Weekly COVID-19 Vaccine Updates

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Introduction

This document summarises the vaccine efficacy and effectiveness, the vaccine specifications, the vaccine development pipeline and the timeline for World Health Organization (WHO) review of the various COVID-19 vaccines in late phase development. The document is updated weekly.

- Vaccine efficacy refers to the performance of a vaccine in a controlled clinical trial (study) situation
- Vaccine effectiveness refers to the performance of a vaccine in a population under real-world conditions

Key messages:

- It is difficult to directly compare the results from the studies as:
    - there are multiple variations in the way the clinical trials and effectiveness studies were undertaken;
    - each used different outcomes;
    - and the definitions for outcomes (e.g. for severity) also varied
- All COVID-19 vaccines in late phase development report high vaccine efficacy against severe COVID-19 and favourable safety profiles
- Pfizer/BioNTech and AstraZeneca both show high vaccine effectiveness in the UK and Israel where the B.1.1.7 (UK) variant is circulating

Other resources on COVID-19 vaccines:

WHO COVID-19 vaccines website: https://www.who.int/emergencies/diseases/novel-coronavirus-2019/covid-19-vaccines
EMA COVID-19 vaccines website: https://www.ema.europa.eu/en/human-regulatory/overview/public-health-threats/coronavirus-disease-covid-19/treatments-vaccines/covid-19-vaccines

New Updates

Key updates to this week's edition include:

- Summaries on:
    1. Vaccine efficacy (and effectiveness) in the elderly and against comorbidities (Page 7)
    2. Serious adverse events (Page 8)
        - AstraZeneca vaccine: No evidence of an overall increased risk of thromboembolic events in >17 million vaccinated people in the European Union and UK
        - Rare serious adverse events following immunisation (AEFI) include reports of central venous sinus thrombosis (CVST) with low platelets.
- Effectiveness data for Moderna and Pfizer vaccines (Page 5)
- Results (not yet peer reviewed) from the AstraZeneca trial in the USA, Chile & Peru showing 79% efficacy against symptomatic infection and 100% efficacy against severe disease (Page 3); and 80% efficacy in those aged ≥65 years (Page 7)
- WHO SAGE has released recommendations for the Johnson & Johnson vaccine (Page 9)
- Moderna, Sinopharm and Sinovac vaccines to receive WHO EUL authorisation in April 2021 at the earliest (Page 11)

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Vaccine Specifications

	ASTRAZENECA	GAMALEYA	JOHNSON & JOHNSON	MODERNA	NOVAVAX	PFIZER/BIONTECH	SINOVAC
VACCINE TYPE	Viral vector (chimpanzee adenovirus ChAdOx1)	Viral vector (recombinant adenovirus types 5 and 26)	Viral vector (recombinant adenovirus type 26)	mRNA	Protein subunit	mRNA	Inactivated virus
Available Through COVAX	✓	-	✓	-	✓	✓	-
Doses Required	8-12 weeks apart* 4 weeks apart (Product Information)	3 weeks apart	1	28 days apart*	3 weeks apart	3 weeks apart*	2 weeks apart (Brazil data suggest higher efficacy with 3 weeks between doses)
Shipping, Storage & Presentation	Normal cold chain requirements (2-8°C); 10-dose vials	-18.5°C (liquid form); 2-8°C (dry form)	2-8°C; 5-dose vials	-25°C to -15°C; 10-dose vials	2-8°C; 10-dose vials	-80°C to -60°C; -25°C to -15°C for up to 2 weeks; 6-dose vials	2-8°C; Single-dose vials
Approval by a Stringent Regulatory Authority (SRA)	WHO EUL, EMA, TGA, MHRA	Under review by WHO SAGE	WHO EUL, EMA, FDA	EMA, FDA	Under review by WHO SAGE	WHO EUL, EMA, FDA, TGA, MHRA	Under review by WHO SAGE

*Based on WHO Strategic Advisory Group of Experts on Immunization (SAGE) recommendations

WHO EUL: WHO Emergency Use Listing
EMA: European Medicines Agency
FDA: Food and Drug Administration (USA)
TGA: Therapeutic Goods Administration (Australia)
MHRA: Medicines and Healthcare Products Regulatory

