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. This 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

- COVID-19 vaccine efficacy results from different trials cannot be directly compared against each other. They must be interpreted in the context of study designs (including case definitions, clinical endpoints, access to testing), target populations, and COVID-19 epidemiologic conditions (including circulation of variants of concern)
- 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 have high vaccine effectiveness against the Delta variant and both vaccines are similarly effective against transmission in the UK. Sinovac has shown high vaccine effectiveness in Chile where the Gamma and Alpha variants are circulating. Sinopharm has shown high vaccine effectiveness in Bahrain and several vaccines have shown effectiveness against mortality in infected adults in Bahrain: Unvaccinated: 1.32% mortality (857 deaths); Sinopharm: 0.46% (112 deaths); Pfizer/BioNTech: 0.15% (3 deaths); Sputnik: 0.09 (3 deaths); AstraZeneca: 0.03% (1 death).[1] The Johnson & Johnson and Moderna vaccines have both shown good vaccine effectiveness against infection in the US. One or 2 doses of the Moderna vaccine is effective against the Alpha variant in Canada, and a single dose is effective against infection and very effective against severe disease with the Delta variant.
- The US FDA, UK MHRA, EU EMA, NZ Medsafe, Health Canada and the Australian TGA have authorised the Pfizer/BioNTech vaccine for emergency use in adolescents aged 12-15 years.[2–6] The EMA, MHRA and TGA have also authorised the Moderna vaccine in this age group.[7–9]
- Mixed vaccine schedules (i.e. delivering different types of vaccine for the first and second dose) are under investigation as these could facilitate better protection against variants of concern and enable vaccination programs to continue if a particular vaccine is unavailable
- Seven intranasal vaccines are in development (6 live-attenuated viruses or virus-vectored vaccines; 1 protein subunit.[10] These may be beneficial in preventing transmission (Page 15)
- A very rare clotting disorder with low platelets (Thrombosis with Thrombocytopaenia Syndrome – TTS) has been associated with the AstraZeneca and Johnson & Johnson vaccines.[11–13] The majority of cases fully recover with adequate treatment. The risk following the first dose of AstraZeneca vaccine has been estimated by the EMA as 1 in 100,000 and by the Australian Technical Advisory Group on Immunisation (ATAGI) as 1 in 50,000.[14,15] Risk of TTS is much lower following the *second* dose of AstraZeneca vaccine: estimate in the UK is 1 in 1.5 million second doses.[16]
- The risk of TTS following the first dose of Johnson & Johnson vaccine has been estimated as 1 in 319,000 in the USA[17]
- The risk of myocarditis/pericarditis is increased following the second dose of Pfizer/BioNTech and Moderna vaccines, particularly in younger males, occurring in >1 in 20,000 males under 25 years of age.[18] Highest rate in in males 16-17 years of age following Pfizer/BioNTech vaccine but no clear difference in risk between Moderna and Pfizer/BioNTech.[19] There is a small increase in risk of myocarditis in females <30 and males >50 years of age.
- Appropriate communication on the benefit-risk profile of COVID-19 vaccines (Page 14) remains crucial to maintain confidence in immunisation programmes and to avoid vaccine hesitancy.

New updates

Key updates include *(also highlighted in yellow text in the document)*:

- Efficacy of Pfizer/BioNTech vaccine over 6 months from a multi-country study (Pages 5, 8 and 25):
  - Infection: 91.3% (89.0-93.2)
  - Infection 7 days to 2 months after second dose: 96.2% (93.3-98.1)
  - Infection after 2-4 months: 96.2% (93.3-98.1)
  - Infection after 4-6 months: 83.7% (74.7-89.9)
  - Infection ≥75 years: 96.2% (76.9-99.9)
  - Severe disease: 96.7% (80.3-99.9)
- Effectiveness against hospitalisation in Scotland, including in those classified as severely clinically vulnerable (high risk) (Pages 6, 8, 23, and 25):
  - Pfizer/BioNTech and Moderna (low risk): 92% (85-99)
  - Pfizer/BioNTech and Moderna (high risk): 72% (51-84)
  - AstraZeneca (low risk): 94% (90-99)
  - AstraZeneca (high risk): 63% (46-75)
- Effectiveness against hospitalisation and death from the Delta variant in Scotland (effectiveness declined rapidly in the first two months after the second dose but more slowly thereafter and remained high) (Pages 6, 8 and 24):
  - Pfizer/BioNTech and Moderna: 91% (88-93)
  - AstraZeneca: 88% (85-90)
- Effectiveness of Pfizer/BioNTech, Moderna and Johnson & Johnson vaccines against hospitalisation in USA:
  - 86% (82-89)
- Effectiveness of Johnson & Johnson vaccine in USA (Pages 6, 7, 23 and 24):
  - Infection: 79% (77-80)
  - Infection (Delta predominance): 78% (73-82)
  - Hospitalisation: 81% (79-84)
  - Hospitalisation (Delta predominance): 85% (73-91)
- Pfizer/BioNTech vaccine trial in children aged 5-11 years in USA from a press release (Page 9):
  - Antibody response following a two-dose regimen of 10 µg (one third of the adult dose) comparable to that in 16-25 year-olds receiving the full dose
  - Safety profile for reactogenicity similar to in 16-25 year-olds
- An expert panel convened in the UK reached consensus on the following vaccine effectiveness estimates based on available data:
  - Infection with Alpha:
    - AZ (single dose): ~60%
    - AZ (2 doses): ~80%
    - PF (single dose): ~60%
    - PF (2 doses): ~85%
  - Infection with Delta:
    - AZ (single dose): ~40%
    - AZ (2 doses): ~65%
    - PF (single dose): ~55%
    - PF (2 doses): ~75%
  - Severe disease with either Alpha or Delta:
    - AZ or PF (single dose): ~85%
    - AZ or PF (2 doses): ~95%

COVID-19 Vaccine Specifications

	ASTRAZENECA	GAMALEYA	JOHNSON & JOHNSON	MODERNA	NOVAVAX	PFIZER/BIONTECH	SINOVAC	SINOPHARM	BHARAT BIOTECH
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	Inactivated virus	Inactivated virus
Available Through COVAX	✓	-	✓	-	✓	✓	-	-	-
Doses Required	8-12 weeks apart* 4-12 weeks apart (Product Information)	3 weeks apart	1	4 weeks apart*	3 weeks apart	3-4 weeks apart*	2-4 weeks apart*	3-4 weeks apart*	3 weeks apart
Shipping, Storage & Presentation	Normal cold chain requirements (2-8°C); 10-dose vials	-18.5°C (liquid form); 2-8°C (dry form)	Shipped at -20°C; 2-8°C for up to 3 months; 5-dose vials	-25°C to -15°C; 10-dose vials	2-8°C; 10-dose vials	-80°C to -60°C; 2-8°C for up to 1 month; 6-dose vials	2-8°C; Single-dose vials	2-8°C; Single-dose vials/ pre-filled syringes	2-8°C; 10-dose or 20-dose vials
Approval by a Stringent Regulatory Authority (SRA)	WHO EUL, EMA, TGA, MHRA	Under review by WHO SAGE	WHO EUL, EMA, FDA, MHRA	WHO EUL, EMA, FDA, TGA	Under review by WHO SAGE	WHO EUL, EMA, FDA, TGA, MHRA	WHO EUL	WHO EUL	-

*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 (US)
TGA: Therapeutic Goods Administration (Australia)
MHRA: Medicines and Healthcare Products Regulatory Agency

