Literature screening report

Covid-19 vaccines in the WHO's Emergency Use List: report (1)

Report submission date:	**30.06.2021**

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Abstract

In this report, we focused on the vaccines accepted in the Emergency Use List (EUL) of the World Health Organisation (WHO) as of June 29, 2021. Those vaccines are 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/BIBP (China), and Sinovac/CoronaVac (China).

We extracted data from phase III clinical trials for each vaccine and summarized it in a synoptic table. In some cases, we used data from observational studies where necessary.

Additional important topics such as top-ups/booster vaccines or vaccine combinations (e.g., mixing mRNA-vaccines) were not covered in the current version of the report.

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 23.4% of the world populations had received at least one dose of a marketed Covid-19 vaccine[1]. To further accelerate the vaccination 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 where several are currently under evaluation for an emergency use Listing (EUL). Of those, 6 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/BIBP (China), and Sinovac/CoronaVac (China)] were assessed and granted an authorization as of June 29, 2021. Here, we aimed to summarize the data from phase III clinical trials - and observational studies where necessary- for those EUL-accepted vaccines.

Methodology

We screened the data for the EUL-accepted vaccines as of June 23, 2021. The methods used were reported previously.

Results

We synthesized the data in a draft table (see below) that will be updated regularly. We cited the phase III clinical trials at the end of this report. Better references management and input changes will be integrated in the next report.

[1] https://ourworldindata.org/covid-vaccinations (accessed on 30.06.2021).
[2] https://www.who.int/teams/regulation-prequalification/eul/ (accessed on 30.06.2021).

Synoptic table about SARS-CoV-2 vaccines accepted in the WHO's Emergency Use List (as of June 29th, 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)[i]**	**Sinopharm/BIBP, China**	**Sinovac CoronaVac, China**
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
Number of participants (vaccine/placebo)	43,448 (21,720/ 21,728)	30420 (15,210/15,210)	17,178 (8597/8581)	39,321 (19,630/19,691)	26917(13459/13458) or 26 914(13465/13458)	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-positive swab: efficacy was 54.1% (95% CI 44.7 to 61.9).	After 14 days, efficacy against moderate to severe or critical Covid-19 was **66.9%** (95% CI 59.0 to 73.4).	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 0-62.0)[ii].
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)[iii]	92.1% (95% CI 68.8 to 99.1; starting at >14 days) - Statistically non-significant reduction before 14 days	72.8% (starting at 22 days up to 60 days)[iv]	Single dose vaccine	Unknown	49.6% (limited observational data)

Asymptomatic prevention in/outside clinical trials	90% (starting at 14 days)[v]	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)[vi].	Efficacy against symptomatic and asymptomatic cases was 64% (95% CI 48.8 to 74.7; in WIV04 vaccine) or 73.5% (95% CI 60.6 to 82.2; in HBO2 vaccine).	Unknown
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)[vii]	Limited data	48% (limited data)	Limited data	Unknown	Unknown
Duration of protection	Limited data (see ref. [viii])	Limited data (see ref. viii)	Limited data (see ref. viii)	Limited data (see ref. viii)	Limited data (see ref. viii)	Limited data (see ref. viii)
Efficacy against variants			No protection against mild to moderate Covid-19 due to the B.1.351 variant[ix]	Efficacy against moderate to severe or critical Covid-19 due to the 20H/501Y.V2 variant was 52.0% (>14 days) and 64.0% (>28 days)[x].	Unknown	49.6% against P.1 (>14 days after 1st dose) and P.2 (Gamma variant)[xi].
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

Safety (adverse events)	Adverse events: 21% in the vaccine and 5% in the placebo. Four related serious adverse events were reported among vaccine recipients (shoulder injury related to vaccine administration, right axillary lymphadenopathy, paroxysmal ventricular arrhythmia, and right leg paresthesia). Other adverse events commonly reported in the vaccine group (pain at the injection site, fatigue, and headache)	Common adverse events: pain at injection site, headache, fatigue, myalgia, arthralgia (all more often or clinically significant in the vaccine group compared to placebo)	Serious adverse events occurred in 168 participants, 79 of whom received the vaccine and 89 of whom received MenACWY or saline control. There were 175 serious adverse events (84 in the vaccine group and 91 in the control group), three of which were possibly related to the intervention: transverse myelitis occurring 14 days after a vaccine booster dose, hemolytic anemia in a control recipient, and fever higher than 40°C in a participant still masked to group allocation.	Systemic reactions such as headache, fatigue, myalgia, and nausea. One case of thrombosis was considered unrelated to the vaccine.	Systemic adverse events (pain at the injection site, headache, fatigue, myalgia, diarrhea, coughing, fever) and unsolicited adverse reactions were similar among the vaccine groups and control group within 7 days.	pain at the injection site, myalgia, Headache, fatigue (similar in the vaccine and placebo groups). Serious adverse events were similar in number in the vaccine and placebo groups (judged unrelated to the vaccine).

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)
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)[xii]. It may be related to new variants.

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[i] https://www.nejm.org/doi/full/10.1056/NEJMoa2101544 (accessed on 25.06.2021).
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[iii] https://www.cdc.gov/mmwr/volumes/70/wr/mm7020e2.htm (accessed on 26.06.2021).
[iv] https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)00432-3/fulltext#tbl1 (accessed on 26.06.2021).
[v] https://www.cdc.gov/mmwr/volumes/70/wr/mm7013e3.htm?s_cid=mm7013e3_w (accessed on 26.06.2021)
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[vii] https://www.nejm.org/doi/full/10.1056/NEJMc2107717?query=featured_coronavirus (accessed on 25.06.2021).
[viii] https://sciencetaskforce.ch/en/policy-brief/protection-duration-after-vaccination-or-infection/ (accessed on 30.06.2021)
[ix] https://www.nejm.org/doi/full/10.1056/NEJMoa2102214 (accessed on 27.26.2021).
[x] https://www.nejm.org/doi/full/10.1056/NEJMoa2101544 (accessed on 27.06.2021).
[xi] https://www.who.int/news-room/feature-stories/detail/the-sinovac-covid-19-vaccine-what-you-need-to-know?gclid=EAIaIQobChMIiaWzmYK98QIVafx3Ch0kowoFEAAYAiAAEgIjvPD_BwE (accessed on 28.06.2021).
[xii] https://www.theguardian.com/world/2021/jun/28/indonesian-covid-deaths-add-to-questions-over-sinovac-vaccine (accessed on 30.06.2021).

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