Supplementary appendix

Supplement to: Effectiveness of the CoronaVac vaccine in older adults population during a Gamma variant-associated epidemic of COVID-19 in Brazil: test-negative case-control study

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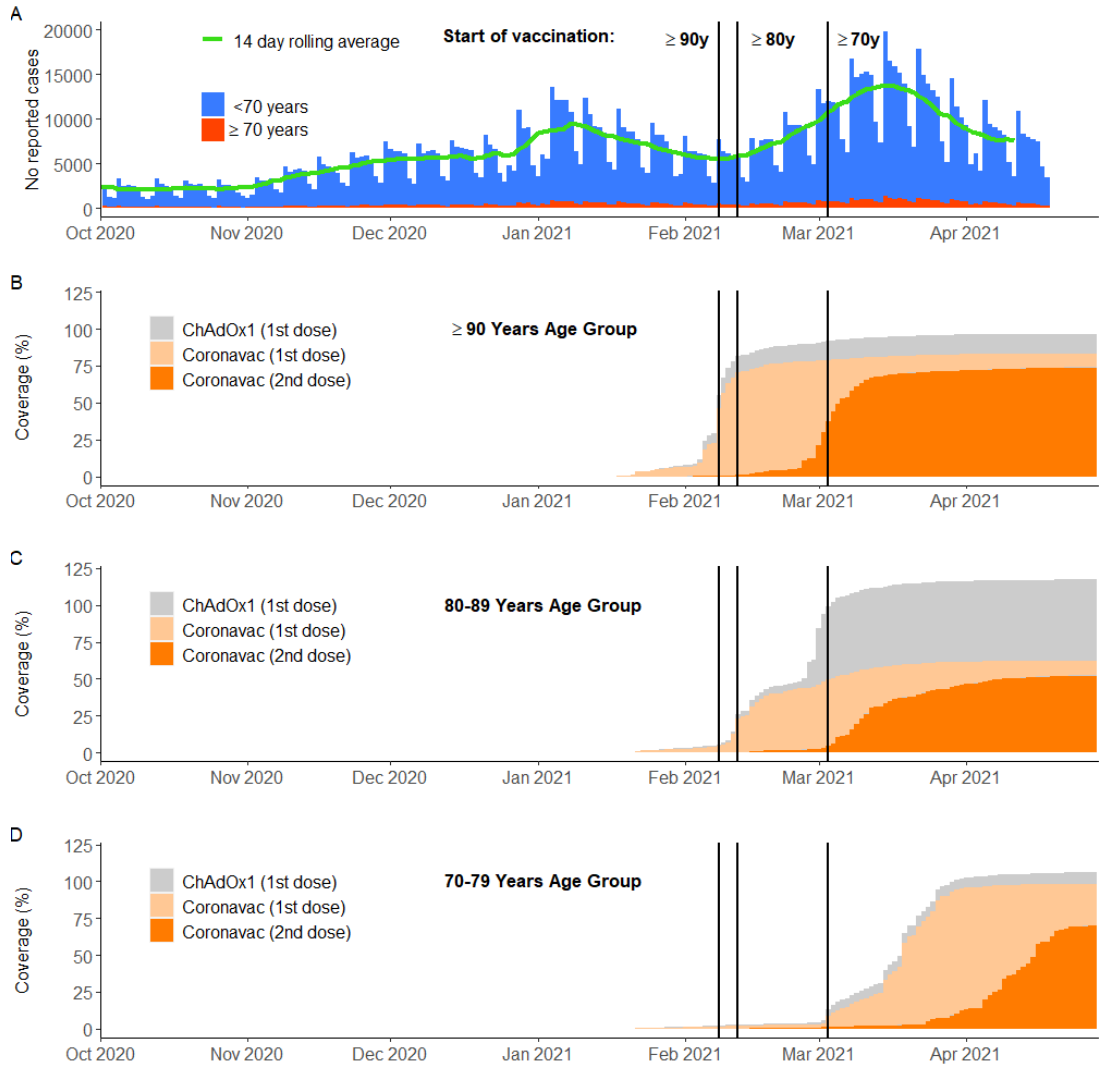
Supplementary Table 1. **Data sources description**

