Australian Government
Department of Health
Therapeutic Goods Administration

COVID-19 vaccines not registered in Australia but in current international use – TGA advice on "recognition"

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TGA Health Safety Regulation

Contents

Executive summary

This document provides an updated assessment by the Therapeutic Goods Administration's (TGA) of the protection offered by certain COVID-19 vaccines that are administered in certain countries but are not currently registered in Australia. It is based on individual assessment of published data and in some cases regulatory information provided in confidence. This advice is subject to change as new information becomes available.

This information does not represent assessment for regulatory approval within Australia. It also does not contemplate approaches to the verification of data provided on vaccination status of individuals vaccinated overseas. It will help inform decisions made by Government to support incoming travel across Australia's international borders and will be updated as new evidence on the effectiveness of vaccines emerges, and as assessments on other vaccines is completed. Note that while certain vaccines may be considered by the TGA as "recognised" decisions on inbound travel the Australian Government may apply additional considerations around vaccine requirements post-border.

The advice has compared the data for selected vaccines that are not registered in Australia with data on efficacy and protection offered by the vaccines approved for use in Australia. This assessment is based on data for two dose schedules of the vaccines not registered in Australia.

In its first assessment of September 2021 the TGA assessed six vaccines that are currently not registered in Australia:

- Peoples Republic of China - Coronavac (Sinovac), BBIBP-CorV (Sinopharm), and Convidecia (Cansino)
- India – Covishield (AstraZeneca-Serum Institute of India), Covaxin (Bharat Biotech)
- Russian Federation - Sputnik V (Gamaleya Research Institute)

Of these vaccines, Coronavac (Sinovac) and Covishield (AstraZeneca-Serum Institute of India) were Recognised for the purposes of travel into Australia effective 1 October 2021.

In a second assessment of November 2021 the TGA further included the Recognition of:

- BBIBP-CorV (Sinopharm)
- Covaxin (Bharat Biotech)

In a third assessment of January 2022 the TGA further included the Recognition of:

- Sputnik V

This assessment updates the Recognition of BBIBP-CorV(Sinopharm) to remove the age limit (e.g. <60 years of age), meaning that it will be Recognised for all ages of traveller.

Potential use of this information

Identifying incoming travellers as being fully vaccinated against COVID-19 helps achieve two main outcomes. Effective vaccination reduces the probability that an incoming traveller would:

1. **transmit COVID-19 infections to others while in Australia.**
2. **become acutely unwell due to COVID, potentially requiring acute healthcare services.**

How the estimates were determined

The protection offered by a vaccine against a person requiring hospital care if they develop COVID is either directly measured in Vaccine Efficacy and Effectiveness (VE) data from clinical trials or inferred from protection against 'severe' infection. VE measures the reduction in the odds of a person developing infection or hospitalisation, after vaccination, compared to unvaccinated people with the same exposure to COVID. Vaccine Efficacy trials directly measure the protection a vaccine offers against a person becoming infected with COVID when exposed to the virus. This can be used as an imperfect surrogate for reducing the chance of transmitting COVID because a person must first be infected with COVID to transmit it. There are also challenges in making accurate comparisons between the effectiveness of vaccines, given the inconsistent effectiveness measures, study confounders and efficacy end points used in clinical trials.

Vaccines approved in Australia

Effectiveness information has been assessed for the four vaccines that are TGA approved for use in Australia (Registered Vaccines) for the sake of completeness and to provide comparative data. **All TGA approved vaccines are recognised for incoming travellers.**

Table 1. Vaccine Efficacy of TGA-registered vaccines.

Vaccine	Outcome prevented	Average Vaccine Efficacy
AstraZeneca (Vaxzevria)[1]	Symptomatic Infection	65%
AstraZeneca (Vaxzevria)[1]	Severe infection/hospitalisation	85%
Pfizer (Comirnaty)[1]	Symptomatic Infection	81%
Pfizer (Comirnaty)[1]	Severe Infection/hospitalisation	88%
Moderna (Spikevax)[1]	Symptomatic Infection	86%
Moderna (Spikevax)[1]	Severe infection/hospitalisation	81%
Janssen (COVID-19 Vaccine Janssen)[1]	Symptomatic Infection	66%
Janssen (COVID-19 Vaccine Janssen)[1]	Severe infection/hospitalisation	85%
Nuvaxovid (Novovax)[2]	Symptomatic Infection	90%
Nuvaxovid (Novoxax)[2]	Severe infection/hospitalisation	87%

1 Adapted from National Centre Immunisation Research and Surveillance update to ATAGI on 13 September 2021
2 ATAGI statement on the use of the Novovax COVID-19 vaccine (Nuvaxovid) 24 January 2022

Of the five vaccines currently granted provisional regulatory approval in Australia, the minimal average vaccine effectiveness (VE) from two doses of Vaxzevria (AstraZeneca) has been used as the minimal effectiveness comparator based on Vaxzevria's published results. **The average VE against symptomatic infection is 65% and severe infection and/or hospitalisation is 85%.**

Recommendations regarding recognition of TGA-registered vaccines

Five COVID-19 vaccines have been granted provisional approval in Australia from the following sponsors:

1. Pfizer Australia Pty Ltd (Comirnaty)
2. AstraZeneca Pty Ltd (Vaxzevria)
3. Janssen-Cilag Pty Ltd (COVID-19 Vaccine Janssen)
4. Moderna Australia Pty Ltd.(Spikevax)
5. Nuvaxovid (Novovax Inc)
6. TGA (and ATAGI) consider people to be fully vaccinated with Comirnaty, Vaxzevria and Spikevax if a) they have completed a two-dose schedule of Comirnaty, Vaxzevria, Nuvaxovid or Spikevax with the two doses at least 14 days apart, or received a single dose of COVID-19 Vaccine Janssen and b) at least 7 days has elapsed since completing their vaccination schedule.