COVID-19 Vaccine Efficacy

VACCINE	VACCINE EFFICACY			
	SYMPTOMATIC INFECTION	MODERATE-SEVERE	SEVERE	HOSPITALISATION/DEATH
AstraZeneca	UK: 66.7% (57.4-74.0)[20] USA, Chile, Peru: 76%[21] (not peer-reviewed) Single dose in UK (22-90 days post-vaccination): 76.0% (59.3 to 85.9)[20] Efficacy with different interval between doses in UK: 12+ weeks: 82.4% (2.7-91.7) <6 weeks: 54.9% (32.7-69.7)[20]	-	Severe/critical and hospitalisation in USA, Chile, Peru: 100%[21] (not peer-reviewed) UK: 100% (15 cases in the placebo group)[20]	Hospitalisation in UK: 100% (9 cases in placebo group)[20]
Gamaleya	Russia: 91.6% (85.6–95.2)[22] SInlge dose (Sputnik Light) in Argentina: 78.6%[23]	Moderate-severe: 100% (20 cases in the placebo group)[22]	-	-
Johnson & Johnson	-	Moderate to severe/critical: All sites: 66.1% (55.0-74.8) USA: 72.0% (58.2-81.7) Latin America: 61.0% (46.9-71.8) South Africa: 64.0% (41.2-78.7)[24,25] South Africa: 67-71%[26]	85.4% (54.2-96.9)[25]	100% (5 deaths in placebo group)[25] Death in South Africa: 96%[26]
Moderna	USA: 94.1% (89.3-96.8)[27] USA: >90%[28] Efficacy in USA: 12-17 years: Symptomatic: 92.7% (67.8-99.2) Infection: 69.8% (49.9-82.1) Asymptomatic infection: 59.5% (28.4-77.3)[29]	-	USA: 100% (30 cases in placebo group)[27] US: >95%[28]	USA: 100% (1 death in placebo group)[27]
Novavax	UK: 89.7% (80.2-94.6)[30] US and Mexico: 90.4% (82.9-94.6)[31]	US and Mexico: 100% (87.0-100)[31]	-	-
Pfizer/BioNTech	Argentina, Brazil, Germany, South Africa, Turkey and the USA: 94.6% (89.9–97.3)[32] Infection over 6 months: 91.3% (89.0-93.2)[33]	-	Argentina, Brazil, Germany, South Africa, Turkey and the USA: 88.9% (20.1–99.7)[32] Severe disease: 96.7% (80.3-99.9)[33]	-
Sinovac	Brazil: 50.7% (35.9-62.0) Chile: 67% (65-69) Indonesia: 65% (20-85)[34] Turkey: 83·5% (65·4-92·1)[35]	Requiring medical assistance in Brazil: 83.7% (58.0-93.7) Moderate-severe: 100% (56.4-100.0)[36]	-	Hospitalisation: Brazil: 100% (56-100) Chile: 85% (83-97) Turkey: 100% (20-100)[34]
Sinopharm	UAE, Bahrain, Egypt and Jordan: 78.1% (64.9-86.3)[34]	-	-	Hospitalisation in UAE, Bahrain, Egypt and Jordan: 78.7% (26.0-93.9)[34]
Bharat Biotech	India: 77.8% (65.2-86.4)[37]	-	India: 93.4% (57.1-99.8)[37]	-

Vaccine Effectiveness Summary at-a-glance

Detailed summary available in Appendix 1.

VACCINE	ANY INFECTION	SYMPTOMATIC INFECTION	HOSPITALISATION/ SEVERE DISEASE	DEATH
AstraZeneca	60-67%[38–40] Single dose 30-67%[38,40–42]	67-78%[43–45] Single dose: 50-68%[42,43,46]	88-100%[44,45,47–49] Single dose: 71-94%[42,49,50]	94-100%[44,45]
Johnson & Johnson	77-79%[51,52]	-	71-85%[26,52]	-
Moderna	76-87%[53,54] Single dose: 72%[41]	88-95%[45,54,55] Single dose: 72%[55,56]	92-98%[45,53,54] Single dose: 96%[41]	98%[54]
Pfizer/BioNTech	63-95%[38,39,42,53,57–63] Single dose: 36-57%[38,40,41]	82-97%[42–45,55,59,63–65] Single dose: 49-61%[43,55,56]	85-98%[42,44,45,49,53,59,60,63,64,66,67] Single dose: 85-94%[49,50]	91-100%[44,45,59,60,63,66,67]
Sinovac	60%[67]	59[44]	86-91%[44,67]	86-95%[44,67]
Sinopharm	-	90%[34]	-	-
Bharat Biotech	Efficacy: 65.2%[37]			

Vaccine Efficacy/Effectiveness Against Delta VOC at-a-glance

Detailed summary and vaccine efficacy against other variants available in Appendix 2

VACCINE	LAB STUDIES	VACCINE EFFECTIVENESS UNLESS OTHERWISE STATED		
		ANY INFECTION	SYMPTOMATIC INFECTION	HOSPITALISATION AND DEATH
AstraZeneca	✓	60-67%[38–40] Single dose 30-67%[38,40,41]	67%[45]	88-94%[45,48,49] Single dose: 71-88%[41,49]
Gamaleya	✓	-	-	-
Johnson & Johnson	✓	78%[52]	-	71-85%[26,52]
Moderna	✓	76%[53] Single dose: 72%[41]	95%[45]	81-98%[45,53] Single dose: 96%[41]
Pfizer/BioNTech	✓	39-88%[38,39,53,57] Single dose: 36-57%[38,40,41]	90%[45]	75-100%[45,49,53,57] Single dose: 78-94%[41,49]
Bharat Biotech	✓	Efficacy: 65.2%[37]	-	-

Vaccine Efficacy/Effectiveness in High-Risk Groups at-a-glance

Detailed summary available in Appendix 3

VACCINE	VACCINE EFFICACY/EFFECTIVENESS			
	DIABETES	OBESITY	AT RISK FOR SEVERE COVID-19	ELDERLY*
AstraZeneca	-	-	Effectiveness of single dose against: Symptomatic infection: 60%[43] Efficacy against symptomatic infection: 76%[21] Effectiveness against symptomatic infection: 80%[43] Effectiveness against hospitalisation: 63%[47]	Effectiveness of single dose against: Symptomatic infection: 53-61%[42,43] Hospitalisation: 80%[68] Death: 83%[56] Efficacy against infection: 85%[21] Effectiveness against: Symptomatic infection: 59-76%[43,45,69] Hospitalisation: 37-73%[69,70] Death: 94%[56]
Gamaleya	-	-	-	Symptomatic infection: 92%[22]
Johnson & Johnson	Efficacy: 23%[24]	Efficacy: 66%[24]	Efficacy: 59%[24]	Efficacy 66%[24]
Moderna	-	-	Efficacy against symptomatic infection: 91%[27]	Efficacy against symptomatic infection: 86%[27] Effectiveness against infection: 83%[54]
Pfizer/BioNTech	Effectiveness against infection: 82%[58] 89%[66]	Effectiveness against infection: 90%[66]	Effectiveness of single dose against symptomatic infection: 56%[43] Efficacy against symptomatic infection: 95%[32] Effectiveness against: Infection: 71-90%[60,66] Symptomatic infection: 89%[43] Hospitalisation: 72-81%[60]	Effectiveness of single dose against: Infection: 76%[42] Symptomatic infection: 40-56%[43,55] Hospitalisation: 71-81%[68,70] Death 77%[56] Efficacy against symptomatic infection: 95-100%[32,33] Effectiveness against: Infection: 70-89%[58,60,66,71] Smptomatic infection: 61-93%[43,45,55,69] Hospitalisation: 43-93%[69–71] Death: 98%[56]
Novavax			Efficacy against infection: 91%[31]	
Sinovac	-	75%[34]	49%[34]	-
Sinopharm	-	81%[34]	-	Effectiveness against symptomatic infection 91%[34]
Bharat Biotech	-	-	Efficacy against infection: 66%[37]	Efficacy against symptomatic infection: 68%[37]

