World Health Organization

Evidence Assessment: Sinovac/CoronaVac COVID-19 vaccine

FOR RECOMMENDATION BY THE STRATEGIC ADVISORY GROUP OF EXPERTS (SAGE) ON IMMUNIZATION

Prepared by the SAGE Working Group on COVID-19 vaccines

EVIDENCE ASSESSMENT: CoronaVac COVID-19 vaccine

Key evidence to inform policy recommendations on the use of CoronaVac

Background

- 2-dose β-propiolactone-inactivated, aluminium hydroxide-adjuvanted COVID-19 vaccine administered on a 0/14-28-day schedule for the prevention of COVID-19 disease
- Authorized by the China National Medical Products Administration on February 6, 2021
- Authorized by 32 countries/jurisdictions for use in adults ≥18 years, with variation in age indication
- 260 million doses have been distributed to the public domestic and overseas markets
- EUL status pending

EVIDENCE ASSESSMENT: CoronaVac COVID-19 vaccine

Key evidence to inform policy recommendations on the use of CoronaVac

The SAGE Working Group specifically considered the following questions:

1. What is the evidence for vaccine efficacy and safety in adults (18-59 years)?
2. What is the evidence for efficacy and safety for certain comorbidities and health states?
3. What is the evidence for use in older age groups?
4. GRADEing of the evidence assessment

EVIDENCE ASSESSMENT: CoronaVac COVID-19 vaccine

Key evidence to inform policy recommendations on the use of CoronaVac

The SAGE Working Group specifically considered the following questions:

1. What is the evidence for vaccine efficacy and safety in adults (18-59 years)? Cristiana Toscano
2. What is the evidence for efficacy and safety for certain comorbidities and health states?
3. What is the evidence for use in older age groups? Cristiana Toscano, Rafael Araos
4. GRADEing of the evidence assessment Melanie Marti

EVIDENCE ASSESSMENT: CoronaVac COVID-19 vaccine

Key evidence to inform policy recommendations on the use of CoronaVac

Clinical database available at the time of review

Total Data Package	Age Group (Years)	Authorized dose/schedule	Alternative dose/schedule	Total by age	Total all ages
Safety	18-59Y	7,603	288	7,891	8,840
	≥60Y	726	223	949	
Immunogenicity	18-59Y	1,589	288	1,987	2,608
	≥60Y	398	223	621	
Efficacy	18-59Y	12,098	0	12,098	12,310
	≥60Y	212	0	212	

EVIDENCE ASSESSMENT: CoronaVac COVID-19 vaccine

Key evidence to inform policy recommendations on the use of CoronaVac

Summary of clinical trials reporting to date

Study Name Trial Registration	**Phase Type (primary outcome)***	**Location**	**Participants & Ages eligible**	**Schedule**	**Study Status**
Corona-01 NCT04352608	Phase 1/2 Safety and immunogenicity	China	Phase 1: 144 healthy participants 18-59 years	2 dose 0/14 day or 0/28-day schedule	Complete
			Phase 2: 600 healthy participants 18-59 years	2 or 3 dose 0/14 day-, 0/28 day-, or 0/28/56-day schedule	
Corona-02 PRO-nCOV-1002 NCT04383574	Phase 1/2 Safety and immunogenicity	China	Phase 1: 72 healthy participants ≥60 years	2-dose 0/28-day schedule	Complete
			Phase 2: 350 healthy participants ≥60 years	2-dose 0/28-day schedule	
Corona-04 PRO-nCOV-3001 NCT04617483	Phase 3 Non-inferiority to commercial lot and to elderly on 0/14 schedule	China	1,040 healthy participants ≥18 years, 25% of participants ≥60 years	2-dose 0/14-day schedule	Complete
PROFISCOV NCT04456595	Phase 3 Vaccine efficacy and safety	Brazil	12,688 healthy participants ≥18 years, healthcare workers who treat patients with COVID-19	2-dose 0/14-day schedule	Interim results available
CoV2-0320 NCT04508075	Phase 3 Vaccine efficacy and lot-to-lot consistency	Indonesia	1,620 healthy participants	2-dose 0/14-day schedule	Interim results available
9026-ASI NCT04582344	Phase 3 Vaccine efficacy	Turkey	13,000 healthy participants 18-59 years	2-dose 0/14-day schedule	Top line efficacy results available
CoronaVac3CL NCT04651790	Phase 3 Safety and immunogenicity	Chile	2,300 healthy participants ≥18 years	2-dose 0/14- and 0/28-day schedule	Interim results available

EVIDENCE ASSESSMENT: CoronaVac COVID-19 vaccine

Key evidence to inform policy recommendations on the use of CoronaVac

Evidence of clinical protection across studies and locations ≥14 days after 2nd dose

Study Location	Population Size	Schedule (days)	Design / Measure of Effect	Circulation of VOCs	Protection against symptomatic COVID-19	Protection against hospitalization
Turkey	13,000	0,14	RCT / Efficacy	Limited	84% (65, 92)	100% (20, 100)
Chile	10.5 million	0,28	Cohort / Effectiveness	P.1, B.1.1.7	67% (65, 69)	85% (83,97)
Indonesia	1,620	0,14	RCT / Efficacy	Limited	65% (20, 85)	Not Estimated*
Brazil	12,688	0,14	RCT / Efficacy	Limited	51% (36, 62)	100% (56, 100)
Brazil	393 case-control pairs	0,14**	TND / Effectiveness	P.1	50% (11, 71)	Not Reported

*No hospitalized cases in either group
**Analysis based on receiving ≥1 dose

RCT=Randomized-Controlled Trial; TND=Test Negative Design.