TGAs updated recommendations on recognition of vaccines not registered in Australia

BBIBP-CorV (Sinopharm China) showed an average VE against symptomatic infection of 67% and an average VE against severe disease/hospitalisation of 82%.

- VE against symptomatic infection (surrogate for transmission) of 67% based on estimates of 73%, 51%, 46%, 87%, 69% and 76% from six studies.
- VE against severe infection/hospitalisation of 82% based on information provided in confidence to TGA and estimates of 45%, 90.5%, 95% and 100% from four studies.

Based on published and pre-print data this suggests that the average efficacy of BBIBP-CoV against symptomatic infection is comparable to Australian approved vaccines and the VE effectiveness against severe infection/hospitalisation is 3% lower than Australian-approved vaccines.

The TGA considers BBIBP-CorV (Sinopharm) is a 'recognised vaccine' (for all ages). In this case TGA has recognised a slightly lower vaccine effectiveness against severe infection/hospitalisation given that this estimate is driven by a single study in which the VE against severe infection/hospitalisation was low and considering that the weight of other available studies the VE is comparable to Australian-approved vaccines. The TGA notes the evolving nature of the pandemic has changed the overall risk of severe disease and hospitalisation in COVID patients, mitigating the lower quality of evidence for vaccine efficacy in older people in studies referenced in previous TGA assessments.

Coronavac (Sinovac) showed an average VE against symptomatic infection of 64% and an average VE against hospitalisation of 90%.

- VE against symptomatic infection (surrogate for transmission) of 54%, 54%, 64%, 66% and 84% in five studies.
- VE against severe infection/hospitalisation of 100%, 100%, 88% and 73% in four trials.

The standard schedule of Coronavac is 2 doses administered 14-28 days apart.

Based on regulatory, published and pre-print data this suggests the efficacy of Coronavac is comparable to the Australian-approved vaccines, although marginally lower in protection against symptomatic infection.

TGA thus considers that the Coronavac (Sinovac) vaccine is a 'recognised vaccine'

Covishield (AstraZeneca/Serum Institute of India) is manufactured using the same ChAdOx1-S recombinant virus as the AstraZeneca (Vaxzevria) vaccine to produce the same dose of virus in the final product. The two are considered interchangeable by the World Health Organisation. TGA considers COVISHIELD to have the same clinical efficacy as Vaxzevria for this assessment. Two major global regulators, the UK Medicines and Health products Regulatory Agency and Health Canada have provided regulatory approvals for the AstraZeneca vaccine manufactured by the Serum Institute of India. These regulators are recognised in regulation as "Comparable Overseas Regulators" by the TGA.

Therefore, the clinical efficacy and effectiveness data for Vaxzevria (AstraZeneca) are relevant in this case. The average VE against symptomatic infection is 65% and severe infection and/or hospitalisation is 85%.

TGA thus considers that the Covishield (AstraZeneca/Serum Institute of India) vaccine is a "recognised vaccine.

Covaxin (Bharat Biotech, India) showed an average VE against symptomatic infection of 78% and an average VE against hospitalisation of 94%.

- VE against symptomatic infection (surrogate for transmission) of 78% in one study.
- VE against hospitalisation of 91% in two studies.

The standard schedule of Covaxin is two doses administered 28 days apart.

TGA considers that Covaxin is a 'recognised vaccine'

Sputnik V (Gamaleya Institute, Russian Federation) showed an average VE against symptomatic infection of 89% and VE against hospitalisation of 100%.

- VE against symptomatic infection (surrogate for transmission) of 92% and 86% from two studies.
- VE against hospitalisation of 100% from one study.

Based on published studies the vaccine efficacy of Sputnik V meets current criteria for efficacy. One study using a single dose of Sputnik V was considered supportive of the efficacy of a full Sputnik V schedule.

TGA considers Sputnik V be a 'recognised vaccine'

For **Convidecia (Cansino)**, there is currently insufficient published data on which to base an assessment of the efficacy of Convidecia and the TGA has not yet been provided with a regulatory dossier.

Because there continues to be insufficient data to evaluate the efficacy of the vaccine. **TGA has not yet reached a conclusion on whether Convidecia (Cansino) should be a 'recognised vaccine'.**

For the unregistered vaccines that are granted recognition, effective vaccination would be considered to extend from 7 days after the last dose of the schedule (which is currently two doses (except for Janssen)) but may be a booster doses six to twelve months after the last dose of the schedule. This is based on generalising the data from duration of immunity studies reviewed in the absence of specific studies in the unregistered vaccines.

Assessment of vaccination status in schedules containing vaccines not registered in Australia

The use of TGA-registered vaccines in Australia to complete vaccine schedules commenced with vaccines not registered in Australia should follow the advice of the Australian Technical Advisory Group on Immunisation (ATAGI).

ATAGI has considered several issues arising from the Recognition of vaccines not currently registered in Australia including;

- The appropriate advice for people who have received vaccines that are not Recognised (either because TGA has not Recognised them or they are not registered in Australia) and wish to become fully vaccinated to undertake activity in Australia.
- The status of mixed-product schedules where both products are Recognised vaccines (e.g. Sinovac/Comirnaty).

The determination of the vaccination status of a person who has received a Recognised vaccine (e.g. fully vaccinated, partially vaccinated, requiring a booster etc) will follow ATAGI's advice on these matters.