*Estimates in those ≥60 years to ≥80 years

Vaccine Efficacy/Effectiveness in Children

VACCINE	VACCINE EFFICACY/EFFECTIVENESS	COUNTRIES VACCINATING CHILDREN BY AGE GROUP
AstraZeneca	Trials suspended when evidence emerged of the higher risk of TTS in younger adults compared to older adults	-
Gamaleya	-	-
Johnson & Johnson	-	-
Moderna	Efficacy in USA, 12-15 years: 96%[72]	Authorised in those aged ≥12 years by EMA and MHRA France, Italy: ≥12 years
Pfizer/BioNTech	Efficacy in USA, 12-15 years: 100%[73] 5-11 years: Antibody response and safety profile for reactogenicity similar to 16-25 year-olds[74]	Authorised in those aged ≥12 years by EMA, FDA, TGA, Medsafe UK, Sweden: 16-17 years and high-risk groups ≥12 years US, Canada, France, Spain, Italy, Netherlands, Germany, Singapore, Australia: ≥12 years The UK Chief Medical Officers have advised the government to offer a single dose to all 12-15 year olds[75]
Novavax	Study in 12-18 years has started recruitment and study in birth-11 years is planned	-
Sinovac	Phase I/II studies complete in 3-17 year olds in China[76]; efficacy studies underway	Indonesia: ≥12 years China: ≥3 years
Sinopharm	Phase I/II studies in 3-17 year olds in China	China: ≥3 years
Bharat Biotech	-	-

Vaccine Efficacy/Effectiveness Against Transmission

There are limitations related to the analysis and comparison of transmission data between studies and vaccines. Criteria for testing vary between studies and may include, for example, random testing, testing at defined intervals, or retrospective serology.

VACCINE	EFFICACY/EFFECTIVENESS AGAINST ASYMPTOMATIC INFECTION	OTHER OUTCOMES
AstraZeneca	EFFICACY (UK only): 22·2% (−9·9-45·0); Symptomatic and asymptomatic combined (UK, SOUTH AFRICA & BRAZIL): 54.1% (44.7-61.9)[20] ENGLAND: Hazard ratio for single dose in vaccinated vs. unvaccinated care facility residents: 0.32 (0.15-0.66)[77]; Odds ratio for household contacts of vaccinated vs non-vaccinated health workers testing positive: 0.52 (0.43-0.62)[78] UK: Regular testing of randomly selected households: 79% (65-88)[79]; Single dose against symptomatic and asymptomatic infection: 60% (49–68)[80] NETHERLANDS: Effectiveness against transmission (secondary attack rate among household contacts): 58% (−12-84)[81]	SCOTLAND: POOLED ANALYSIS OF PFIZER/BIONTECH AND ASTRAZENECA: Hazard ratio for household contacts of vaccinated vs non-vaccinated health workers testing positive: 0.70 (0.63-0.78)[82]
Johnson & Johnson	EFFICACY (multiple countries): Asymptomatic infection: 59.7% (32.8-76.6)[24] UK: Single dose against symptomatic and asymptomatic infection: 60% (49–68)[80] Netherlands: Effectiveness against transmission (secondary attack rate among household contacts): 77% (6-94)[81]	USA (Kentucky): OR for reinfection in unvaccinated vs vaccinated with Johnson & Johnson, Moderna or Pfizer/BioNTech): 2.34 (1.58–3.47)[83]
Moderna	USA: Asymptomatic infection: 72.7% (53.4-84.0)[54] USA: POOLED ANALYSIS OF PFIZER/BIONTECH AND MODERNA: 88.7% (68.4-97.1)[84]; 90% (68%-97)[85]; single dose: 80% (59-90)[85]; Relative risk of infection in asymptomatic pre-surgical patients >10 days after first dose compared to unvaccinated residents: 0.21 (0.12-0.37)[86]; Incident cases in unvaccinated nursing home residents decreased from 4.3% within 14 days of the first vaccination clinic to 0.3% after 42 days[87] MODELLING: Reduced potential for transmission: at least 61%[88] UK: Single dose against symptomatic and asymptomatic infection: 60% (49–68)[80] Netherlands: Effectiveness against transmission (secondary attack rate among household contacts): 88% (50-97)[81]	USA (Kentucky): OR for reinfection in unvaccinated vs vaccinated with Johnson & Johnson, Moderna or Pfizer/BioNTech): 2.34 (1.58–3.47)[83]
Pfizer/BioNTech	ENGLAND: 86% (76-97) 7 days after 2 doses; 72% (58-86) 21 days after 1 dose[89] ISRAEL: 92% (88-95)[64]; 91.5% (90.7-92.2)[59]; 65% (45-79%)[90]; single dose: 75% (72-84)[91]; Effectiveness against transmission: 88.5% (82.3-94.8)[92]; Effectiveness against infection in the household: 78% (30-94)[93] USA: Asymptomatic screening: 90% (78-96)[65] USA: POOLED ANALYSIS OF PFIZER/BIONTECH AND MODERNA: 88.7% (68.4-97.1)[84]; 90% (68%-97)[85]; single dose: 80% (59-90)[85]; Relative risk of infection in asymptomatic pre-surgical patients >10 days after first dose compared to unvaccinated residents: 0.21 (0.12-0.37)[86]; Incident cases in unvaccinated nursing home residents decreased from 4.3% within 14 days of the first vaccination clinic to 0.3% after 42 days[87] UK: single dose: 4-fold decrease in risk amongst HCWs ≥12 days post-vaccination[94]; Regular testing of randomly selected households: 80% (73-85)[79]; Single dose against symptomatic and asymptomatic infection: 72% (63–79)[80]; 60% (49–68)[80] FINLAND: Effectiveness against transmission to unvaccinated household contacts: 2 weeks after first dose: 8.7% (-28.9-35.4); 10 weeks after first dose: 42.9% (22.3-58.1)[95] Netherlands: Effectiveness against transmission (secondary attack rate among household contacts): 70% (61-77)[81] Finland: Effectiveness against transmission to unvaccinated household contacts of vaccinated cases: 42.9% (22.3-58.1)[95]	ISRAEL: Lower viral load in vaccine failure cases 12-37 days after the first dose of vaccine compared to within the first 11 days, indicating potentially lower infectiousness[96]; Data from 223 communities: strong correlation between community vaccination rate and a later decline in infection among children under 16 years of age who were unvaccinated[97]; Substantially decreased viral load for infections occurring 12-37 days after the first dose of vaccine, indicating likely lower infectiousness[96] Detectable transmission in long-term care facilities in Spain reduced by 90% (76-93)[98] ENGLAND: Odds ratio for household contacts of vaccinated health workers vs non-vaccinated health workers testing positive: 0.54 (0.47-0.62)[78] SCOTLAND: POOLED ANALYSIS OF PFIZER/BIONTECH AND ASTRAZENECA: Hazard ratio for single dose in vaccinated vs. unvaccinated care facility residents: 0.35 (0.17-0.71)[77] USA (Kentucky): OR for reinfection in unvaccinated vs vaccinated with Johnson & Johnson, Moderna or Pfizer/BioNTech): 2.34 (1.58–3.47)[83]
Bharat Biotech	EFFICACY IN INDIA: Asymptomatic: 63.6% (29.0-82.4); Symptomatic and asymptomatic combined: 68.8% (46.7-82.5)[37]	-

* Nationwide vaccination program including Pfizer/BioNTech, Moderna and Johnson & Johnson vaccines

Mixed Dose Vaccine Safety and Immune Responses

Mixed vaccine schedules (i.e. delivering different types of vaccine for the first and second dose) could be particularly useful to facilitate better protection against variants of concern and enable vaccination programs to continue if a particular vaccine is unavailable.