EVIDENCE ASSESSMENT: CoronaVac COVID-19 vaccine

Key evidence to inform policy recommendations on the use of CoronaVac

Characteristics of Phase 3 trials to inform variations in estimated efficacy

Country (N)	Population	Mean Age (SD)	Proportion with comor-bidity	Incidence in placebo group /100py	Proportion of Grade 4+ COVID-19 in placebo group	Case definition for primary analysis	Median follow up time	VE against symptomatic COVID-19 (95%CI)	VE against Grade 4+ COVID-19 (95%CI)
Brazil	Healthcare workers treating patients with COVID-19	39.50 (10.75)	56%	22.34	6%	Case definition 1	73 days	Vaccine: 85/4953 Placebo: 168/4870 VE: 51% (36, 62)	Vaccine: 0/5717 Placebo: 10/5714 VE: 100% (56, 100)
Turkey	Medical staff (10%) & General population (90%)	Not reported	Not reported	19.22	19%	Case definition 3	Not reported	Vaccine: 9/6659 Placebo: 32/3471 VE: 84% (65, 92)	Vaccine: 0/6550 Placebo: 6/3445 VE: 100% (20, 100)
Indonesia	General population	35.82 (11.4)	Not reported	11.25	0%	National case definition	~2.5 months	Vaccine: 7/798 Placebo: 18/804 VE: 65% (20, 85)	Vaccine: 0/798 Placebo: 0/804 VE: NE

EVIDENCE ASSESSMENT: CoronaVac COVID-19 vaccine

Key evidence to inform policy recommendations on the use of CoronaVac

Trial	Case definition used for primary endpoint
Brazil (NMPA-recommended)	Individuals with at least two type A symptoms, or at least one type B symptom, or radiologic characteristics of COVID-19 vaccine. Meanwhile, with positive PCR test of COVID-19 (including saliva sample). **1) Clinical symptom** Symptom A (for at least 2 days): Fever (Axillary temperature ≥37.5ºC), chills, sore throat, fatigue, nasal congestion or runny nose, muscle pain, headache, nausea or vomiting, diarrhoea. Symptom B: Cough (for at least 2 days), loss of smell or taste (for at least 2 days), shortness of breath or difficulty breathing. **2)Radiologic characteristics of COVID-19**
Turkey	At least one of the following symptoms and lasts for at least two days, and nucleic acid positive of SARS-CoV-2 (exclude nucleic acid positive of saliva sample). Fever or cold; Cough; Shortness of breath or difficulty breathing; Fatigue; Muscle or physical pain; Have a headache; Loss of smell or taste; Sore throat; Stuffy or runny nose; Nausea or vomiting; Diarrhoea.
Indonesia	Clinically confirmed or suspected COVID-19 cases (referring to the case definition of the national guidelines for the diagnosis and treatment of COVID-19).

EVIDENCE ASSESSMENT: CoronaVac COVID-19 vaccine

Key evidence to inform policy recommendations on the use of CoronaVac

Vaccine efficacy in Phase 3 trial in Brazil

Group/Subgroup	Vaccine Group		Placebo Group		Vaccine Efficacy % (95% CI)
	No. at risk	No. of cases	No. at risk	No. of cases	
Overall	4953	85	4870	168	50.7 (35.9, 62.0)
Hospitalization (Grade 4+)	4953	0	4870	10	100.0 (56.4, 100.0)
Severe	4953	0	4870	6	100.0 (16.9, 100.0)
Age group					
18-59 years	4741	83	4663	164	50.7 (35.8, 62.1)
≥60 years	212	2	207	4	51.1 (-166.9, 91.0)
Interdose interval					
<21 days	4184	77	4148	149	49.1 (33.0, 61.4)
21-28 days	769	8	722	19	62.3 (13.9, 83.5)
Comorbidity					
Any	2731	44	2730	86	48.9 (26.6, 64.5)
Cardiovascular disease	621	6	608	10	39.5 (-66.4, 78.0)
Hypertension	335	0	330	7	100.0 (28.4,100.0)
Obesity	1099	13	1112	50	74.9 (53.7, 86.4)
Type 2 diabetes mellitus	175	3	159	5	48.6 (-115.3, 87.7)

EVIDENCE ASSESSMENT: CoronaVac COVID-19 vaccine

Key evidence to inform policy recommendations on the use of CoronaVac

Use in individuals with underlying disease

- Clinical protection
  - Efficacy stratified by underlying disease only available from Brazil: VE amongst participants with any underlying disease was 48.9% (95%CI 26.6, 64.5)
  - When stratified by specific morbidities, efficacy was demonstrated amongst participants with obesity [VE=74.9% (95%CI 53.7, 86.4)] and hypertension VE=100.0% (95%CI 28.4,100.0). There were insufficient numbers in other subgroups.
- Safety
  - Safety profile in Phase 3 study in Brazil was consistent when limiting the analysis to those with comorbidities

EVIDENCE ASSESSMENT: CoronaVac COVID-19 vaccine

Key evidence to inform policy recommendations on the use of CoronaVac

Clinical safety summary

- No safety concerns from pre-clinical or repro/tox studies
- Clinical safety database: 8,840 participants who received any dose/schedule of Sinovac product, of which 94% received authorized dose/schedule
- Most AEs were mild/moderate
- Most common adverse events were pain at the injection site, headache, fatigue, and myalgia
- Safety follow up of limited inadvertently vaccinated pregnant women in clinical trials is ongoing
- Phase 3 trial in Brazil:
    - No imbalance in the number of reported SAEs or Grade 3+ adverse events between vaccine and placebo group. All SAEs classified as "unlikely" or "unrelated" to vaccination
    - 3 deaths in the trial: 2 in placebo group (COVID-19 and cardiopulmonary arrest) and 1 in vaccine group (suicide)
    - Few allergic reactions, all Grade 1 or 2