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COVID-19 Vaccine Efficacy

VACCINE	VACCINE EFFICACY				
	ASYMPTOMATIC	MILD - MODERATE-SEVERE	SEVERE	HOSPITALISATION/DEATH	OTHER OUTCOMES
AstraZeneca	2.0% (-50.7-36.2)[1] Symptomatic and asymptomatic combined: 54.1% (44.7-61.9)[1]	-	UK: 100% (15 cases in the placebo group)[1] USA, Chile, Peru: 100%[2] (not peer-reviewed)	UK: Hospitalisation: 100% (9 cases in placebo group)[1]	Symptomatic infection: 66.7% (57.4-74.0)[1] Symptomatic infection: 79%[2] (not peer-reviewed) Symptomatic infection using a SINGLE DOSE (22-90 days post-vaccination): 76.0% (59.3 to 85.9)[1] Efficacy higher with longer time interval between doses: 12+ weeks: 82.4% (2.7-91.7) <6 weeks: 54.9% (32.7-69.7)[1]
Gamaleya	-	Moderate-severe: 100% (20 cases in the placebo group)[3]	-	-	Symptomatic infection: 91.6% (85.6–95.2)[3]
Johnson & Johnson	-	≥28 days post-vaccination: All sites: 66.1% (55.0-74.8) US: 72.0% (58.2-81.7) Latin America: 61.0% (46.9-71.8) South Africa: 64.0% (41.2-78.7)[4]	85.4% (54.2-96.9)[4]	100% (7 deaths in placebo group)[4]	Preserved for all ages and virus variants including B1.351[4]
Moderna	-	-	100% (30 cases in placebo group)[5]	100% (1 death in placebo group)[5]	Symptomatic infection: 94.1% (89.3-96.8)[5]
Novavax	-	-	-	-	Symptomatic infection: 89.3% (75.2-95.4)[6] (not peer reviewed)
Pfizer/BioNTech	-	-	88.9% (20.1–99.7)[7]	-	Symptomatic infection: 94.6% (89.9–97.3)[7]
Sinovac	-	-	-	-	Symptomatic infection: Brazil: 50.4%; Indonesia: 65.3%; Turkey 91.3% (not peer reviewed)

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COVID-19 Vaccine Effectiveness

VACCINE	SEVERE	HOSPITALISATION / DEATH	OTHER OUTCOMES
AstraZeneca	-	SINGLE DOSE in Scotland: 94% (73-99)[8]	-
Moderna	-	-	Pooled analysis of Moderna and Pfizer vacines in USA: Infections in nonvaccinated: 234 of 8969; 2.61% (2.29-2.96) Fully vaccinated: 4/8121; 0.05% (0.01-0.13)[9]
Pfizer/BioNTech	Israel: 92% (75-100)[10]	SINGLE DOSE in Scotland: 85% (76-91)[8] England: 86% (76-97) 7 days after 2 doses 72% (58-86) 21 days after 1 dose[11]	Pooled analysis of Moderna and Pfizer vacines in USA: Infections in nonvaccinated: 234 of 8969; 2.61% (2.29-2.96) Fully vaccinated: 4/8121; 0.05% (0.01-0.13)[9] Symptomatic infection in Israel: 94% (87-98)[10] Documented infection in Israel: 92% (88-95)[10]

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Vaccine Efficacy Against Variants

Refer to previous table for vaccine effectiveness results for the Pfizer/BioNTech vaccine in Scotland, England and Israel, where all locations had predominant B.1.1.7 circulation.

VACCINE	VACCINE EFFICACY			
	B.1.1.7 (UK) VARIANT	B1.351 501Y.V2 (SOUTH AFRICA) VARIANT		B.1.1.28.P1 AND B.1.1.28.P2 (BRAZIL) VARIANTS
	MILD/MODERATE	MILD/MODERATE	SEVERE	SEVERE
AstraZeneca	74.6% (41.6-88.9) (84% (70.7-91.4) against wild variant in UK)[12]	10.4% (−76.8 to 54.8)[13]	Study underway [4]	-
Johnson & Johnson	-	-	Moderate to severe/critical: 64.0% (41.2-78.7) Severe/critical: 81.7% (46.2-95.4)[4]	Moderate to severe/critical: 68.1% (48.8-80.7) Severe/critical: 87.6% (7.8-99.7)[4]
Novavax	85.6%[6] (not peer reviewed)	60.0% (19.9-80.1) against mild, moderate and severe COVID-19 in HIV-negative[6] 49.4% (6.1-72.8) overall against mild, moderate and severe COVID-19[6] (not peer reviewed)	-	-