SCHEDULE	SAFETY	IMMUNE RESPONSES OR EFFECTIVENESS	COUNTRIES USING SCHEDULE
AstraZeneca followed by Pfizer/BioNTech	Spain: Similar side effects to those receiving 2 doses of the same vaccine; no safety concerns (not peer reviewed)[99] UK: Greater systemic side effects (mild-moderate symptoms) following the booster dose than with 2 doses of the same vaccine; no safety concerns[100] Germany: greater reactogenicity with first dose of AstraZeneca than with the Pfizer/BioNTech booster[101] Increased reactogenicity (54.4%; 49.4-59.5) vs AstraZeneca-AstraZeneca (33.5%; 28.0-39.2)[102] Total adverse event reporting in Korea: 0.28% (vs AZ-AZ: 0.22%; and PF-PF: 0.31%)	Spain: ≥8 week dose interval: Stronger immune response following Pfizer/BioNTech than after 2 doses of AstraZeneca vaccine (not peer reviewed)[99] Spain: 8-12 week dose interval: robust antibody response[103] UK: 4 week dose interval: stronger antibody and cellular response than after 2 doses of AstraZeneca vaccine[104] Germany: 9-12 week dose interval: Significantly stronger immune response following Pfizer/BioNTech booster than AstraZeneca, and slightly stronger than after 2 doses of Pfizer/BioNTech (not peer reviewed)[105] Germany: 4-fold greater immune response than 2 doses of AstraZeneca[106] South Korea: 6-fold greater neutralising antibody response than 2 doses of AstraZeneca Germany: Higher neutralising antibody response against wild-type, Alpha, Beta, Gamma and Delta variants than AZ-AZ[107]	Canada, Denmark, Finland, France, Germany, Sweden, Norway, Spain and South Korea[108]
Pfizer/BioNTech followed by AstraZeneca	UK: Greater systemic side effects (mild-moderate symptoms) following the booster dose than with 2 doses of the same vaccine; no safety concerns[100] Greater reactogenicity with first of homologous and heterologous prime-boost immunisation with BNT162b2 and ChAdOx1-nCoV19: a prospective cohort study increased reactogenicity (55.2%; 46.1-64.1) vs Pfizer/BioNTech-Pfizer/BioNTech (33.3%; 23.4-44.5)[102]	UK: 4 week dose interval: weaker antibody response than after 2 doses of Pfizer/BioNTech vaccine (but stronger than after 2 doses of AstraZeneca vaccine)[104]	-
Pfizer/BioNTech or Johnson & Johnson followed by Moderna	-	USA: Trial underway with 12-20 week dose interval[109]	-
AstraZeneca, Moderna and Pfizer/BioNTech	-	Canada: Trial underway mixing and matching all three vaccines with study arms assessing 4 week and 16 week dose intervals[110] Denmark: Vaccine effectiveness against infection: AZ-PF or AZ-MO: 88% (83-92)[111]	AstraZeneca followed by either Moderna or Pfizer/BioNTech: Denmark, Finland, France, Germany, Sweden, Norway and Spain[108]
Sinovac followed by AstraZeneca	-	-	Thailand

Adverse Events Following Immunisation with WHO EUL Vaccines

Adverse events following immunisation (AEFIs) are any reactions occurring after immunisation. They can be either expected or unexpected. The vaccine may not actually cause the AEFI; it may occur coincidentally as millions of people are being vaccinated so some people may get sick after vaccination but this does not necessarily mean that it is due to the vaccine. Special investigations determine whether they are due to the vaccine. Adverse events of special interest (AESIs) are of scientific and medical concern that are found through active surveillance, that have the potential to be causally associated with a vaccine and that need to be carefully monitored and confirmed by further special studies.

For all injectable vaccines, appropriate medical treatment and supervision should always be readily available in case of an anaphylactic event following administration.

	ASTRAZENECA	MODERNA	PFIZER/BIONTECH	JOHNSON & JOHNSON	SINOPHARM	SINOVAC
Adverse events following immunisation (AEFIs)*	Very common (more than 1 in 10 people): headache, nausea, muscle pain, joint pain, injection site tenderness/ pain/ warmth/ itch, fatigue, malaise, fever, chills Common (between 1 in 10 and 1 in 100 people): injection site swelling/ redness[112]	Injection site pain (92%)/ swelling (15%)/ redness (10%), fatigue (70%), headache (65%), muscle pain (62%), joint pain (46%), fever (16%), chills (45%), nausea/vomiting (23%), axillary swelling/tenderness (20%)[113]	Very common: headache, muscle pain, joint pain, injection site pain/ swelling, fatigue, fever, chills; Common: nausea, injection site redness[112] Uncommon (between 1 in 100 and 1 in 1000 people): lymphadenopathy, insomnia, pain in extremity of vaccinated arm, malaise, injection site itch; Rare: (between 1 in 1000 and 1 in 10,000): acute peripheral facial paralysis[6]	Injection site pain/ redness/ swelling, headache, fatigue, muscle pain, nausea, fever[114]	Injection site pain (16%)/ itch (1%)/ swelling (2%)/ redness (1%), fever (4%), fatigue (3%), nausea (1%), headache (1%), diarrhoea (1%), muscle pain (<1%), itch (non-injection site) (1%)[115]	Fatigue (8.3%), fever (3.3%), diarrhoea (0.8%), nausea (1.7%), headache (2.5%), muscle pain (1.7%), injection site pain (10.0%)/ redness (0%)/ swelling (0%)[116]
Adverse events of special interest (AESIs)	Thrombosis with thrombocytopaenia syndrome (TTS) (see page 13 for estimated risk); EMA PRAC: Guillain-Barre syndrome (GBS)[117] Australia: Guillain-Barre syndrome: 52 cases (10.4 per million doses)[118]	USA: Myocarditis/pericarditis: 40.6 males and 4.2 females aged 12-29 years per million second doses of mRNA vaccine; and 2.4 males and 1.0 females aged 30+;[119] >1 in 20,000 males under 25 years of age[18] Immune thrombocytopaenia (ITP)**[120]	USA: Myocarditis/pericarditis: 40.6 males and 4.2 females aged 12-29 years per million second doses of mRNA vaccine; and 2.4 males and 1.0 females aged 30+;[119] >1 in 20,000 males under 25 years of age[18] Israel: 1 to 5 cases of myocarditis per 100,000 persons[121,122] ITP**[120]	TTS (see page 14 for estimated risk) USA: Guillain-Barre Syndrome: 100 preliminary reports of GBS following 12.5 million doses of vaccine administered (mostly males >50 years)[123]	-	-

*Details for AstraZeneca, Moderna, Pfizer/BioNTech and Johnson & Johnson from product information sheets in SRA countries, based on data from clinical trials; Sinopharm and Sinovac details from published clinical trials
**The ITP cases are mostly without the thrombotic events characteristic of TTS

Serious Adverse Events

Caution is required when comparing safety profiles as definitions and reporting systems vary in trials and in particular phase IV studies.