EVIDENCE ASSESSMENT: CoronaVac COVID-19 vaccine

Key evidence to inform policy recommendations on the use of CoronaVac

Post-authorization safety summary

No unexpected signals from post-authorization passive surveillance have been identified to date, although limited to data from China, Indonesia, Brazil, and Chile

- **China**: Based on 35.8 million doses distributed, and 49 serious AEs reported, including anaphylaxis, Henoch-Schonlein purpura, laryngeal odema, demyelination, cerebral hemorrhage (n≤6)
- **Brazil/Indonesia**: Based on ~17 million doses distributed, and 162 serious AEs reported, including fever, dyspnea, death, and headache (n≤16)
- **Chile**: Based on 3.7 million doses distributed, and 90 serious AEs reported. Most common were clinical symptoms of anaphylaxis for a reporting rate of 1.7/100,000 doses, lower than reported for another COVID vaccine

EVIDENCE ASSESSMENT: CoronaVac COVID-19 vaccine

Key evidence to inform policy recommendations on the use of CoronaVac

Use in older age groups (≥60 years)

- Clinical Protection
  - Vaccine efficacy was not demonstrated in Phase 3 trial in Brazil (2 cases in vaccine group vs. 4 cases in placebo group, VE=51.1 (95%CI -166.9, 91.0)
  - Vaccine effectiveness was demonstrated in large Phase 4 study in Chile (next slides)
- Safety
  - Clinical trials: similar safety profile compared to younger adults, but with lower reactogenicity in older adults
  - Post-authorization: most countries have prioritized older age groups for vaccination, so the majority of reports tend to be in this age group

Ministerio de Salud

Gobierno de Chile

Early Estimates of CoronaVac Vaccine's Effectiveness in Chile

Rafael Araos, MD, MMSc
Advisor to the Undersecretariat of Public Health
Instituto de Ciencias e Innovación en Medicina
Facultad de Medicina
Clínica Alemana Universidad del Desarrollo

April 27, 2021

STUDY DESIGN: vCOVID CHILE COHORT

› 2 February – 1 April 2021

› Study groups (exposures)

- Unvaccinated
- Partially vaccinated (≥14 days after the first dose)
- Fully vaccinated (≥14 days after the second dose)

› Outcomes

- SARS-CoV-2 infection
- Covid-19 symptomatic (cases confirmed by RT-PCR or antigen test for SARS-CoV-2)
- Hospital admissions (date of first symptoms)
- ICU admissions (date of first symptoms)
- Deaths due to Covid-19 (U07.1) (date of first symptoms)

› Covariables (potential confounders): age, gender, region of residence, income, comorbidities, nationality

* We included a subgroup analysis for those above 60 yo

STATISTICAL APPROACH

We estimated hazard ratios using the Andersen-Gill extension of the Cox proportional hazards model, accounting for time-varying vaccination status.

We calculated hazard ratios of unvaccinated person-days to partial immunization person-days (≥14 days after the first dose) and full immunization person-days (≥14 days after the second dose) separately.

We excluded the 13 days between vaccine administration and partial or full immunization at-risk person-time because immunity status is still indeterminate.

We estimated the unadjusted vaccine effectiveness as $100\% \cdot (1 - hazard\ ratio)$. We also show results for the adjusted vaccine effectiveness, including covariates as controls.

Table 2: Characteristics of FONASA affiliates cohort, with confirmed SARS-CoV-2 infections and percentage receiving one or more doses of Coronavac vaccine. Follow up period: February 2nd - April 1st, 2021.