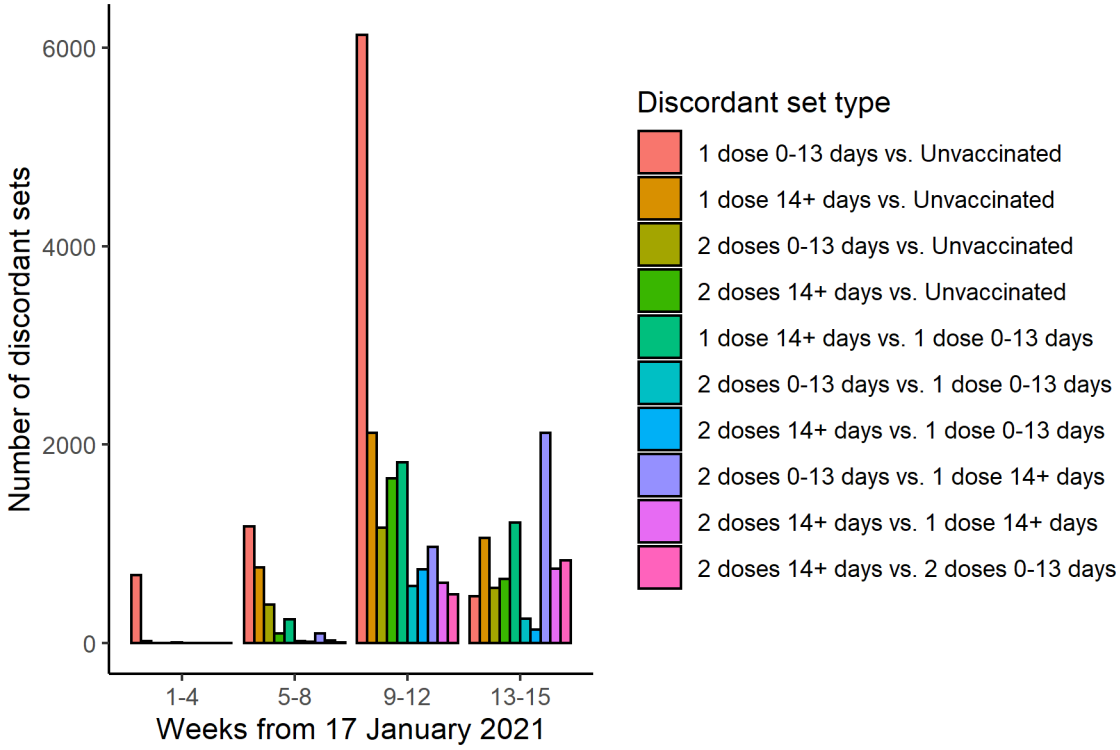
Database acronym	**Domain**	**Comment**
“Vacina Já”	State COVID-19 vaccination registry	The state vaccination system transfers the data daily to the National Immunization System (SIPNI)
SIVEP-Gripe (“Sistema de Informação da Vigilância Epidemiológica da Gripe”)	National surveillance database of severe acute respiratory illnesses	Contains all COVID-19 suspected or confirmed hospitalizations and deaths. In São Paulo State, there is a protocol for RT-PCR post-mortem SARS-CoV-2 testing for suspected COVID-19 deaths that are also notified to SIVEP-Gripe.
e-SUS	National surveillance system of suspected cases of COVID-19 from mild to moderate "influenza like illness"	Notifications from primary health care and specialty outpatient visits.
GAL (“Gerenciador de Ambiente Laboratorial”)	State laboratory testing registry of the network of public health laboratories	In São Paulo State, diagnostic tests performed in GAL is already imputed in eSUS-VE or SIVEP-Gripe, increasing the coverage of e-SUS and SIVEP-Gripe

Supplementary Figure 1**. Daily cases of COVID-19 and cumulative vaccination coverage from Oct 01, 2020 to Apr 29, 2021 in São Paulo State, Brazil**