VACCINE	VACCINE SAFETY
AstraZeneca	108 SAEs in 12,282 (0.9%) vaccine recipients and 127 in 11,962 (1.1%) placebo recipients; 7 deaths all considered unrelated to vaccination (2 vaccine, 5 placebo)[20] US Phase III study: No serious safety concerns involving 32,449 participants[21] (not peer-reviewed) EMA investigation: possible link between the AstraZeneca vaccine and Thrombosis with Thrombocytopaenia Syndrome (TTS) Blood clots affected the brain (central venous sinus thrombosis, CVST) and abdomen (splanchnic vein thrombosis) There have been reports of 169 cases of CVST and 53 cases of splanchnic vein thrombosis in ~34 million vaccinated people in Europe The EMA confirmed the overall benefits of the vaccine in preventing COVID-19 outweigh the risks of side effects[12] UK: Risk factors for death in patients with TTS following the AstraZeneca vaccine: baseline platelet count; and intracranial haemorrhage[124] TTS reported to occur in ~1 in 50,000 vaccinated adults in Australia[15] Several countries introduced age recommendations for the vaccine: >60 years in Germany and Australia; >55 years in France and Canada; >40 years in the UK[125–127] EMA has started a review of reports of capillary leak syndrome following 5 cases of this very rare disorder post vaccination[128] WHO GACVS reports Guillain Barre Syndrome (GBS) rates following adenovirus vector vaccines: EU/EEA: 4.4; AUS: 9.7; KOR: 0.4; PHL: <1[129]
Gamaleya	45 SAEs in 16,427 (0.3%) vaccine recipients and 23 in 5,435 (0.4%) placebo recipients; 4 deaths all considered unrelated to vaccination (3 vaccine, 1 placebo)[22]
Johnson & Johnson	83 SAEs in 21,895 (0.4%) vaccine recipients and 96 in 21,888 placebo recipients (0.4%); 19 deaths all considered unrelated to vaccination (3 vaccine, 16 placebo)[24] EMA investigation of 8 reports of TTS. Most cases occurred in women <60 years of age but specific risk factors have not been confirmed[13] The CDC and FDA have now recommenced the vaccination program in the USA following a thorough safety review[130] 15 cases of TTS have been reported in 7.98 million people vaccinated in USA[11] Guillain-Barre Syndrome: 100 preliminary reports of GBS following 12.5 million doses of vaccine administered in USA (mostly males >50 years)[123] WHO GACVS reports Guillain Barre Syndrome (GBS) rates following adenovirus vector vaccines: USA: 7.8; KOR: 0.9; EU/EEA: AZ: 2.1[129]
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)[27] Anaphylaxis reported in the US at a rate of 2.5 per million doses[131] No obvious safety signals among pregnant women who received mRNA COVID-19 vaccines in USA[132] USA: Myopericarditis highest in males 18-34 years: 37.7 cases per million doses[19] USA: Myo/pericarditis reported in 40.6 males and 4.2 females aged 12-29 years per million second doses of mRNA vaccine; and 2.4 males and 1.0 females aged 30+[119]
Novavax	SAEs at low levels and similar between vaccine and placebo groups[133]
Pfizer/BioNTech	SAEs and deaths were low and comparable between vaccine and placebo groups (total 37,586 participants)[32] Anaphylaxis reported in the US at a rate of 4.7 per million doses[131] No obvious safety signals among pregnant women who received mRNA COVID-19 vaccines in USA[132] USA: Myopericarditis highest in males 16-17 years: 71.5 cases per million doses[19] USA: Myopericarditis reported in 40.6 males and 4.2 females aged 12-29 years per million second doses of mRNA vaccine; and 2.4 males and 1.0 females aged 30+[119] Brazil: SAEs: 5.4/100,000 doses
Sinovac	Brazil: SAEs: 79.7/100,000 doses

Risk of Rare Unusual Blood Clotting with Low Blood Platelets (Thrombosis with Thrombocytopaenia Syndrome – TTS)

Estimated number of TTS that potentially might occur in Pacific Island Countries if all adults received the AstraZeneca or Johnson & Johnson vaccines, based on most recent official estimate of the adult population in each country and the incidence of these events in Europe and Australia.

COUNTRY	TOTAL POPULATION	ESTIMATED POPULATION AGED 18 YEARS AND OVER*	POTENTIAL NUMBER OF TTS CASES IF ALL ADULTS IN EACH COUNTRY RECEIVED ASTRAZENECA VACCINE**	POTENTIAL NUMBER OF TTS CASES IF ALL ADULTS IN EACH COUNTRY RECEIVED JOHNSON & JOHNSON VACCINE***
American Samoa	55,519	33,311	<1	<1
Cook Islands	15,300	9,180	<1	<1
Federated States of Micronesia	102,300	61,380	0.6-1.2	<1
Fiji	867,000	520,200	5.2-10.4	1.6
French Polynesia	275,918	165,551	1.7-3.3	<1
Guam	159,358	95,615	1.0-1.9	<1
Kiribati	113,400	68,040	0.7-1.4	<1
Marshall Islands	54,900	32,940	<1	<1
Nauru	10,900	6,540	<1	<1
New Caledonia	271,407	162,844	1.6-3.3	<1
Niue	1,611	967	<1	<1
Northern Mariana Islands	53,883	32,330	<1	<1
Palau	18,000	10,800	<1	<1
Papua New Guinea	7,744,700	4,646,820	46.5-92.9	14.6
Samoa	195,979	117,587	1.2-2.4	<1
Solomon Islands	642,000	385,200	3.9-7.7	1.2
Tokelau	1,160	696	<1	<1
Tonga	99,419	59,651	0.6-1.2	<1
Tuvalu	10,507	6,304	<1	<1
Vanuatu	272,173	163,304	1.6-3.3	<1
Wallis and Futuna	11,558	6,935	<1	<1
All Pacific Island Countries	10,976,992	6,586,195	65.9-131.7	20.8

* Based on estimate of 60% of population aged ≥18 years[134]
** Based on estimates of TTS occurring in ~1 in 100,000 vaccinated adults by the European Medicines Agency and ~1 in 50,000 in Australia[14,15]
*** Based on estimates of TTS occurring in ~1 in 319,000 vaccinated adults in USA (may be an underestimate as only cerebral venous sinus thrombosis are reported)[17]

Who Can be Vaccinated Based on WHO SAGE Recommendations?

So far, WHO SAGE have made recommendations for use of AstraZeneca, Moderna, Pfizer/BioNTech, Johnson & Johnson and Sinopharm vaccines: https://www.who.int/groups/strategic-advisory-group-of-experts-on-immunization/covid-19-materials

	ASTRAZENECA	MODERNA	PFIZER/BIONTECH	JOHNSON & JOHNSON	SINOPHARM	SINOVAC
Minumum Age	18 years	18 years	12 years	18 years	18 years	18 years
Maximum Age (SAGE WHO)	None	None	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	Yes if high priority group & approved by health provider	Yes if high priority group & approved by health provider
Breastfeeding	Yes	Yes	Yes	Yes	Yes	Yes
Timing after previous SARS-CoV-2 infection	May delay 6 months; Within 90 days if VOCs associated with reduced effectiveness are circulating (e.g. Beta)	May delay 6 months; Within 90 days if VOCs associated with reduced effectiveness are circulating (e.g. Beta)	May delay 6 months; Within 90 days if VOCs associated with reduced effectiveness are circulating (e.g. Beta)	May delay 6 months; <6 months may be advisable if VOCs with reduced neutralisation activity are circulating	May delay 6 months; <6 months may be advisable if VOCs associated with reduced effectiveness are circulating	May delay 6 months; <6 months may be advisable if VOCs associated with reduced effectiveness are circulating
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	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)	Yes (unless the allergy is to the vaccine or its components)	Yes (unless the allergy is to the vaccine or its components)

Vaccine Development Pipeline

WHO has recommended that vaccines adopted by countries have WHO SAGE EUL and/or Stringent Regulatory Approval. Last updated 8 September 2021.

VACCINE TYPE	NUMBER OF VACCINE CANDIDATES AT EACH PHASE OF DEVELOPMENT				
	PRE-CLINICAL	PHASE I/II	PHASE III	PHASE IV	IN USE*
RNA	27	10	3	2	2 (Pfizer/BioNTech, Moderna)
DNA	17	7	3	0	1 (Zydus Cadila Healthcare Limited)
Vector (non-replicating)	27	7	2	3	4 (CanSino, Gamaleya, Johnson & Johnson, AstraZeneca)
Vector (replicating)	18	6	1	0	0
Inactivated	7	7	8	2	8 (Sinopharm/BIBP; Sinopharm/WIBP; Sinovac; Bharat; Chumakov; Research Instutute for Biological Safety Problems; Shenzhen Kangtai Biological Products; Shifa Pharmed)
Live-attenuated	2	1	0	0	0
Protein subunit	73	23	12	1	6 (Vector institute; Anhui Zhifei Longcom Biopharmaceutical Chinese Academy of sciences; Center for Genetic Engineering and Biotechnology; Instituto Finlay de Vacunas, Cuba [peptides 1 and 2]; Medigen Vaccine Biologics, Taiwan)
Virus-like particle	20	4	1	0	0
Other/unknown	32	5	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.