The relevance of Omicron COVID Variant of Concern to TGA Assessment

The TGA notes that the emergence of the Omicron Strain of COVID (B.1.1.529) in late November 2021 has posed challenges for assessing the efficacy of vaccines based on clinical trials conducted in other COVID variants. It is likely that extended schedules (e.g. 'boosters') will be required in some populations to provide protection.

The use of 2-dose primary schedules for vaccines not registered in Australia should be considered in conjunction with ATAGI recommendations for the requirement and appropriate products (e.g. mRNA vaccines) of third or further doses, and its advice regarding the definition of 'fully vaccinated' status.

Appendix 1 BBIP-CorV

Product	BBIBP-CorV (CorV)
Product Developer	Sinopharm
Country of origin	China
Vaccine Type	Inactivated virus/ alum adjuvanted
Schedule	Strain SARS-CoV-WIV04

Countries deployed

Sinopharm is deployed in 91 countries and WHO recognised for emergency use.

Algeria	Angola	Antigua and Barbuda	Argentina	Armenia	Bahrain
Bangladesh	Barbados	Belarus	Belize	Bolivia (Plurinational State of)	Bosnia and Herzegovina
Brazil	Brunei Darussalam	Burkina Faso	Burundi	Cambodia	Cameroon
Chad	China	Comoros	Cuba	Dominica	Dominican Republic
Egypt	Equatorial Guinea	Ethiopia	Gabon	Gambia	Georgia
Guinea	Guinea-Bissau	Guyana	Hungary	Indonesia	Iran (Islamic Republic of)
Iraq	Jordan	Kazakhstan	Kenya	Kyrgyzstan	Lao People's Democratic Republic
Lebanon	Madagascar	Malawi	Malaysia	Maldives	Mauritania
Mauritius	Mexico	Mongolia	Montenegro	Morocco	Mozambique
Myanmar	Namibia	Nepal	Nicaragua	Niger	Nigeria
North Macedonia	Pakistan	Papua New Guinea	Paraguay	Peru	Philippines
Republic of Moldova	Republic of the Congo	Rwanda	Senegal	Serbia	Seychelles

Sierra Leone	Solomon Islands	Somalia	South Africa	Sri Lanka	Sudan
Suriname	Thailand	Togo	Trinidad and Tobago	Tunisia	United Arab Emirates
United Republic of Tanzania	Vanuatu	Venezuela (Bolivarian Republic of)	Viet Nam	West Bank	Zambia
Zimbabwe					

Table 2. Main clinical efficacy and effectiveness data using standard schedules

Study	Population	Strain	Schedule	Primary Endpoint	VE	Study	Population	Strain	Schedule	Primary Endpoint
(Al Kaabi et al. 2021)	People >18 years of age without known history of COVID, MERS or SARS, or symptoms at screening.	Not noted	Two 5µg dose at day 0 and 21	Laboratory confirmed symptomatic COVID from 14 days after the second dose	64%	72.8%			• Randomised	• Strain prevalent in the trial not noted • Mainly enrolled healthy young men, mean age of 36.2%.
(Xia et al. 2021)	192 healthy people aged 18-80 with negative screening.	Not relevant 2 to 8 µg	Two does on day 0 and day 14,21 or 28	Phase I/II safety study with seroconversion endpoints						

Study	Population	Strain	Schedule	Primary Endpoint	VE	Study	Population	Strain	Schedule	Primary Endpoint
Silva-Valencia, Javier et al 2021 PREPRINT	400 000 HCW	Lamba and Gamma	Two doses Interval unknown	Symptomatic infection and Death		50.4%		94%	• Large real-world study in 400 000 people in Peru • Provides estimate of protection against death.	• Lambda and Gamma strain • Only reported VE against symptomatic infection and death in tabulated results • Not peer-reviewed (Pre-print)
(AlQahtani et al. 2021)	569054 people residents of Bahrain	Beta and Delta	Two doses	Symptomatic infections, hospitalisations, ICU admissions, Deaths		45.5%	44.5% (72% over 50 years old)	63%	• Large study • Includes delta strain	• Relatively young population
(Al-Hosani 2021) PREPRINT	176640 residents of UAE	Alpha and Beta	Two doses	Hospitalisation, ICU admissions and Death			79.8%	97.1%	• Large study	• Relatively young population • Observational • Not peer reviewed

Study	Population	Strain	Schedule	Primary Endpoint	VE	Study	Population	Strain	Schedule	Primary Endpoint
Rearte, A et al 2022	237,330 individuals in Argentina >60 years	Gamma, Lambda and Alpha	Two doses	Hospitalisation and Death	44%			85%	• Large study in high power journal • Looking at efficacy in older populations	• No reporting on ability of vaccine to reduce severe illness, only death
Petrovic, V. et al 2022	118,000 individuals in Serbia >60 years	Alpha	Two doses	Infection, Mild Infection (symptomatic without lower respiratory symptoms), Severe Infection (pneumonia and oxygenation)		86.9%	90.50% (LRTI and oxygen)		• Large study looking at older population (>60 years)	• Short period of observation – follow up only for 4 weeks post second dose • Observational
• Mousa, M. et al 2022	3782 individuals, average age 32.76 years	Delta	Two doses	Hospitalisation			95%		• Efficacy study during predominant delta outbreak	• Manuscript submission • Observational study

Study	Population	Strain	Schedule	Primary Endpoint	VE	Study	Population	Strain	Schedule	Primary Endpoint
Ma, C. et al 2022	92 fully vaccinated individuals	Delta	Two doses	Symptomatic, Severe Illness (RR.30, Sats <93% or worse)		75.5%	100%		• Real world study looking at close contact of confirmed cases	• Small study size

Main Safety Data

(Saeed et al. 2021) was a cross-sectional survey of recipients of BBIBP-CorV in the UAE between January and April 2021. The survey was voluntary and self-administered, and offered to potential recipients over 18 years of age who had received 1 or 2 doses of vaccine by email or social media sites. 1102 survey responses were received, of whom 1080 were included in the study as being from people 18 years and old. The number of vaccines administered to the survey population was not reported.