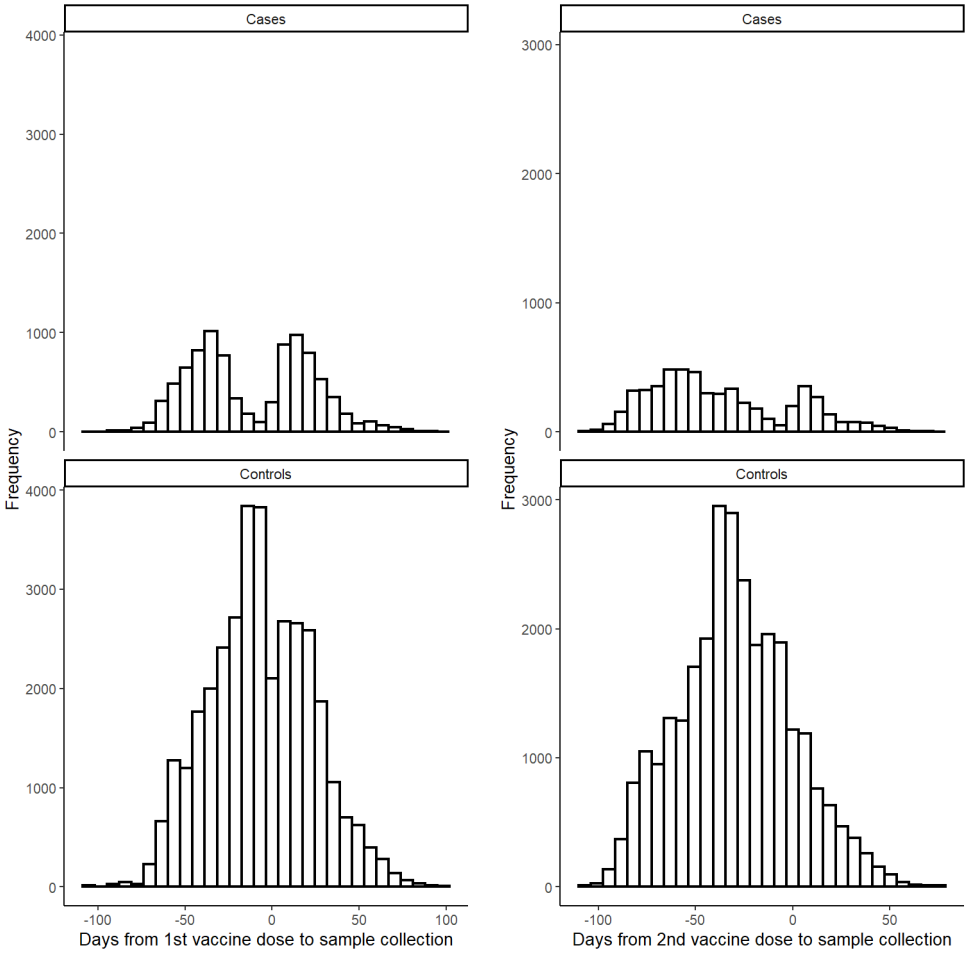
Panel A shows the daily cases of reported COVID-19 from Oct 01, 2020 to Apr 29, 2021 in São Paulo State, Brazil, with the green line representing the 14-day roling average of counts. Panels B, C and D show the cumulative vaccination coverage for age groups >90y, 80y-89y, and 70y-79y, respectively. Population estimates for age groups were obtained from national projections for 2020. Vertical bars, from left to right in each panel, show the dates that adults ≥90, 80-89 and 70-79 years of age in the general population became eligible for vaccination.



Supplementary Figure 2. **Timing of enrolment of case-control sets with discordant cases and controls by vaccination category**



Supplementary Figure 3. **Timing of RT-PCR sample collection date relative to first (left column) and second (right column) vaccine dose date, among cases (top row) and controls (bottom row) who were vaccinated during the study period.**



Supplementary Table 2**. Distribution of matched case-control sets with discordant case and control vaccine status.**

	Case vaccine status				
Vaccine status of at least one control in matched set	Unvaccinated	Single dose, dose 1 within 0-13 days	Single dose, dose 1 ≥14 days	Two doses, dose 2 within 0-13 days	Two doses, dose 2 ≥14 days
Unvaccinated	8,370	996	587	232	190
Single dose, dose 1 within 0-13 days	1,320	1,036	476	74	39
Single dose, dose 1 ≥14 days	635	521	1,029	383	185
Two doses dose 2 within 0-13 days	339	158	502	440	158
Two doses, dose 2 ≥14 days	407	152	224	232	412

Supplementary Table 3. **Characteristics of adults ≥70 years of age who were eligible for matching and selected into case-test negative pairs for the hospitalisation analysis.**

	Eligible cases and controls		Matched pairs	
Characteristics*	**Test-negative (n=17,622)^**	**Test-positive (n=26,433)^**	**Controls (n=23,265)^**	**Cases (n=7,043)^**
Demographics				
Age, mean (SD), years	77.53 (6.78)	76.71 (6.19)	76.47 (5.87)	76.83 (6.12)
Age categories, n (%)				
70-79 years	12,123 (68.8)	19,673 (74.4)	17639 (75.8)	5191 (73.7)
80-89 years	4,301 (24.4)	5,437 (20.6)	4801 (20.6)	1519 (21.6)
≥90 years	1,198 (6.8)	1,323 (5.0)	825 (3.5)	333 (4.7)
Male sex, n (%)	7,689 (43.6)	12,431 (47.0)	10972 (47.2)	3380 (48.0)
Self-reported race[†], n (%)'				
White/Branca	13,415 (76.1)	19,796 (74.9)	19251 (82.7)	5742 (81.5)
Brown/Pardo	3,192 (18.1)	4,983 (18.9)	3530 (15.2)	1077 (15.3)
Black/Preta	785 (4.5)	1,258 (4.8)	404 (1.7)	165 (2.3)
Yellow/ Amarela	226 (1.3)	390 (1.5)	80 (0.3)	59 (0.8)
Indigenous/Indigena	4 (0.0)	6 (0.0)	-	-
Residence in "Grande São Paulo" Health Region, n (%)	12,381 (70.3)	16,538 (62.6)	6166 (26.5)	2613 (37.1)
Comorbidities				
Reported number[‡], n (%)				
None	10,027 (56.9)	12,668 (47.9)	12948 (55.7)	1986 (28.2)
One or two	6,984 (39.6)	12,548 (47.5)	9375 (40.3)	4461 (63.3)
Three or more	611 (3.5)	1,217 (4.6)	942 (4.0)	596 (8.5)
Cardiovascular disease , n (%)	5,293 (30.0)	10,079 (38.1)	7035 (30.2)	3813 (54.1)
Diabetes, n (%)	3,233 (18.3)	6,533 (24.7)	4525 (19.4)	2508 (35.6)
Prior SARS-CoV-2 exposure[**]				