Vaccine Efficacy/Effectiveness in the Elderly and Against Comorbidities

VACCINE	VACCINE EFFICACY UNLESS OTHERWISE STATED			
	DIABETES	OBESITY	AT RISK FOR SEVERE COVID-19	ELDERLY
AstraZeneca	-	-	79% against symptomatic infection in a sample where 60% had comorbidities, including diabetes, severe obesity or cardiac disease[2] (not peer-reviewed)	In ≥65 years: 80%[2] (not peer-reviewed) Effectiveness against hospitalisation at 28-34 days after a SINGLE DOSE (pooled analysis of AstraZeneca and Pfizer vacines) 18-64 years: 85% (68-93) 65-79 years: 79% (17-95) ≥80 years: 81% (65-90)[8]
Gamaleya	-	-	-	Against symptomatic infection in >60 years: 91.8% (67.1–98.3)[3]
Johnson & Johnson	Against moderate to severe/critical: 23.0% (-90.1-69.8)[4]	Against moderate to severe/critical: 65.9% (47.8-78.3)[4]	Against moderate to severe/critical: With any comorbidity: 58.6% (40.6-71.6)[4] No comorbidity: 68.8% (59.0-76.6)[4]	Against moderate-severe/critical disease ≥28 post vaccination: 18-59 years: 66.1% (53.3-75.8) 60+ years: 66.2% (36.7-83.0)[4]
Moderna	-	-	Against symptomatic infection, based on presence of comorbidities, including diabetes and obesity: In low risk: 95.1% (89.6-97.7) In high risk: 90.9% (74.7-96.7)[5]	Against symptomatic infection: 18-64 years: 95.6% (90.6-97.9) ≥65 year olds: 86.4% (61.4-95.2)[5]
Pfizer/BioNTech	-	-	Against symptomatic infection: With any comorbidity or obesity: 95.3% With no comorbidity: 94.7%[7]	Against symptomatic infection: >55 years: 93.7% (80.6-98.8) >65 years: 94.7% (66.7-99.9) >75 years: 100% (-13.1-100)[7] Effectiveness against hospitalisation at 28-34 days after a SINGLE DOSE (pooled analysis of AstraZeneca and Pfizer vacines) 18-64 years: 85% (68-93) 65-79 years: 79% (17-95) ≥80 years: 81% (65-90)[8]

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Serious Adverse Events

VACCINE	VACCINE SAFETY
AstraZeneca	108 SAEs in 12,282 (0.9%) vaccine recipients and 127 in 11,962 (1.1%) placebo recipients 12 thromboembolic events (4 vaccine; 8 placebo) 7 deaths, all considered unrelated to vaccination (2 vaccine, 5 placebo)[1] No safety concerns in US Phase III study involving 32,449 participants[2] (not peer-reviewed) No evidence of increased risk of thromboembolic events in >17 million vaccinated people in the European Union and UK (total 15 events of deep vein thrombosis and 22 events of pulmonary embolism, lower than would be expected in that population)[14] Rare reports in Germany and Scandinavian countries of central venous sinus thrombosis (CVST) with thrombocytopenia 7-14 days following the vaccine (not peer reviewed)[15]
Gamaleya	45 SAEs in 16,427 (0.3%) vaccine recipients and 23 in 5,435 (0.4%) placebo recipients All SAEs were considered unrelated to vaccination 4 deaths, all considered unrelated to vaccination (3 vaccine, 1 placebo)[3]
Johnson & Johnson	83 SAEs in 21,895 (0.4%) vaccine recipients and 96 SAEs in 21,888 placebo recipients (0.4%) 19 deaths all considered unrelated to vaccination (3 vaccine, 16 placebo)[4]
Moderna	153 SAEs in 15,166 (1.0%) placebo recipients and 147 in 15,185 (1.0%) vaccine recipients 5 deaths considered unrelated to vaccine (2 vaccine, 3 placebo)[5] Anaphylaxis reported in the US at a rate of 2.5 per million doses[16]
Novavax	SAEs at low levels and similar between vaccine and placebo groups[6]
Pfizer/BioNTech	SAEs and deaths were low and comparable between vaccine and placebo groups (total 37,586 participants)[7] Anaphylaxis reported in the US at a rate of 4.7 per million doses[16]

SAEs: Serious Adverse Events

Who Can be Vaccinated Based on WHO SAGE Recommendations?

So far, WHO SAGE have reviewed AstraZeneca, Moderna and Pfizer/BioNTech and have made recommendations for use.