Table 3. Rate of adverse events reported in survey of recipients, Saeed et al (PREPRINT)

Adverse event reported	After 1st dose (rate)	After 2nd dose (rate)
Number of participants	**1080**	**1080**
Local pain (normal)	456	352
Local pain (severe)	28	88
Tenderness	56	108
Local pruritis	12	12
Local redness	8	16
Headache	104	108
Fatigue	132	176
Lethargy	100	148
Myalgia	68	
Nausea	16	12
Diarrrhoea	8	8
Cough	12	8
Hypersensitivity	12	0
Fever	12	32
Abdominal pain	20	16
Backpain	44	32
Other	8	8

Adverse event reported	After 1st dose (rate)	After 2nd dose (rate)
None	264	152

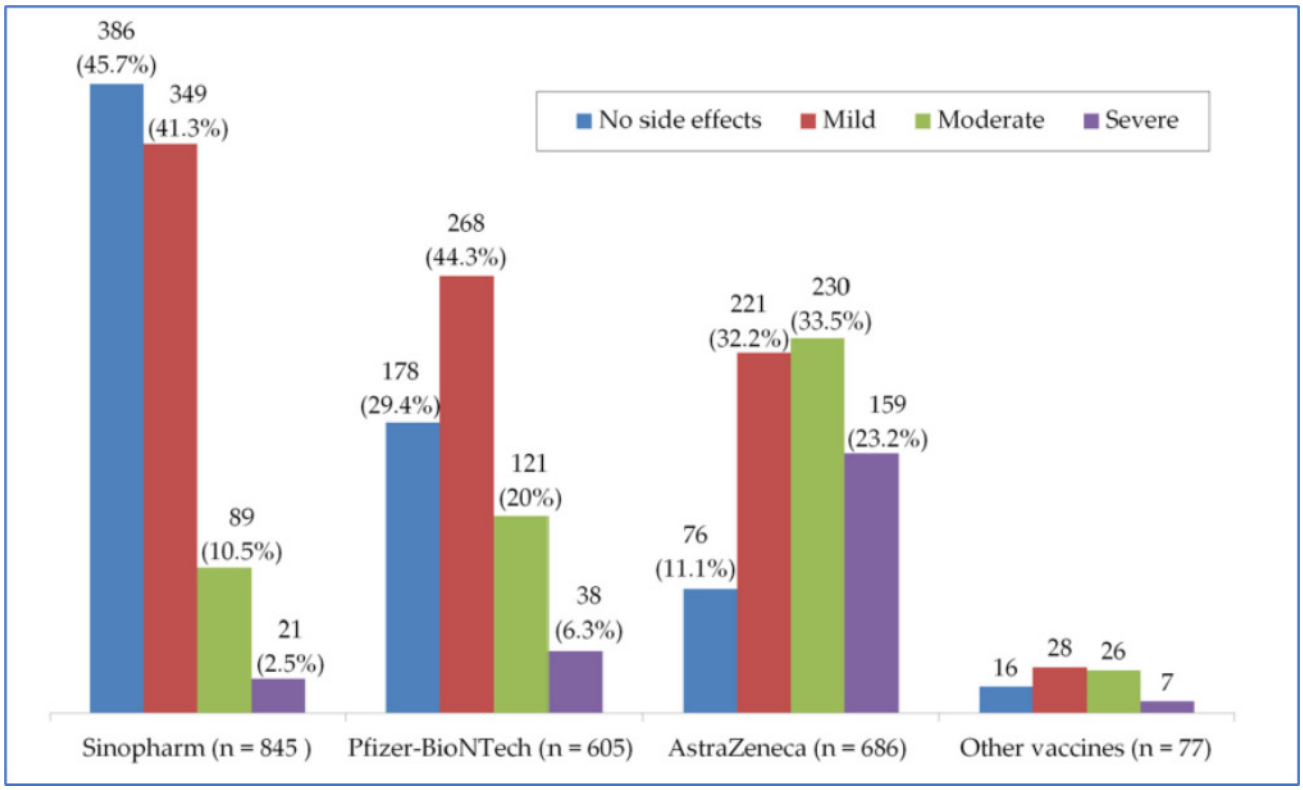
(Hatmal et al. 2021) was a study that administered a self-administered survey to a randomised cross section of the adult Jordanian population between 9 and 15 April 2021. Participants were invited through social media (Whatsapp, Facebook, Instagram) to go to the survey website, and a total of 2213 participants provided information. The vaccinated population of Jordan was 550000, who had received Comirnaty (BNT162b2), Vaxzevria (AZ1222) or BBIBP-CorV. The response rate was not reported.