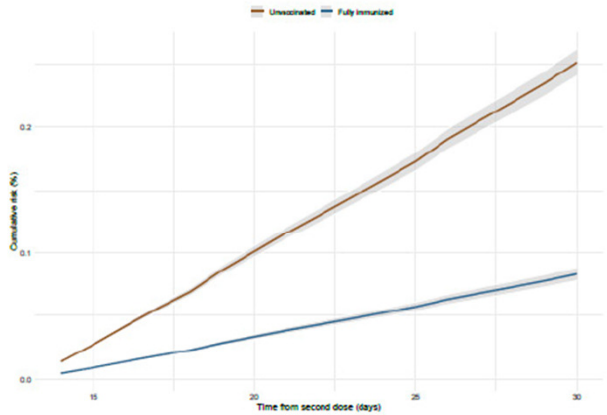
		Covid19		Unvaccinated	Vaccinated		
					1 dose	2 doses	
Characteristic	No. (column %)	No. (row %)	p-value	No. (row %)	No. (row %)	No. (row %)	p-value
Total	10,550,329 (100.0)	156,618 (1.5)	-	6,266,701 (59.3982)	1,735,619 (16.4509)	2,548,009 (24.1510)	-
Cohort location							
Arica	129,401 (1.2)	1,998 (1.5)	< 2.22e-16	90,251 (69.75)	11,809 (9.126)	27,341 (21.13)	< 2.22e-16
Tarapacá	178,767 (1.7)	3,317 (1.9)		125,910 (70.43)	16,375 (9.16)	36,482 (20.41)	
Antofagasta	303,463 (2.9)	4,398 (1.4)		202,867 (66.85)	44,369 (14.62)	56,227 (18.53)	
Atacama	176,300 (1.7)	1,398 (0.79)		115,765 (65.66)	22,944 (13.01)	37,591 (21.32)	
Coquimbo	489,107 (4.6)	5,657 (1.2)		309,319 (63.24)	73,446 (15.02)	106,342 (21.74)	
Valparaíso	1,153,266 (11)	14,496 (1.3)		659,497 (57.19)	201,763 (17.49)	292,006 (25.32)	
Metropolitana	3,899,480 (37)	45,904 (1.2)		2,300,354 (58.99)	663,705 (17.02)	935,421 (23.99)	
L.G.B. O'Higgins	597,267 (5.7)	7,682 (1.3)		347,322 (58.15)	107,705 (18.03)	142,240 (23.82)	
Maule	721,992 (6.8)	11,149 (1.5)		421,361 (58.36)	123,952 (17.17)	176,679 (24.47)	
Ñuble	326,086 (3.1)	5,049 (1.5)		176,342 (54.08)	60,585 (18.58)	89,159 (27.34)	
Biobío	984,234 (9.3)	22,614 (2.3)		552,084 (56.09)	170,639 (17.34)	261,511 (26.57)	
Araucanía	646,883 (6.1)	15,400 (2.4)		388,989 (60.13)	101,880 (15.75)	156,014 (24.12)	
Los Ríos	253,932 (2.4)	6,370 (2.5)		153,215 (60.34)	39,533 (15.57)	61,184 (24.09)	
Los Lagos	546,226 (5.2)	9,498 (1.7)		339,139 (62.09)	77,698 (14.22)	129,389 (23.69)	
Aysén	56,251 (0.53)	396 (0.7)		36,695 (65.23)	6,296 (11.19)	13,260 (23.57)	
Magallanes	87,674 (0.83)	1,292 (1.5)		47,591 (54.28)	12,920 (14.74)	27,163 (30.98)	
Sex							
Female	5,635,671 (53)	85,557 (1.5)	< 2.22e-16	3,160,462 (56.08)	931,503 (16.53)	1,543,706 (27.39)	< 2.22e-16
Male	4,914,658 (47)	71,061 (1.4)		3,106,239 (63.2)	804,116 (16.36)	1,004,303 (20.43)	
Age group							
16 - 19	717,923 (6.8)	8,601 (1.2)	< 2.22e-16	685,745 (95.52)	25,452 (3.545)	6,726 (0.9369)	< 2.22e-16
20 - 29	2,051,953 (19)	35,538 (1.7)		1,729,529 (84.29)	180,298 (8.787)	142,126 (6.926)	
30 - 39	1,903,366 (18)	32,500 (1.7)		1,525,410 (80.14)	205,131 (10.78)	172,825 (9.08)	
40 - 49	1,623,587 (15)	26,327 (1.6)		1,203,548 (74.13)	285,048 (17.56)	134,991 (8.314)	
50 - 59	1,529,693 (14)	25,002 (1.6)		657,692 (43)	728,708 (47.64)	143,293 (9.367)	
60 - 69	1,378,878 (13)	16,374 (1.2)		261,109 (18.94)	234,435 (17)	883,334 (64.06)	
70 - 79	871,403 (8.3)	7,977 (0.92)		121,430 (13.93)	49,119 (5.637)	700,854 (80.43)	
80 or more	473,526 (4.5)	4,299 (0.91)		82,238 (17.37)	27,428 (5.792)	363,860 (76.84)	
Comorbidities							
None	7,175,492 (68)	104,973 (1.5)	< 2.22e-16	5,067,879 (70.63)	1,008,253 (14.05)	1,099,360 (15.32)	< 2.22e-16
mayor 1	3,374,837 (32)	51,645 (1.5)		1,198,822 (35.52)	727,366 (21.55)	1,448,649 (42.93)	
Nationality							
Chilean	9,831,611 (93)	147,332 (1.5)	< 2.22e-16	5,656,466 (57.53)	1,667,500 (16.96)	2,507,645 (25.51)	< 2.22e-16
Foreigners	718,718 (6.8)	9,286 (1.3)		610,235 (84.91)	68,119 (9.478)	40,364 (5.616)	

Table 3: Sinovac vaccine effectiveness in preventing SARS-CoV-2 associated outcomes among FONASA affiliates by immunization status. Study period February 2nd to April 1st, 2021