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	SK Bio: Authorised 15/02/21 EU nodes: Authorised 16/04/21 CSL, Australia: Authorised 09/07/21 Daiichi Sankyo, Japan: Authorised 09/07/21
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	Authorised: 07/05/2021
Sinovac	SARS-CoV-2 Vaccine (Vero Cell), Inactivated	Inactivated	In progress	Authorised 01/06/2021
Moderna	mRNA-1273	mRNA	In progress (to use abridged procedure relying on EMA)	Authorised 30/04/2021
Johnson & Johnson	Ad26.COV2.S	Adenoviral vector	Final decision made	Authorised 12/03/21
The Gamaleya National Center	Sputnik V	Adenoviral vector	On hold, awaiting completion of rolling submission	Will be determined when all data are submitted
CanSinoBIO	Ad5-nCoV	Adenoviral vector	Rolling data assessment started 9 August 2021	-
Novavax	NVX-CoV2373	Protein subunit	Pre-submission meeting held; rolling data starting in August 2021	-
CureVac	Zorecimeran	mRNA	Expression of interest accepted; Pre-submission meeting planned for Q4 2021	-
Bharat Biotech	Covaxin; BBV152	Inactivated	Rolling data assessment started 6 July 2021	-
Clover Biopharmaceuticals	SCB-2019 (CpG 1018/Alum)	Protein subunit	Pre-submission meeting being planned	-

Source: WHO Guidance Document: Status of COVID-19 Vaccines within WHO EUL/PQ evaluation process. Available at: https://www.who.int/teams/regulation-prequalification/eul/covid-19

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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

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Weekly COVID-19 Vaccine Updates
Number 27, 23 September 2021

Appendix 1: COVID-19 Vaccine Effectiveness

VACCINE	SEVERE / HOSPITALISATION / DEATH	INFECTION AND OTHER OUTCOMES
AstraZeneca	Single dose in Scotland: 94% (73-99)[50] Risk of death in vaccine failures compared to unvaccinated cases in England reduced by: 55% (41-66)[135] (not peer reviewed) Single dose against hospitalisation in Spain: 92% (46-99)[42] Pooled analysis of AstraZeneca, Pfizer/BioNTech and Moderna vaccines in Italy: Hospitalisation: 89% (85-91); Death: 93% (89-96)[136] Chile: Hospitalisation: 100%; ICU admission: 100%; Death: 100%[44] Scotland: Hospitalisation: 94% (90-99)[47]	Pooled analysis of Pfizer/BioNTech and AstraZeneca vaccines in elderly care home residents in UK: Reduction in risk of infection 4 weeks after-single dose: 56% Reduction in risk of infection 5 weeks after single dose: 62%[137] Pooled analysis of Pfizer/BioNTech and AstraZeneca vaccines: reduced odds of infection post-second dose: 70% (62-77)[138] Single dose in Spain: Any infection: 44% (31-54); Symptomatic infection: 50% (37-61)[42] Pooled analysis of AstraZeneca, Pfizer/BioNTech and Moderna vaccines in Italy: Infection: 78% (76-79)[136] Single dose against symptomatic infection in multiple European countries: 68% (39-83)[46] Symptomatic infection in 16-64 years in UK: single dose: 50.2% (40.8-58.2); 2 doses: 78.0% (69.7-84.0)[43] Symptomatic infection in Chile: 68.7% (39.8-83.7)[44]
Johnson & Johnson	USA: Hospitalisation: 81% (79-84)[52]	USA: Any infection: 76.7% (30.3-95.3)[51] USA: Infection: 79% (77-80)[52]
Moderna	Pooled analysis of AstraZeneca, Pfizer/BioNTech and Moderna in Italy: Hospitalisation: 89% (85-91); Death: 93% (89-96)[136] Pooled analysis of Pfizer/BioNTech and Moderna against hospitalisation: 2-12 weeks after second dose: 86% (82%-90%) 13-24 weeks after second dose: 84% (77%-90%)[139] USA: Hospitalisation: 95.8% (90.7-98.1); Death: 97.9% (66.9-99.9)[54] Pooled Pfizer/BioNTech and Moderna against hospitalisation in Scotland: 92% (85-99)[47]	Pooled analysis of Moderna and Pfizer/BioNTech vaccines in USA: Infections in nonvaccinated: 234 of 8969; 2.61% (2.29-2.96) Fully vaccinated: 4/8121; 0.05% (0.01-0.13)[140] Pooled analysis of Moderna and Pfizer/BioNTech vaccines against infection in USA: Fully vaccinated: 90% (68–97) Two weeks after first dose: 80% (59–90)[141] Pooled analysis of AstraZeneca, Pfizer/BioNTech and Moderna vaccines in Italy: Infection: 78% (76-79)[136] Single dose against symptomatic disease in the UK: Age 15-39 years: 72% (46-86)[56] Minnesota, USA: January to July 2021 (Delta variant <0.7% in May): Infection: 86% (81-91); Hospitalisation: 92% (81-97) July (Delta variant >70%): Infection: 76% (58-87); Hospitalisation: 81% (33-96)[53] Infection in USA (98% vaccines used Pfizer/BioNTech and Moderna): Pre-Delta variant predominant: 91% (81–96); Delta variant predominant: 66% (26–84)[142] Infection in Canada: 1 dose: 72% (63-80); 2 doses: 94% (86-97)[55] USA: Any infection: 87.4% (84.8-89.6); Symptomatic infection: 88.3% (86.1-90.2)[54]
Pfizer/BioNTech	Severe in Israel: 92% (75-100)[64] Severe/critical in Israel: 97.5% (97.1-97.8)[59] Single dose against hospitalisation in Scotland: 85% (76-91)[50] Risk of death in vaccine failures compared to unvaccinated cases in England reduced by: Single dose: 44% (32-53) Fully vaccinated: 69% (31-86)[135] (not peer reviewed) Israel: Hospitalisation: 97.2% (96.8-97.5); Death: 96.7% (96.0-97.3)[59] Hospitalisation in Spain: 94% (60-99)[42] Priority groups in Denmark: Hospitalisation: 93% (89-96); Death: 94% (90-96)[60] Pooled analysis of AstraZeneca, Pfizer/BioNTech and Moderna vaccines in Italy: Hospitalisation: 89% (85-91); Death: 93% (89-96)[136] USA care facility: Hospitalisation: 94.4 (73.9-98.8); Death 94.4 (44.6–99.4)[63] Uruguay: Hospitalisation: 97.8% (96.0-98.8); Death: 96.2 (95.4-96.8)[67] Israel: Hospitalisation: 93·4% (91·9-94·7); Death: 91·1% (86·5-94·1)[66] Chile: Hospitalisation: 97.2% (96.6-97.6); ICU admission: 98.3% (97.6-98.8); Death: 100%[44] Pooled analysis of Pfizer/BioNTech and Moderna against hospitalisation: 2-12 weeks after second dose: 86% (82%-90%) 13-24 weeks after second dose: 84% (77%-90%)[139] Pooled analysis of Moderna and Pfizer/BioNTech against hospitalisation or death: 98% (83-100)[55] Pooled Pfizer/BioNTech and Moderna against hospitalisation in Scotland: 92% (85-99)[47]	Pooled analysis of Moderna and Pfizer/BioNTech vaccines in USA: Infections in nonvaccinated: 234 of 8969; 2.61% (2.29-2.96) Fully vaccinated: 4/8121; 0.05% (0.01-0.13)[140] Pooled analysis of Moderna and Pfizer/BioNTech vaccines in USA: Fully vaccinated: 90% (68–97); Two weeks after first dose: 80% (59–90)[141] Symptomatic infection in Israel: 94% (87-98)[64] Any infection in Israel: 90% (79-95)[58] Israel: Any infection: 95.3% (94.9-95.7); Symptomatic infection: 97.0% (96.7-97.2)[59] Pooled analysis of Pfizer/BioNTech and AstraZeneca vaccines in elderly care home residents in UK: 4 weeks after first dose: 56%; 5 weeks after first dose: 62%[137] Documented infection in Israel: incidence decreased from 9.4 infections per 1,000 HCWs in the week following first dose to <1.0 infection per 1,000 HCWs per week from 1 week after the second dose[143] Pooled analysis of Pfizer/BioNTech and AstraZeneca vaccines: reduced odds of infection post-second dose: 70% (62-77)[138] Spain: Any infection: 65% (56-73); Symptomatic infection: 82% (73-88)[42] Infection in priority groups in Denmark: 82% (79-84)[60] USA: Symptomatic infection: 84% (75-90)[65] Denmark: Infection in care facility residents: >14 days after first dose:17% (4-28); >7 days after second dose: 64% (14-84)[61] USA: Single dose against infection in 2 care facilities: 63% (33-79)[62] A care facility in USA: Infection 66% (41-81); Symptomatic illness 87% (66-95)[63] Pooled analysis of AstraZeneca, Pfizer/BioNTech and Moderna vaccines in Italy: Infection: 78% (76-79)[136] Uruguay: Infection: 78.1% (77.0-79,1)[67] Israel: Infection: 93·0% (92·6-93·4)[66] Single dose against symptomatic disease in the UK: Age 15-39 years: 61% (56-66)[56] Symptomatic infection in multiple European countries: single dose: 61% (39-75); 2 doses: 87% (74-93)[46] Symptomatic infection in 16-64 years in UK: single dose: 48.6% (27.9-63.3); 2 doses: 93.3% (85.8-96.8)[43] Symptomatic infection in Chile: 87.7% (87.3-88.1)[44] Minnesota, USA: January to July 2021 (Delta variant <0.7% in May): Infection: 76% (69-81); Hospitalisation: 85% (73-93) July (Delta variant >70%): Infection: 42% (13-62); Hospitalisation: Hospitalisation: 75% (24-94)[53] Infection in USA (98% vaccines used Pfizer/BioNTech and Moderna): Pre-Delta variant predominant: 91% (81–96); Delta variant predominant: 66% (26–84)[142] Infection in Canada: 1 dose: 59% (55-62); 2 doses: 91% (88-93)[55]
Sinovac	Uruguay: Hospitalisation: 90.9% (88.6-92.7); Death: 94.7% (93.4-95.7)[67] Chile: Hospitalisation: 86.0% (85.6-86.5); ICU admission: 89.7% (89.1-90.2); Death: 86.4% (85.6-87.2)[44]	Uruguay: Infection: 59.9% (59.1-60.7)[67] Symptomatic infection in Chile: 58.5% (58.0-59.0)[44]
Sinopharm	-	Symptomatic infection in Bahrain: 90% (88-91)[34]

