

#### 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 (6months-11): Ongoing trials  

#### No available data

### 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%)$^{37}$

#### 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%)

#### No available data

### Ongoing clinical trial$^{42}$

#### 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
### 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%)[^37]
Few reported cases of acute myocarditis and pericarditis (mainly in males)[^45]
Children (6months-11):
Ongoing trials[^40]

### Adverse events (6%)
Severe adverse events (1.7%)[^37]

### Injection-site pain
(13%)
Fever (25%)[^44]

### HETEROLOGOUS VACCINATION

<table>
<thead>
<tr>
<th>Heterologous vaccines schedule</th>
<th>BNT162b2/ChAdOx 1</th>
<th>ChAdOx1/mRNA-1273</th>
<th>ChAdOx1/BNT162b2</th>
<th>Not Applicable (one dose schedule)</th>
<th>BBIBP/BNT162b2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Administration of ChAdOx1 as second/booster dose</td>
<td>Administration of mRNA-1273 as second/booster dose</td>
<td>Administration of BNT162b2 as second/booster dose</td>
<td></td>
<td></td>
<td>Press releases have confirmed that Thailand will use the AstraZeneca vaccine as the second dose for individuals whose</td>
</tr>
</tbody>
</table>

[^37]: Few reported cases of acute myocarditis and pericarditis (mainly in males)[^45]
[^40]: Ongoing trials[^40]
[^44]: Injection-site pain (13%)
[^45]: Fever (25%)
<table>
<thead>
<tr>
<th>Heterologous vaccines immunogenicity</th>
<th>GMCs of SARS-CoV-2 anti-spike IgG at 28 days post booster:</th>
<th>*Spike-specific IgG antibodies: Heterologous (3602 BAU/mL) vs. Homologous (4189 BAU/mL)(^46)</th>
<th>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(^47)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Heterologous (7133 ELU/mL, CI 6415-7932) vs. Homologous (14,080 ELU/mL, CI 12491-15871)(^46)</td>
<td>*Neutralizing antibodies: Heterologous (100%) vs. Homologous (100%)(^48)</td>
<td>IgG antibody titres: Heterologous (3684 BAU/mL) vs. Homologous (101.2 BAU/mL) at day 14(^47) Neutralizing antibodies: Heterologous (100%) at day 14 vs. Homologous (30%) at day 14(^47)</td>
</tr>
<tr>
<td></td>
<td>SFC frequency (T0cell ELISpot): Heterologous (99 SFC/10⁶ PBMCs) vs. Homologous (80 SFC/10⁶ PBMCs)(^46)</td>
<td></td>
<td>Not Applicable (one dose schedule)</td>
</tr>
<tr>
<td></td>
<td>*Results based on immunosuppressed population</td>
<td></td>
<td>Unknown</td>
</tr>
</tbody>
</table>

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### Literature screening report: COVID-19 vaccines in the WHO’s Emergency Use Listing (EUL): report (2) - 16.08.2021 - Sabina Rodriguez Velásquez, Gabriela Guizzo Dri

**Heterologous vaccines reactogenicity**

<table>
<thead>
<tr>
<th>Adverse events in heterologous:</th>
<th>Adverse events in homologous:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adverse events (90)</td>
<td>Adverse events (81)</td>
</tr>
<tr>
<td>Grade 1 (54.4%)</td>
<td>Grade 1 (59.3%)</td>
</tr>
<tr>
<td>Grade 2 (37.8%)</td>
<td>Grade 2 (39.5%)</td>
</tr>
<tr>
<td>Grade 3 (7.8%)</td>
<td>Grade 3 (1.2%)</td>
</tr>
<tr>
<td>Grade 4 (0%)</td>
<td>Grade 4 (0%)</td>
</tr>
<tr>
<td>Arthralgia, Migraine, Back Pain</td>
<td>Arthralgia, Migraine, Back Pain</td>
</tr>
</tbody>
</table>

*Adverse events in heterologous and homologous vaccination groups were very similar*[^46]

*Majority of adverse events self-reported were Pain at injection site, Swelling at injection site, Fever, Headaches, Fatigue, Chills, GI effects, Myalgia, Arthralgia[^48]*

*Results based on immunosuppressed population*

<table>
<thead>
<tr>
<th>Adverse events in heterologous:</th>
<th>Severity of adverse events in heterologous:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headache (44%)</td>
<td>Mild (68%)</td>
</tr>
<tr>
<td>Myalgia (43%)</td>
<td>Moderate (30%)</td>
</tr>
<tr>
<td>Malaise (42%)</td>
<td>Severe (2%)</td>
</tr>
<tr>
<td>Fever (2%)</td>
<td></td>
</tr>
<tr>
<td>Injection site pain (88%)</td>
<td></td>
</tr>
<tr>
<td>Induration (35%)</td>
<td></td>
</tr>
<tr>
<td>Erythema (31%)[^47]</td>
<td></td>
</tr>
</tbody>
</table>

Not Applicable (one dose schedule)

Unknown (on-going clinical trial)[^49]

Unknown

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[^46]: Observed increase in systemic reactogenicity after boost in heterologous schedules in comparison with homologous schedules[^46]

[^47]: Severity of adverse events in heterologous: Mild (68%), Moderate (30%), Severe (2%)[^47]

[^48]: Adverse events in heterologous: Headache (44%), Myalgia (43%), Malaise (42%), Fever (2%), Injection site pain (88%), Induration (35%), Erythema (31%)[^47]

[^49]: Results based on immunosuppressed population
| 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. | Phase II booster trial of three booster doses are ongoing. 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. | Preliminary results on tolerability and immunogenicity of third dose of ChAdOx1 vaccines showed strong boost to the immune response. Preprint reported that antibody levels 28 days after third dose were significantly higher than second dose antibodies after 28 days and that third dose provided higher antibody titters against Alpha, Beta, and Delta variants. | 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. 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. All other adverse events were considered unrelated to the vaccination. The third shot is considered to be safe. 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.iii

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 response53.

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iii 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/
| 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. | 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] iv |

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References


38. Study to Evaluate the Safety, Tolerability, and Immunogenicity of an RNA Vaccine Candidate Against COVID-19 in Healthy Children <12 Years of Age. In: https://ClinicalTrials.gov/show/NCT04816643.


40. A Study to Evaluate Safety and Effectiveness of mRNA-1273 COVID-19 Vaccine in Healthy Children Between 6 Months of Age and Less Than 12 Years of Age. In: https://ClinicalTrials.gov/show/NCT04796896.


42. Immuno-bridging Study of Inactivated SARS-CoV-2 Vaccine in Healthy Population Aged 3-17 vs Aged 18 Years Old and Above. In: https://ClinicalTrials.gov/show/NCT04917523.