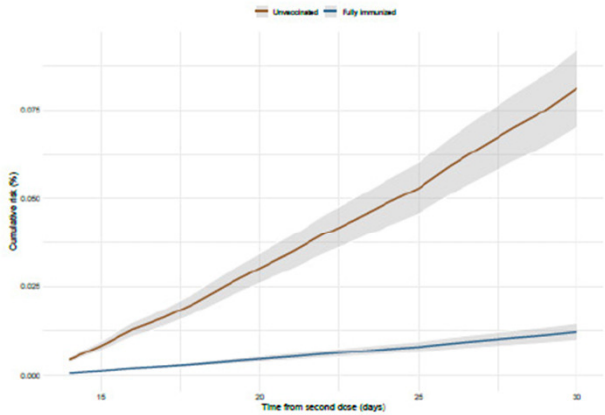
Immunization status	Person-days	No.	Incidence rate (1,000 person-days)	Effectiveness (%) Unadjusted (95% CI)	Adjusted[1] (95% CI)	Adjusted[2] (95% CI)
Infection						
Unvaccinated	469,466,302	158,925	0.338523	-	-	-
Partially immunized (≥ 14 days after first dose)	45,960,768	14,879	0.323733	19.89 (18.51 ; 21.24)	5.98 (4.17 ; 7.76)	15.25 (13.62 ; 16.85)
Fully immunized (≥ 14 days after second dose)	14,379,196	2,663	0.185198	65.21 (63.81 ; 66.54)	56.48 (54.63 ; 58.25)	62.55 (60.97 ; 64.07)
COVID-19						
Unvaccinated	470,339,828	122,948	0.261402	-	-	-
Partially immunized (≥ 14 days after first dose)	46,059,097	11,708	0.254195	19.02 (17.44 ; 20.56)	7.10 (5.07 ; 9.08)	16.13 (14.30 ; 17.92)
Fully immunized (≥ 14 days after second dose)	14,405,753	1,840	0.127727	68.34 (66.82 ; 69.80)	61.84 (59.90 ; 63.69)	66.96 (65.28 ; 68.55)
Hospitalization						
Unvaccinated	472,989,520	11,225	0.023732	-	-	
Partially immunized (≥ 14 days after first dose)	46,367,936	2,156	0.046498	-67.35 (-75.49 ; -59.60)	29.33 (25.48 ; 32.98)	35.65 (32.13 ; 38.99)
Fully immunized (≥ 14 days after second dose)	14,477,772	222	0.015334	52.42 (45.43 ; 58.51)	83.15 (80.58 ; 85.39)	84.84 (82.52 ; 86.85)
ICU hospitalization						
Unvaccinated	473,169,786	4,012	0.008479	-	-	-
Partially immunized (≥ 14 days after first dose)	46,425,723	671	0.014453	-40.52 (-52.79 ; -29.24)	35.51 (29.21 ; 41.25)	42.70 (37.07 ; 47.82)
Fully immunized (≥ 14 days after second dose)	14,484,537	46	0.003176	72.41 (62.91 ; 79.48)	87.12 (82.53 ; 90.50)	88.55 (84.46 ; 91.56)
Confirmed death						
Unvaccinated	473,241,713	1,069	0.002259	-	-	-
Partially immunized (≥ 14 days after first dose)	46,428,543	527	0.011351	-315.52 (-363.91 ; -272.17)	34.54 (26.30 ; 41.86)	40.22 (32.63 ; 46.97)
Fully immunized (≥ 14 days after second dose)	4,484,178	54	0.003728	-132.63 (-217.40 ; -70.51)	78.32 (70.29 ; 84.17)	80.44 (73.16 ; 85.75)

Adjusted[1] is the result based on the model including age and sex as predictors. Adjusted[2] is the result based on the model including age, gender, region, nationality, income, and comorbidities as predictors

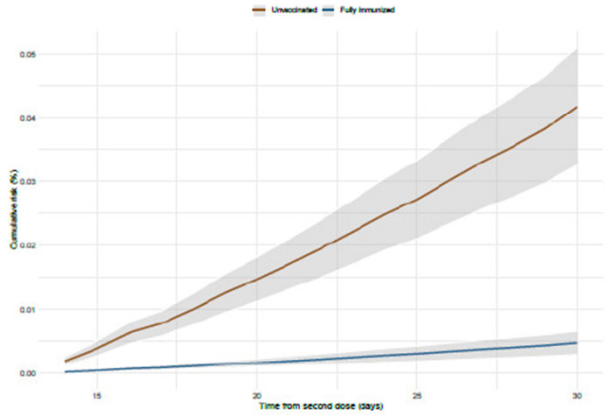
Fully immunized group



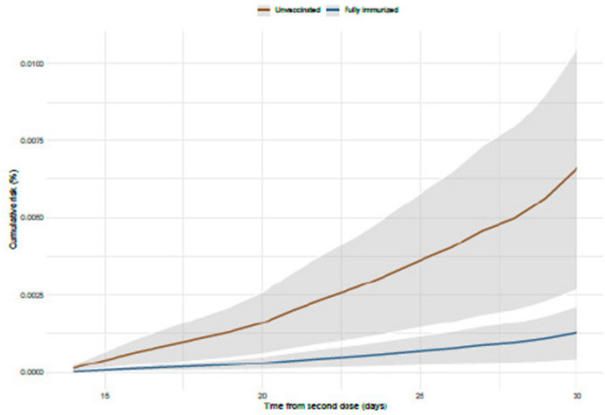
(a) Covid-19



(b) Hospitalization



(c) ICU hospitalization



(d) Confirmed death

SUMMARY OF RESULTS

EFFECTIVENESS OF CORONAVAC®
14 DAYS AFTER THE SECOND DOSE

67% (65% - 69%)	85% (83% - 87%)	89% (84% - 92%)	80% (73% - 86%)
Effectiveness to prevent **Symptomatic Covid-19**	Effectiveness to prevent **Hospital admission**	Effectiveness to prevent **ICU admission**	Effectiveness to prevent **Death**

Institución ▾ | Áreas ISP ▾ | Vigilancia Sanitaria ▾ | Productos y Servicios ▾ | Atención al Ciudadano ▾ | Normativa ▾ | Resoluciones