Table 4. Adverse reactions by vaccine type reported in (Hatmal et al. 2021)

		Vaccines				χ^2	*p*-Value
		Sino.	Pfizer.	Astra.	O.		
Severity of side effects	Non Mild Moderate Severe	386 349 89 21	178 268 121 38	76 221 230 159	16 28 26 7	12.24	0.00 **
Infected after vaccination	Yes No	33 812	39 566	39 647	2 75	2.57	0.11
Tiredness	Present Absent	354 105	319 108	563 47	52 9	0.36	0.55
Fever	Present Absent	168 291	187 240	434 176	38 23	2.33	0.13
Headache	Present Absent	276 183	260 167	460 150	44 17	0.01	0.92
Haziness or lack-of-clarity in eyesight	Present Absent	84 375	57 370	147 463	11 50	1.68	0.19
Injection site pain and swelling	Present Absent	281 178	373 54	484 126	45 16	45.68	0.00 **
Joint pain	Present Absent	220 239	201 226	456 154	41 20	0.01	0.92
Swollen ankles and feet	Present Absent	26 433	19 408	53 557	4 57	0.14	0.71
Myalgia	Present Absent	221 238	219 208	455 155	42 19	0.40	0.53
Nausea	Present Absent	107 352	96 331	193 417	20 41	0.01	0.92
Abdominal pain	Present Absent	97 362	68 359	141 469	11 50	1.80	0.18
Diarrhea	Present Absent	55 404	52 375	110 500	8 53	0.00	1.00
Vomiting	Present Absent	17 442	16 411	52 558	3 58	0.03	0.86
Bruises on the body	Present Absent	20 439	12 415	34 576	3 58	0.39	0.53
Bleeding gums	Present Absent	11 448	1 426	15 595	1 60	2.22	0.14 *
Nosebleed	Present Absent	9 450	2 425	11 599	2 59	0.99	0.32 *
Chills	Present Absent	207 252	238 189	481 129	45 16	5.63	0.02 **
Itchy skin, or irritation and allergic reactions	Present Absent	47 412	31 396	62 548	9 52	0.97	0.32
Sweating for no reason	Present Absent	93 366	71 356	224 386	13 48	0.69	0.41
Cold, numbness, and tingling in limbs	Present Absent	140 319	115 312	278 332	25 36	0.55	0.46
Dizziness	Present Absent	168 291	131 296	288 322	28 33	1.61	0.20
Clogged nose	Present Absent	115 344	70 357	108 502	15 46	5.42	0.02 **
Runny nose	Present Absent	111 348	66 361	114 496	16 45	5.52	0.02 **
Dyspnea	Present Absent	71 388	54 373	127 483	12 49	0.53	0.47
Chest pain	Present Absent	60 399	63 364	139 471	14 47	0.14	0.71
Sleepiness and laziness	Present Absent	308 151	230 197	420 190	46 15	9.06	0.00 **
Irregular heartbeats	Present Absent	66 393	72 355	158 452	13 48	0.34	0.56
Abnormal blood pressure	Present Absent	46 413	50 377	95 515	7 54	0.19	0.66
Sore or dry throat	Present Absent	153 306	100 327	180 430	21 40	5.52	0.02 **
Cough	Present Absent	61 398	57 370	100 510	12 49	0.01	0.92
Number of side effects	0 1–6 7–12 >12	386 205 169 86	178 202 147 78	76 146 248 216	16 17 24 19	18.85	0.00 **

Sino., Sinopharm; Pfizer., Pfizer-BioNTech; Astra., AstraZeneca; O., other vaccines including Sputnik V, Moderna, Covaxin, and Johnson & Johnson vaccines. * One of the expected cell frequencies is smaller than 5. ** Significant difference.

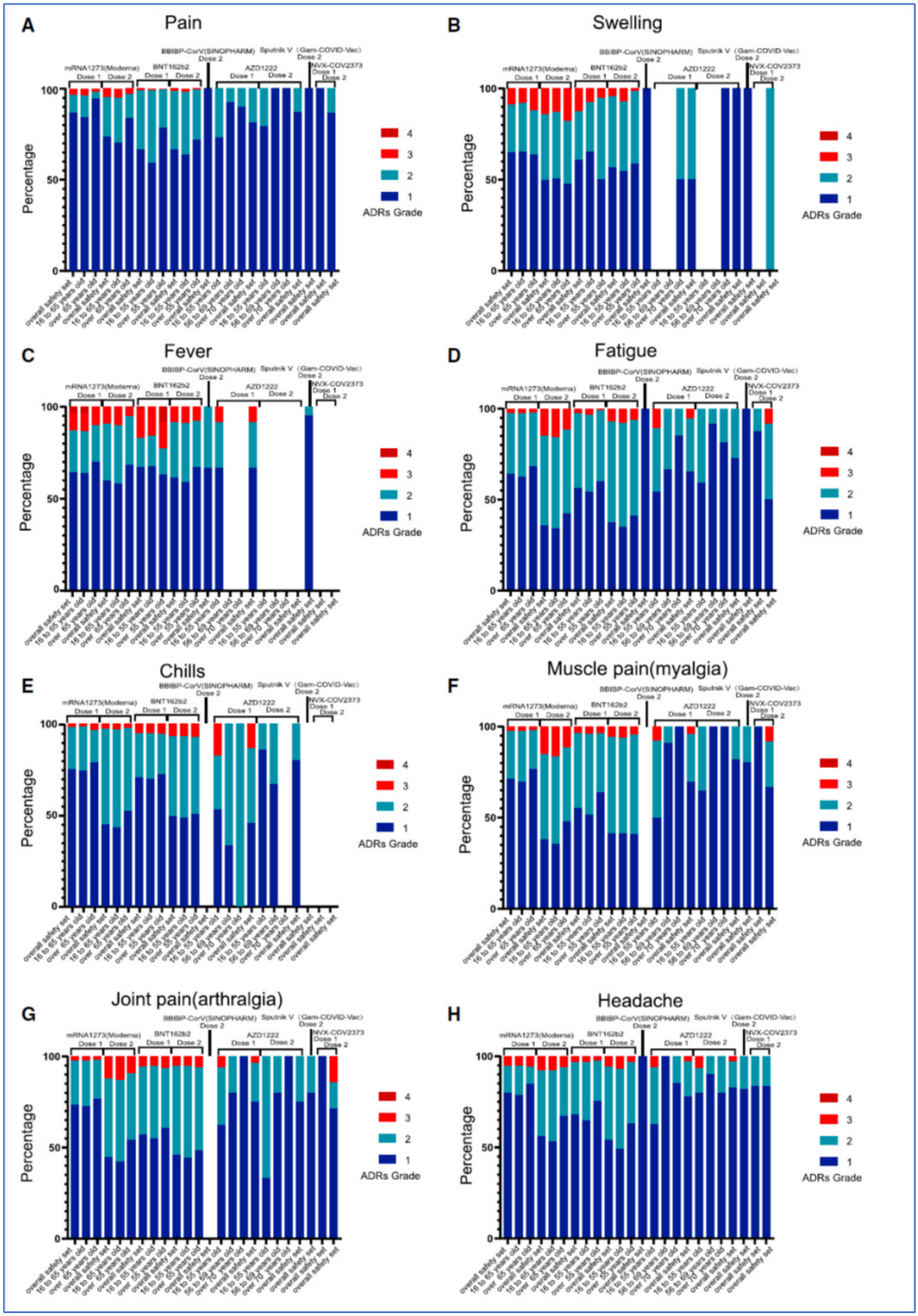
Figure 1. Adverse event severity by vaccine type from (Hatmal et al. 2021)