	ASTRAZENECA	MODERNA	PFIZER/BIONTECH	JOHNSON & JOHNSON
Minumum Age	18 years	18 years	16 years	16 years
Maximum Age (SAGE WHO)	None	None	None	None
Pregnancy	Yes if high priority group & approved by health provider	Yes if high priority group & approved by health provider	Yes if high priority group & approved by health provider	Yes if high priority group & approved by health provider
Breastfeeding	Yes if high priority group	Yes if high priority group	Yes if high priority group	Yes if high priority group
Immunocompromised Including HIV	✓	✓	✓	✓
People Previously Infected by SARS-CoV-2 (PCR Confirmed)	Yes, although that person may choose to delay vaccination by 6 months	Yes, although that person may choose to delay vaccination by 6 months	Yes, although that person may choose to delay vaccination by 6 months	Yes, although that person may choose to delay vaccination by 6 months
History of Anaphylaxis (Severe Allergy)	Yes (unless the allergy is to the vaccine or its components)	Yes (unless the allergy is to the vaccine or its components)	Yes (unless the allergy is to the vaccine or its components)	Yes (unless the allergy is to the vaccine or its components)

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Vaccine Development Pipeline

WHO has recommended that vaccines adopted by countries have WHO SAGE EUL and/or Stringent Regulatory Approval.

VACCINE TYPE	NUMBER OF VACCINE CANDIDATES AT EACH PHASE OF DEVELOPMENT				
	PRE-CLINICAL	PHASE I/II	PHASE III	PHASE IV	IN USE*
RNA	28	7	1	2	2 (Pfizer/BioNTech, Moderna)
DNA	16	8	2	0	0
Vector (non-replicating)	26	7	4	1	4 (CanSino, Gamaleya, Johnson & Johnson, AstraZeneca)
Vector (replicating)	18	5	0	0	0
Inactivated	9	5	4	2	5 (Sinopharm/BIBP, Sinopharm/WIBP, Bharat, Chumakov, Sinovac)
Live-attenuated	2	1	0	0	0
Protein subunit	73	20	6	0	2 (Vector institute; Anhui Zhifei Longcom Biopharmaceutical Chinese Academy of sciences)
Virus-like particle	19	2	1	0	0
Other/unknown	34	3	0	0	0

*Not all vaccines in use have SRA (as recognised by WHO) approval (see Vaccine specifications table and WHO SAGE Emergency Use Listing and prequalification timeline for approval status of vaccines).

Source: London School of Hygiene and Tropical Medicine COVID-19 vaccine tracker.

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WHO SAGE Emergency Use Listing and Prequalification Timeline

MANUFACTURER	NAME OF VACCINE	PLATFORM	STATUS OF ASSESSMENT	ANTICIPATED DECISION DATE
Pfizer/BioNTech	BNT162b2/COMIRNATY Tozinameran (INN)	mRNA	Final decision made	Authorised 31/12/20
AstraZeneca	AZD1222	Adenoviral vector	Final decision made	Authorised 15/02/21
Serum Institute of India	Covishield (ChAdOx1_nCoV19)	Adenoviral vector	Final decision made	Authorised 15/02/21
Sinopharm/Beijing Institute of Biological Products (BIBP)	SARS-CoV-2 Vaccine (Vero Cell), Inactivated (InCoV)	Inactivated	In progress	Earliest April
Sinovac	SARS-CoV-2 Vaccine (Vero Cell), Inactivated	Inactivated	Additional submission required	Earliest April
Moderna	mRNA-1273	mRNA	In progress	Earliest April
Johnson & Johnson	Ad26.COV2.S	Adenoviral vector	Final decision made	Authorised 12/03/21
The Gamaleya National Center	Sputnik V	Adenoviral vector	Clinical review ongoing	Will be determined when chemistry, manufacturing and control data are submitted
CanSinoBIO	Ad5-nCoV	Adenoviral vector	Rolling data assessment to start in April 2021	-
Novavax	NVX-CoV2373	Protein subunit	Expression of interest submitted 23/02/21. Pre-submission meetings required prior to commencing assessment	-

Source: WHO Guidance Document: Status of COVID-19 Vaccines within WHO EUL/PQ evaluation process (17th March 2021)

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Murdoch Children's Research Institute
50 Flemington Rd, Parkville
Victoria 3052 Australia
ABN 21 006 566 972

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The University of Melbourne

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Compiled by Dr John Hart

Technical leads: Professor Fiona Russell and Professor Kim Mulholland

Quality checks: Professor Julie Bines, Associate Professor Nigel Crawford and Associate Professor Margie Danchin

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