Buscador de contenidos

Inicio / Información y Medidas ISP COVID-19 / Notas Farmacovigilancia

Notas Farmacovigilancia

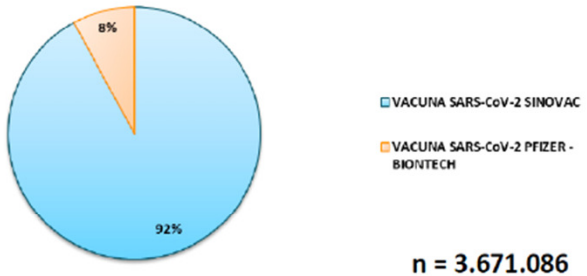
- Vacuna SARS-CoV-2 Chadox1-S recombinante de Astrazeneca y casos de eventos trombóticos combinados con Trombocitopenia
- Tercer Informe Estadístico: ESAVI serios asociados a la administración de las vacunas SARS-CoV-2 en Chile (24 diciembre 2020 - 02 marzo 2021)
- Reacciones anafilácticas asociadas a la administración de las vacunas SARS-CoV-2: Evaluación de reportes de ESAVI y recomendaciones para las vacunas PFIZER-Biontech y Coronavac
- Ficha Informativa Vacuna COVID-19 AstraZeneca
- Ficha Informativa Vacuna COVID-19 Pfizer-BioNTech
- Ficha informativa vacuna COVID-19 CoronaVac
- Segundo Informe Estadístico: ESAVI asociados a la administración de la vacuna SARS-CoV-2 en Chile
- Informe estadístico ESAVI asociados vacuna SARS-CoV
- Implementación de la Farmacovigilancia para las vacunas SARS-CoV-2 en Chile
- Orientación para la monitorización de efectos adversos en pacientes con COVID-19 en tratamientos con cloroquina o hidroxicloroquina
- Guidelines for monitoring adverse effects in covid-19 patients treated with chloroquine or hydroxychloroquine.

https://www.ispch.cl/isp-covid-19/notas-farmacovigilancia/

THIRD STATISTICAL REPORT –SAEs associated with CoronaVac®

December 20, 2020 – March 02, 2021

Number and proportion of doses according to the type of vaccine

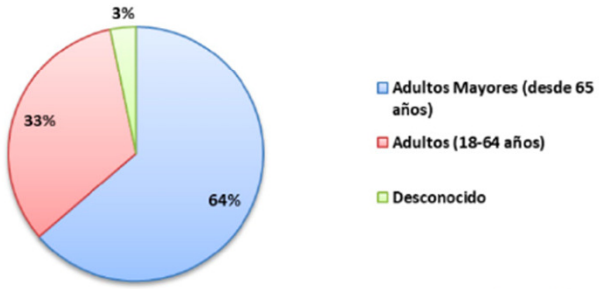


n = 3.671.086

Total number of doses	Total number of notifications	CoronaVac®	Pfizer-BioNTech	Unknown
3,672,086	4,677 (0.13)	1,911	2,553	213

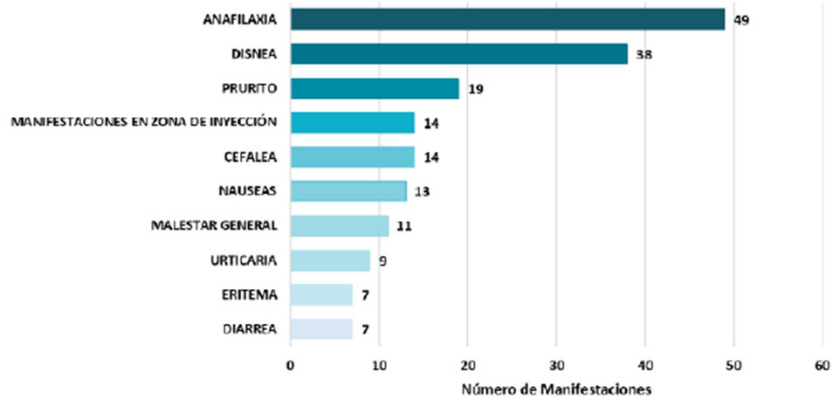
Total number of SAEs	CoronaVac®	Pfizer-BioNTech	Unknown
124	90 (2.67/100,000)	30 (10.26/100,000)	4

Proportion of SAEs according to age groups



n = 124

Most frequent clinical manifestations of SAEs with CoronaVac®



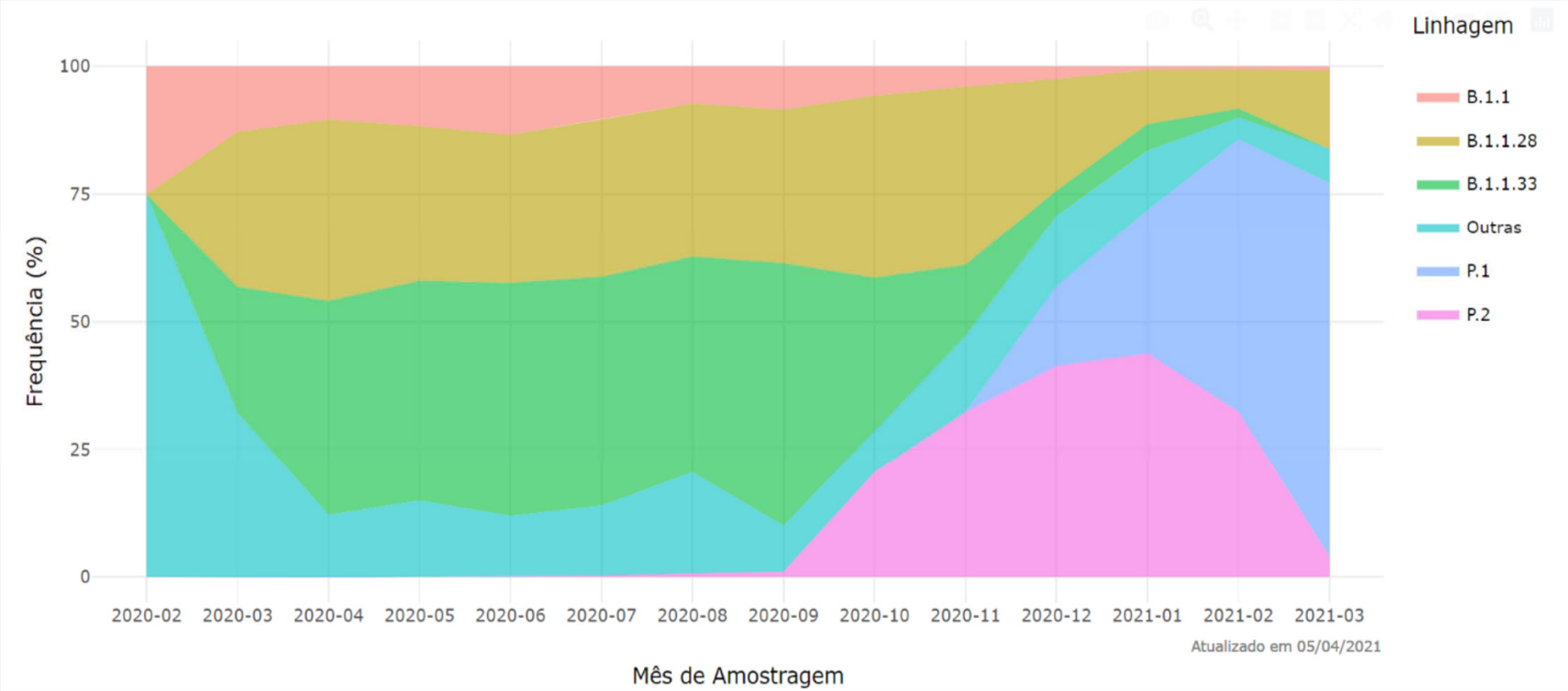
Sinovac Inactivated Vaccine Phase 4 studies in Brazil