The most common adverse events with BBIPB-CorV were fever, tiredness, headache, and injection site pain. Overall, more BBIBP-CorV recipients reported no adverse events or milder adverse events than recipients of Comirnaty or Vaxzevria. Other vaccines in this analysis included small numbers of Covaxin, Sputnik V and other vaccines.

(Cai et al. 2021) is a significant meta-analysis of published studies of several vaccines, including BBIBP-CorV, which examined reported adverse events. It has referenced the main studies used in the analyses of efficacy presented in this Assessment.

Figure 2. Reported adverse events for Comirnaty, Vaxzevria, BBIBP-CorV, Sputnik V and Spikevax from (Cai et al. 2021)



The paper only presents the vaccine subanalysis graphically, although there is a tabulated comparison of adverse events by platform (e.g. non-replicating virus vs mRNA) but this merges several products. Overall the low rate of severe adverse events compared to Cominaty and Vaxzevria reported by (Hatmal et al. 2021) using real world data is repeated in this analysis. The Evaluator notes that there appears to be no data for BBIPB-CorV on the incidence of myalgia, arthralgia or chills, which may reflect the limitations of published trial data, but these are reported in the survey based studies.

The WHO (SAGE 2021) has reported two serious adverse events potentially linked to vaccination with BBIBP-CorV in clinical trial data it has reviewed. These are Inflammatory Demyelination Syndrome/Disseminated Encephalomyelopathy and Severe Nausea.

Additional information

None

Evaluators comments

Al Kaabi, Zhang et al. 2021) is an interim analysis of the the main phase III data available for the Sinopharm/WIV04 vaccine. The study was conducted in 40411 healthy adults in the UAE between Jul and Dec 2020. Subjects were randomised equally to receive either BBIBP-CorV, another inactivated vaccine strain (HBO2) or alum adjuvant only, giving 13066 subjects with two doses of BBIBP-CorV and 13071 with alum only. The study enrolled mainly men (84%) of young age (mean 36.2 years). The primary endpoint was PCR confirmed symptomatic COVID, with a vaccine efficacy of 72.8% (95%CI 58.1-82.4). A post-hoc analysis identified an additional 42 asymptomatic cases, which would lower the total vaccine efficacy (symptomatic and asymptomatic) to 64% (95%CI 48.4-74.7). There were only 2 'severe' cases of COVID and the Authors note this as a limitation in the study, giving an estimate VE of 100% but with very broad confidence intervals. The grading scale for symptoms used was not described in the publication.

WHO's sage committee provided TGA with a summary of updated data at a median of 112 days followup. This indicated that there was a VE against hospitalisation of 78.7% (95%CI 26-93.9). Vaccine Efficacy in people >60 years of age was not estimated.

Table 5. SAGE estimate of vaccine efficacy

Vaccine efficacy in multi-country Phase 3 Trial (median follow up time 112 days)

	BBIBP-CorV Group		Placebo Group		Vaccine Efficacy
Group/Subgroup	No. at risk	No. of cases	No. at risk	No. of cases	% (95% CI)
Overall	13,765	21	13,765	95	78.1 (64.9, 86.3)
Hospitalization	13,765	3	13,765	14	78.7 (26.0, 93.9)
Severe	13,765	0	13,765	2	NE
Sex					
Male	11,598	18	11,642	83	78.4 (64.1, 87.0)
Female	2,167	2	2,123	13	75.6 (13.3, 93.1)
Age group					
18-59 years	13,556	21	13,559	95	78.1 (64.9, 86.3)
≥60 years	209	0	206	0	NE
Comorbidities					
Hypertension	374	0	367	4	NE
Diabetes	300	2	308	6	63.7 (-79.8, 92.7)
Obesity	3,040	7	3,080	36	80.7 (56.7, 91.4)
Baseline SARS-CoV-2 serostatus					
Baseline positive	NR	0	NR	1	NE
Baseline negative	NR	16	NR	83	80.8 (67.2, 88.8)

NE=Not estimated

The SAGE summary noted that there was a 'low level of confidence' that 2 doses of BBIBP-CorV provides efficacy against infection in older adults.

(Xia et al. 2021) was a phase I/II study that mainly examined safety in escalating doses of BBIBP-CorV, as well as seroconversion. In part 1 of the study, subjects were randomised equally to receive either placebo or vaccine at 2, 4, or 8 µg doses on day 0 and 28. In part 2 of the study, subjects were randomised equally to receive placebo of vaccine at 8 µg on days 0 and day 14, 21 or 28. The mean age of participants was 53 years of age. The study was conducted in China in 2020 (exact dates unclear).