Appendix 2: Vaccine Efficacy/Effectiveness Against Variants

Refer to Appendix 1 for vaccine effectiveness results for the Pfizer/BioNTech vaccine in Scotland, England and Israel, where all locations had predominant B.1.1.7 circulation.
There are four Variants of Concern listed by WHO.[144] The WHO recommends labelling SARS-CoV-2 variants with letters of the Greek alphabet, as in the table below.[145]

VACCINE	VACCINE EFFICACY/EFFECTIVENESS (EFFECTIVENESS AGAINST INFECTION UNLESS SPECIFIED)			
	B.1.1.7 (ALPHA) VARIANT	B.1.351 (BETA) VARIANT	P.1 (GAMMA) VARIANT	B.1.617.2 (DELTA) VARIANT
AstraZeneca	UK: 70·4% (43·6-84·5) (vs. 81·5% (67·9-89·4) against wild variant)[146] England: ≥21 days after one dose: 48.7% (45.2-51.9); ≥14 days after two doses: 74.5% (68.4-79.4)[38] Scotland: 73% (66-78)[39] Canada: Single dose: 64% (60-68)[41] UK: Single dose: 63% (55-69); 2 doses: 79% (56-90)[40] Severe disease in Canada: Single dose: 85% (81-88)[41]	South Africa: 10.4% (−76.8 to 54.8)[147] Study against severe disease underway[24]	-	England: ≥21 days after one dose: 30.0% (24.3-35.3); ≥14 days after second dose: 67.0% (61.3-71.8)[38] Scotland: 60% (53-66)[39] Canada: Single dose: 67% (44-80)[41] UK: Single dose: 46% (35-55); 2 doses: 67% (62-71)[40] Symptomatic infection in England: 66.7% (66.3-67.0)[45] Hospitalisation in England: 1 dose: 71% (51-83); 2 doses: 92% (75-97)[45]; 93.9% (91.3-95.7)[45] Death in England: 94.1% (91.8-95.8)[45] Severe disease in Canada: Single dose: 88% (60-96)[41] Hospitalisation and death in Scotland: 88% (85-90)[48]
Johnson & Johnson	-	Moderate to severe/critical: 64.0% (41.2-78.7) Severe/critical: 81.7% (46.2-95.4)[24] Efficacy against hospitalisation in South Africa: 67%[26]	Moderate to severe/critical: 68.1% (48.8-80.7); Severe/critical: 87.6% (7.8-99.7)[24]	Efficacy against hospitalisation in South Africa: 71%[26] USA: Infection: 78% (73-82); Hospitalisation: 85% (73-91)[52]
Moderna	Canada: Single dose: 83% (80-86); 2 doses: 92% (86-96)[41] Severe disease in Canada: Single dose: 79% (74-83); 2 doses: 94% (89-97)[41]	-	-	Canada: Single dose: 72% (57-82)[41] Minnesota, USA: 76% (58-87)[53] England: 95.2% (94.4-95.9)[45] Severe disease in Canada: Single dose: 96% (72-99)[41] Severe disease in Minnesota: 81% (33-96)[53] Hospitalisation in England: 97.5% (82.3-99.7)[45] Pooled Pfizer/BioNTech and Moderna against hospitalisation and death in Scotland: 91% (88-93)[48]
Novavax	UK: 86.3% (71.3-93.5) (vs. 96.4% (73.8-99.5) against wild variant)[30]	South Africa: 51.0% (−0.6 to 76.2)[148]	-	
Pfizer/BioNTech	Case-control study in Israel: After one dose, vaccinees were disproportionally infected with B.1.1.7 (OR: 26:10) [149] Qatar: 89.5% (85.9-92.3)[150] England: ≥21 days after one dose: 47.5% (41.6 to 52.8) ≥14 days after second dose: 93.7% (91.6-95.3)[38] Scotland: 92% (90-93)[39] Canada: Single dose: 66% (64-68); 2 doses: 89% (86-91)[41] UK: Single dose: 59% (52-65); 2 doses: 78% (68-84)[40] Severe disease in Qatar: 100% (81.7-100)[150] Severe disease in Canada: Single dose: 80% (78-82); 2 doses: 95% (92-97)[41]	Israel case-control study: Vaccinees infected at least 1 week after the second dose were disproportionally infected with B.1.351 (odds ratio: 8:1)[149] Qatar: 75.0% (70.5-78.9)[150] South Africa: 100% (53.5-100)[151] Severe disease in Qatar: 100% (73.7-100)[150]	-	England: ≥21 days after one dose: 35.6% (22.7-46.4); ≥14 days after second dose: 88.0% (85.3-90.1)[38] Scotland: 79% (75-82)[39] Canada: Single dose: 56% (45-64); 2 doses: 87% (64-95)[41] Effectiveness in Israel: Infection: 64%; Symptomatic illness: 64%[152] Israel 6m after roll out: 39.0% (9.0-59.0)[57] Minnesota, USA: 42% (13-62)[53] UK: Single dose: 57% (50-63); 2 doses: 80% (77-83)[40] England: 89.8% (89.6-90.0)[45] Hospitalisation in England: 1 dose: 94% (46-99); 2 doses: 96% (86-99)[49]; 99.7% (97.6-100.0)[45] Death in England: 98.2% (95.9-99.2)[45] Severe disease in Canada: Single dose: 78% (65-86)[41] Hospitalisation in Israel: 93%[152] Severe disease in Israel: 91.4% (82.5-95.7)[57] Severe disease in Minnesota: 75% (24-94)[53] Pooled Pfizer/BioNTech and Moderna against hospitalisation and death in Scotland: 91% (88-93)[48]
Sinovac	Chile: 67% (65-69)*[34]	-	Brazil: 1 or 2 doses: 37.9% (−46.4-73.6)[153] Chile: 67% (65-69)*[34] Brazil: ≥70 years: 41.6% (26.9-53.3); 70-74 years: 61.8% (34.8-77.7); 75-79 years: 48.9% (23.3-66.0); ≥80 years: 28.0% (0.6-47.9)[154]	China (combined Sinovac and Sinopharm): Single dose: 13.8% (-60.2-54.8);; 2 doses: 59.0% (16.0-81.6) Severe disease: 100%[155]
Sinopharm				China (combined Sinovac and Sinopharm): Single dose: 13.8% (-60.2-54.8); 2 doses: 59.0% (16.0-81.6) Severe disease: 100%[155]
Bharat Biotech	- -	- -	- -	Efficacy against infection in India: 65.2% (33.1-83.0)[37]