Hitchings MDT, et al. Effectiveness of CoronaVac in the setting of high SARS-CoV-2 P.1 variant transmission in Brazil: A test-negative case-control study. 2021. April 7th https://www.medrxiv.org/content/10.1101/2021.04.07.21255081v1

de Faria, et al. Performance of vaccination with CoronaVac in a cohort of healthcare workers (HCW) - preliminary report. April 15th https://doi.org/10.1101/2021.04.12.21255308

Proportion of SARS-CoV2 samples tested by lineage, Brasil, 2020-2021

P1 accounted for 28% of samples in Jan 2021 → 73% of tested samples in March 2021



Source: Fiocruz, Genomahcov, March 2021

Hitchings MDT, et al. – Sinovac Effectiveness study, Manaus – Brazil, 2021

Objectives

- Effectiveness of at least one dose of Sinovac inactivated vaccine

Population

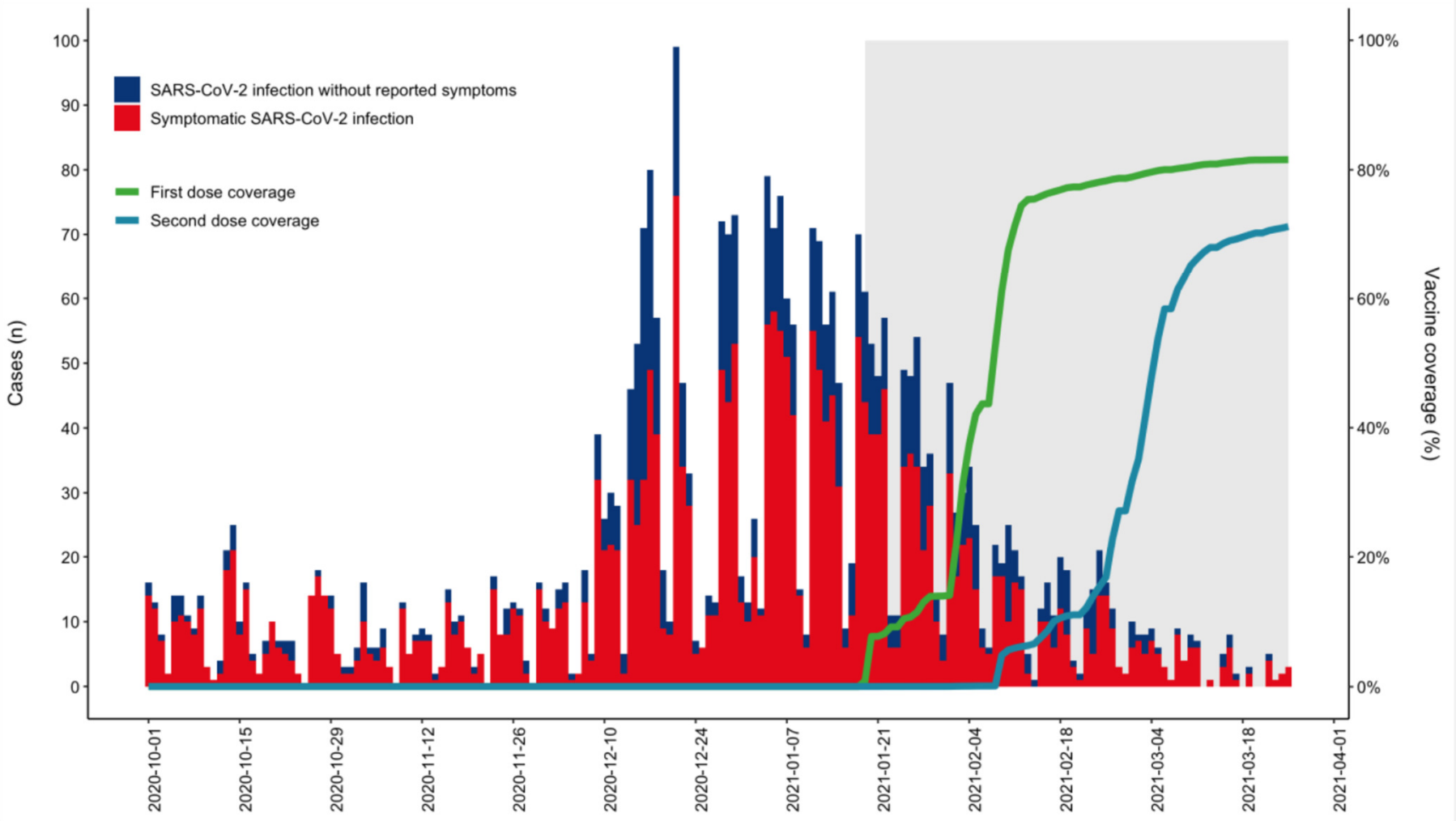
- Healthcare workers (HCW) working in Manaus
- Priority group for vaccination, Vaccine introduced in mid-Jan 2021