Figure 3. Seroconversion following BBIBP-CorV vaccination in phase I/II study.

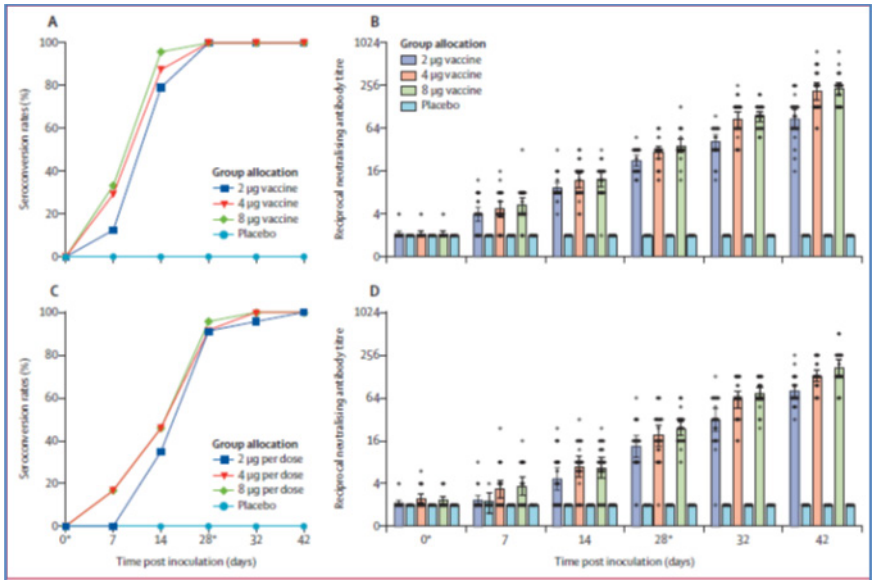


Figure 2: **Seroconversion ratios and neutralising antibody titres for and 60 years and older**
Seroconversion rates (A) and neutralising antibody titres (B) for participants aged 18–59 years; and seroconversion rates (C) and neutralising antibody titres (D) for participants aged 60 years and older. We defined the seroconversion as at least a four-fold increase in post-vaccination titre from baseline. The negative in neutralisation antibody detection is represented as a GMT of 2. *Days of vaccination.

The Study indicates that seroconversion occurs in response to vaccination, with uncertain relevance to clinical outcomes given there is not a clear correlate of immunity for COVID.

(Silva-Valencia) was a large study examining vaccine efficacy and mortality among 400 000 Peruvian healthcare workers between Feb and Jun 2021. The pre-print of the study was in Spanish and so the Evaluator cannot comment on methodology, however the table presents clinical endpoints which translate readily into English. The results of this trial were reported in English in Reuters, at https://www.reuters.com/world/americas/peru-study-finds-sinopharm-covid-vaccine-504-effective-against-infections-2021-08-13/.

(AlQahtani et al. 2021) is a study from the deployment of several vaccines, including Sinopharm, in Bahrain between December 2020 and July 2021. In this, 569 054 individuals with a median age of 38 years were vaccinated. Delta and Beta strain COVID were isolated from PCR results during the period of deployment. The paper does not present vaccine effectiveness, which the Evaluator has calculated from the rates of endpoints presented below. This is notable in that there is a relatively low level of effectiveness even against Death compared to other trials.

Table 6. Pairwise comparisons of effectiveness of Sinopharm BBIBP-CorV in Bahrain

(b)

	Unvaccinated vs Sinopharm											
	ALL				Over 50				Under 50			
	Rate (Unvax)	Rate (Sino)	p	OR	Rate (Unvax)	Rate (Sino)	p	OR	Rate (Unvax)	Rate (Sino)	p	OR
Infections	642.96	350.53	<.001	1.72	781.32	366.57	<.001	2.02	631.66	345.52	<.001	1.70
Hospitalizations	51.06	28.36	<.001	1.78	225.55	62.11	<.001	3.49	33.98	14.74	<.001	2.35
ICU admissions	6.39	2.29	<.001	2.70	41.44	6.62	<.001	5.92	2.65	0.49	**<.05**	5.09
Deaths	4.42	1.64	<.001	2.72	37.17	5.45	<.001	6.56	1.35	0.16	**NS**	7.65

Table 7. Outcomes from Silva-Valencia, J et al. Note the IC 95% is not the CI for the Vaccine Efficacy

Tabla 2. Efectividad de la Vacuna BBIBP-Cor-V para infección, muerte por todas las causas y muerte por COVID-19 en trabajadores de salud del Perú, 2021

Desenlace	HR/RTI*	IC 95%	Efectividad (1-HR x 100)
Infección por SARS-CoV-2			
Inmunización parcial	0.83	0.80 - 0.85	17.2%
Inmunización completa	0.50	0.48 - 0.51	50.4%
Mortalidad por todas las causas			
Inmunización parcial	0.49	0.39 - 0.62	51.0%
Inmunización completa	0.10	0.08 - 0.13	90.1%
Mortalidad por COVID-19			
Inmunización parcial	0.54	0.41 - 0.70	46.3%
Inmunización completa	0.06	0.04 - 0.09	94.0%

* HR: Hazard Ratio calculado para Mortalidad por todas las causas y Mortalidad por COVID-19, RTI: Razones de Tasas de Incidencia calculadas para Infección por SARS-CoV-2. Todos los estimados están ajustados por edad, sexo, infección previa por COVID-19, departamento de procedencia, profesión, obesidad y las comorbilidades diabetes, hipertensión, asma, EPOC, estado de inmunosupresión, insuficiencia renal crónica y cáncer

Figura 2. Efectividad de la Vacuna BBIBP-Cor-V para infección, muerte por todas las causas y muerte por COVID-19 en trabajadores de salud del Perú, 2021.