* While it is known P.1. and B.1.1.7 were circulating at the time of the study, the extent is unknown based on available surveillance

Appendix 3: Vaccine Efficacy/Effectiveness in High-Risk Groups

VACCINE	VACCINE EFFICACY UNLESS OTHERWISE STATED			
	DIABETES	OBESITY	AT RISK FOR SEVERE COVID-19	ELDERLY
AstraZeneca	-	-	76% against symptomatic infection in a sample where 60% had comorbidities, including diabetes, severe obesity or cardiac disease[21] (not peer-reviewed) Effectiveness against symptomatic infection in the UK in those with comorbidities and ≥65 years: Single dose: 60.0% (46.5-70.1); 2 doses: 79.7% (61.6-89.3)[43] Hospitalisation in Scotland: 63% (46-75)[47]	In ≥65 years: 85%[21] (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)[50] Effectiveness of single dose against hospitalisation in England: ≥80 years: 73% (60-81)[70] Effectiveness in England: Symptomatic infection ≥70 years: 73% (27-90); Hospitalisation ≥80 years: 37% (3-59)[69] Hospitalisation following single dose in the UK: ≥80 years: 80.4% (36.4-94.5)[68] Single dose in Spain: ≥60 years: 53% (19-72) vs. 18-59 years: 50% (34-62)[42] Effectiveness against death in the UK: ≥65 years: Single dose: 83% (78-86); Two doses: 94% (80-98)[56] Effectiveness against symptomatic infection in the UK, ≥65 years: single dose: 60.9% (49.0-70.0); 2 doses: 76.4% (58.8-86.5)[43]
Gamaleya	-	-	-	Against symptomatic infection in >60 years: 91.8% (67.1–98.3)[22]
Johnson & Johnson	Against moderate to severe/critical: 23.0% (-90.1-69.8)[24]	Against moderate to severe/critical: 65.9% (47.8-78.3)[24]	Against moderate to severe/critical: With any comorbidity: 58.6% (40.6-71.6)[24] No comorbidity: 68.8% (59.0-76.6)[24]	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)[24]
Moderna	-	-	Against symptomatic infection, comorbidities, including diabetes and obesity: In low risk: 95.1% (89.6-97.7) In high risk: 90.9% (74.7-96.7)[27] Pooled Pfizer/BioNTech and Moderna against hospitalisation in Scotland: 72% (51-84)[47]	Against symptomatic infection: 18-64 years: 95.6% (90.6-97.9) ≥65 years: 86.4% (61.4-95.2)[27] Pooled Moderna and Pfizer vaccines against hospitalisation ≥65 years: 94% (49-99)[156] Infection in Canada: 1 dose ≥70 years: 54% (31-69); 2 doses ≥70 years: 95% (83-98)[55]
Pfizer/BioNTech	Effectiveness in Israel: Diabetes or cardoiovascular disease: 82% (62-92)[58] Effectiveness against infection in Israel: (88·9% (87·3-90·2)[66]	Effectiveness against infection in Israel: (89·7% (88·6-90·7)[66]	Against symptomatic infection: With any comorbidity or obesity: 95.3% With no comorbidity: 94.7%[32] Denmark: Infection: 71% (58-80); Hospitalisation: 81% (49-93)[60] Effectiveness against infection in Israel: Hypertension: (89·7% (88.6-91.7)[66] Effectiveness against symptomatic infection in the UK in those with comorbidities and ≥65 years: Single dose: 56.4% (46.2-64.6) 2 doses: 88.5% (81.5-92.9)[43] Pooled Pfizer/BioNTech and Moderna against hospitalisation in Scotland: 72% (51-84)[47]	Efficacy against infection ≥75 years: 96.2% (76.9-99.9)[33] 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)[32] Effectiveness against hospitalisation 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)[50] England 80-83 years: Documented infection: 70.1% (55.1-80.1) Hospital attendance: 78.9% (60.0-89.9); Hospital admission: 75.6% (52.8-87.6)[71] Reduction in incidence of infection in vaccinated people aged >60 years and unvaccinated people aged 20-39 years, respectively: Documented infection: 45% versus 28%; Hospitalisation: 68% versus 22%[157] Pooled Moderna and Pfizer vaccines against hospitalisation ≥65 years: 94% (49-99)[156] Effectiveness in England: Symptomatic infection ≥70 years: 61% (51-69); Hospitalisation ≥80 years: 43% (33-52); Death ≥80 years (vaccine failure vs non-vaccinated): 51% (37-62)[69] Effectiveness against hospitalisation in England ≥80 years: Single dose: 81% (76-85) Fully vaccinated: 93% (89-95)[70] (not peer reviewed) Effectiveness in Israel: 65-74 years: 82% (63-92); ≥75 years: 82% (61-91)[58] Hospitalisation following single dose in the UK: ≥80 years: 71.4% (43.1-86.2)[68] Single dose in Spain: ≥60 years: 76% (55-87) vs. 18-59 years: 85% (74-91)[42] Effectiveness against infection in Denmark: ≥80 years: 77% (50-89)[60] Effectiveness against infection in Israel: ≥70 years: 89·1% (83-93)[66] Effectiveness against death in the UK: ≥65 years: Single dose: 77% (72-81); Two doses: 98% (94-99)[56] Effectiveness against symptomatic infection in the UK, ≥65 years: single dose: 56.6% (47.6-64.1); 2 doses: 86.7% (80.1-91.1)[43] Infection in Canada: 1 dose ≥70 years: 40% (29-50); 2 doses ≥70 years: 93% (82-98)[55]
Novavax			Against any infection with comorbidity, age ≥65 years or frequent COVID-19 exposure in USA and Mexico: 91.0% (83.6-95.0)[31]	
Sinovac	-	74.9% (53.7-86.4)[34]	Any comorbidity: 48.9% (26.6-64.5)[34]	-
Sinopharm	-	80.7% (56.7-91.4)[34]	-	Effectiveness against symptomatic infection in Bahrain: ≥60 years: 91% (87-94)[34]
Bharat Biotech	-	-	Efficacy against any infection with comorbidity: 66.2% (33.8-84.0)[37]	Efficacy against symptomatic infection in India: ≥60 years: 67.8% (8.0-90.0) vs 18-59 years: 79.4% (66.0-88.2)[37]