Study endpoints:

- Primary: Symptomatic SARS-CoV-2 infection during the period 14 days or more after receiving the first dose
- Secondary: all RT-PCR-confirmed SARS-CoV-2 infections

Test negative matched case control study

SARS-CoV-2 infections and vaccination coverage amongst 67,718 healthcare workers (HCW) in Manaus, Brazil. October 2020 to 25 March 2021.



Hitchings MDT, et al. – Test negative, Manaus
Main findings

53,176 eligible HCWs, 46,884 (88%) received at least one vaccine dose

393 case-control pairs with symptomatic illness

135 case-control pairs without symptomatic illness

Estimated effectiveness against symptomatic COVID-19 after at least one vaccine dose

- VE 49.6% (95% CI 11.3-71.4)

Not effective against SARS-COV2 infection without symptoms

- VE 35.1% (95% CI, -6.6 - 60.5)

Study limitations:

- no genotyping of cases
- pre-existing immunity prior to vaccination not evaluated

EVIDENCE ASSESSMENT: CoronaVac COVID-19 vaccine

Key evidence to inform policy recommendations on the use of CoronaVac

Protection against variants of concern

- Cross-neutralization studies suggest reduced neutralization against P.1 and “530” strain containing mutations D614G, N501Y, K417N, and E484K
- Interim efficacy against variants of concern could not be assessed in the Phase 3 clinical trials
- Two vaccine effectiveness studies have been conducted in the presence of circulating variants
  - Vaccine effectiveness in Manaus, Brazil, from 14 days after at least one dose was 49.6% (95%CI 11.3, 71.4) at a time when ~75% of genotyped viruses were P.1.
  - VE in Chile 14 days after two doses was 67% (95%CI 65,69). 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

EVIDENCE ASSESSMENT: CoronaVac COVID-19 vaccine

Key evidence to inform policy recommendations on the use of CoronaVac

Evidence gaps for policy

- Duration of protection, need for booster doses, and future risk of vaccine-associated enhanced disease
- Protection against variants of concern
- Safety in pregnancy
- Safety and clinical protection in people with older adults, those with underlying disease and other subpopulations
- Evaluation of rare adverse events detected through post-authorization safety monitoring

EVIDENCE ASSESSMENT: CoronaVac COVID-19 vaccine

Key evidence to inform policy recommendations on the use of CoronaVac

Ongoing/planned studies

- Continued follow up of trial participants:
  - 6 months follow up: Phase 1/2 trials, Phase 3 in Indonesia
  - 1 year follow up: Phase 3 trials in Brazil and Turkey
- Pediatric immunogenicity and safety in China
- Phase 4 vaccine effectiveness stepped wedge cluster-randomized trial in Brazil
- Other clinical studies assessing safety/immunogenicity in special populations such as persons living with HIV/AIDS, rheumatic disease, chronic liver disease, and breast and lung cancer receiving active chemotherapy
- Retrospective study of safety in pregnant and lactating women, including data on abortion, teratogenesis, fetal arrest, pregnancy and childbirth complications, and COVID-related outcomes
- Coadministration study with 23-valent pneumococcal polysaccharide vaccine and inactivated influenza vaccine

GRADEing of Evidence	Statement on quality of evidence	SAGE Working Group Judgement
Efficacy against PCR confirmed COVID-19 (Adults)	**High level of confidence**	We are very confident that 2 doses of CoronaVac are efficacious in preventing PCR confirmed COVID-19 in adults (18-59 years).
Safety-serious adverse events (Adults)	**Moderate level of confidence**	We are moderately confident that the risk of serious adverse events following one or two doses of CoronaVac in adults (18-59 years) is low.
Efficacy PCR confirmed COVID-19 (Older adults)	**Moderate level of confidence**	We are moderately confident that 2 doses of CoronaVac are efficacious in preventing PCR confirmed COVID-19 in older adults (≥60 years).
Safety-serious adverse events (Older adults)	**Low level of confidence**	We have low confidence in the quality of evidence that the risk of serious adverse events following one or two doses of CoronaVac in older adults (≥60 years) is low.
Efficacy PCR confirmed COVID-19 (*Individuals with comorbidities or health states that increase risk for severe COVID-19*)	**Moderate level of confidence**	We are moderately confident that 2 doses of CoronaVac are efficacious in preventing PCR confirmed COVID-19 in individuals with comorbidities or health states that increase risk for severe COVID-19 as included in the clinical trial.
Safety-serious adverse events (*Individuals with comorbidities or health states that increase risk for severe COVID-19*)	**Low level of confidence**	We have low confidence in the quality of evidence that the risk of serious adverse events in individuals with comorbidities or health states that increase risk for severe COVID-19 following one or two doses of CoronaVac is low.