(Al-Hosani 2021) is an observational study based on administrative records from the deployment of BBIP-CorV in the UAE between September 2020 and May 2021. A total of 214940 cases of COVID were reported to the UAE Dept of Health, of whom 176 640 could be linked to vaccine status records and were included in the study. The estimate of vaccine effectiveness is not presented stratified by age.

(Ferenci and Sarkadi 2021) published a review of neutralising antibody levels after two doses of BBIBP-CorV. This study found that age was a significant factor in the antibody response to BBIBP-CorV. 25% of recipients at 60 years of age, and 50% of recipients at 80% of age did not produce protective antibodies.

Given the above results, more recent studies have attempted to fill the knowledge gap in relation to vaccine efficacy within older populations. (Rearte, A et al 2022) retrospectively assessed vaccine efficacy at reducing infection and risk of death in 237,330 individuals over the age of 60 in line with Argentina's vaccine rollout. Estimated vaccine effectiveness after 2 doses at reducing overall infection and death with COVID-19 was 44% and 85% retrospectively. (Petrovic, V. et al 2022) assessed early vaccine efficacy at reducing overall, mild and severe COVID-19 infections in individuals aged >60 years using surveillance registry data in Vojvodina, Serbia. Severe infection was defined as those cases where pneumonia was confirmed, and

oxygenation was required. Follow up was performed only 4 weeks after administration of vaccine second dose. The estimated vaccine effectiveness at reducing symptomatic, mild and severe infection after 2 doses of vaccine was 87%, 86% and 91% respectively. This represented significantly higher efficacy then represented in previous studies, which may represent the early window of follow up.

(Voko, Z et al 2022) offers a nationwide observational perspective from Hungary, across various age groups. It correlates other quoted efficacy figures and acknowledges that vaccine effectiveness at preventing infection reduces with increasing age, from 71.1% at age 65-74 to 43.1% from age 85 onwards. This is observed also with mortality rates, with 100% adjusted vaccine effectiveness for those aged below 55, 86.7% aged 75-84 and 67.3% aged above 85.

Table 8: Effectiveness measures from Voko, Z et al. with breakdown by age group

Estimated unadjusted and adjusted effectiveness of five different vaccine types against SARS-CoV-2 infection and COVID-19-related death in the fully vaccinated study population ≥7 days after the second dose in Hungary

Vaccinated person			Vaccine effectiveness							
			SARS-CoV-2 infection				COVID-19-related mortality			
Vaccine	Age	n	Unadjusted	95% CI[a]	Adjusted	95% CI[a]	Unadjusted	95% CI[a]	Adjusted	95% CI[a]
Sinopharm	16–24	65 720	97.4%	(93.7%–98.9%)	67.3%	(21.3%–86.4%)	100.0%	(NA–100.0%)	100.0%*	(NA–NA)
	25–34	91 946	98.5%	(96.7%–99.3%)	84.6%	(65.8%–93.1%)	100.0%	(NA–100.0%)	100.0%*	(NA–NA)
	35–44	104 018	95.6%	(93.5%–97.1%)	69.0%	(53.7%–79.3%)	100.0%	(NA–100.0%)	100.0%*	(NA–NA)
	45–54	80 960	95.8%	(94.0%–97.1%)	78.6%	(69.2%–85.2%)	100.0%	(NA–100.0%)	100.0%*	(NA–NA)
	55–64	126 028	85.6%	(84.2%–86.9%)	66.1%	(62.6%–69.3%)	92.5%	(86.8%–95.8%)	87.9%	(78.5%–93.1%)
	65–74	281 725	87.1%	(86.3%–87.8%)	71.1%	(69.0%–73.1%)	94.1%	(92.6%–95.2%)	91.1%	(88.9%–92.9%)
	75–84	130 323	82.2%	(80.6%–83.7%)	66.4%	(63.1%–69.4%)	90.0%	(87.8%–91.8%)	86.7%	(83.7%–89.1%)
	85+	14 745	69.8%	(62.1%–76.0%)	43.1%	(28.3%–54.9%)	75.7%	(64.7%–83.3%)	67.3%	(52.3%–77.6%)
Total		895 465	86.9%	(86.4%–87.5%)	68.7%	(67.2%–70.1%)	66.1%	(61.3%–70.3%)	87.8%	(86.1%–89.4%)

Finally, two more recent trials have suggested positive efficacy of BBIBP-CorV towards the Delta variant. (Ma, C. et al 2022) looked at rates of symptomatic, pneumonia and severe infection amongst vaccinated and unvaccinated close contacts to individuals infected with the delta strain. It showed strong efficacy across both inactivated vaccines (including BBIBP-CorV) at reducing severe infection, the parameters of which would often be indication for hospitalisation (tachypnoea, hypoxia etc). (Mousa, M et al) is a manuscript submitted comparing efficacy data for BBIBP-CorV preventing hospitalisation during a delta outbreak within the UAE. Fully vaccinated individuals had a VE of 95% at reducing hospitalisation, albeit apparently skewed towards a younger population, with mean age of 32 years. Both these trials observe in their conclusions the need for larger, retrospective studies.

The Evaluator concludes that from the above data, early studies suggested a wide range for the VE of BBIBP-CorV, with (AlQhatani et al) representing a significant outlier. Newer studies sought to provide more information in relation to vaccine efficacy within the older populations and against delta infection. Averaging the documented effectiveness measures equates to a VE against infection of 66.6% (including outlier studies) and VE against hospitalisation of 82.0% (including outlier studies).

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