Previous symptomatic events notified to the surveillance systems**, n (%)	685 (3.9)	354 (1.3)	18 (0.1)	15 (0.2)
Positive SARS-CoV-2 test result [††], n (%)	66 (0.4)	13 (0.0)	0 (0.0)	2 (0.0)
Interval between symptoms onset and RT-PCR testing, median (p25-p75), days	3 [2-5]	4 [2-6]	3 [1-5]	4 [2-6]
Hospitalisations, n (%)	4,524/17,484 (25.9)	12,987/26,221 (49.5)	6,767/23,148 (29.2)	7,043/7,043 (100)
Deaths, n (%)	1,594/16,710 (9.5)	7,054/24,508 (28.8)	2,527/21,915 (11.5)	3,369/6,057 (55.6)
Interval between symptoms onset and hospitalization, median (p25-p75), days	3 [2-6]	7 [4-10]	4 [2-7]	7 [4-10]
Interval between symptoms onset and deaths, median (p25-p75), days	8 [4-13]	14 [9-21]	8 [4-16]	16 [10-22]
Vaccination status				
Not vaccinated, n (%)	11,986 (68.0)	17,233 (65.2)	14583 (62.7)	4583 (65.1)
Single dose, within 0-13 days, n (%)	1,446 (8.2)	2,976 (11.3)	2926 (12.6)	897 (12.7)
Single dose, ≥14 days, n (%)	1,797 (10.2)	3,312 (12.5)	2723 (11.7)	855 (12.1)
Two doses, within 0-13 days, n (%)	1,041 (5.9)	1,533 (5.8)	1449 (6.2)	361 (5.1)
Two doses, ≥14 days, n (%)	1,352 (7.7)	1,379 (5.2)	1584 (6.8)	347 (4.9)
Interval between first and second dose, mean (SD), days	25 (6)	30 (12)	25 (7)	29 (12)
Interval between first dose and RT-PCR testing, mean (SD), days	28 (19)	23 (16)	23 (17)	22 (17)
Interval between second dose and RT-PCR testing, mean (SD), days	20 (15)	17 (14)	18 (15)	18 (15)

*Continuous variables are displayed as mean (SD); categorical variables are displayed as n (%).

^These numbers refer to RT-PCR tests and represent 43,774 individuals for the eligible cases and controls and 13,716 individuals in the matched cases and controls.

[†]Race/skin colour as defined by the Brazilian national census bureau (Instituto Nacional de Geografia e Estatísticas).

[‡]Comorbidities included: cardiovascular, renal, neurological, haematological, or hepatic comorbidities, diabetes, chronic respiratory disorder, obesity, or immunosuppression.

[**]Prior to the start of the study on 17 January, 2021 and after systematic surveillance was implemented on 1 February, 2020.

** Reported illness with COVID-19 associated symptoms in the eSUS and SIVEP-Gripe databases.

[††] Defined as a positive SARS-CoV-2 RT-PCR or antigen detection test result.

Supplementary Table 4. **Characteristics of adults ≥70 years of age who were eligible for matching and selected into case-test negative pairs for the death analysis.**

	Eligible cases and controls		Matched pairs	
Characteristics*	**Test-negative (n=17,622)^**	**Test-positive (n=26,433)^**	**Controls (n=11,075)^**	**Cases (n=3,549)^**
Demographics				
Age, mean (SD), years	77.53 (6.78)	76.71 (6.19)	76.91 (6.06)	77.31 (6.29)
Age categories, n (%)				
70-79 years	12,123 (68.8)	19,673 (74.4)	8079 (72.9)	2522 (71.1)
80-89 years	4,301 (24.4)	5,437 (20.6)	2556 (23.1)	834 (23.5)
≥90 years	1,198 (6.8)	1,323 (5.0)	440 (4.0)	193 (5.4)
Male sex, n (%)	7,689 (43.6)	12,431 (47.0)	5614 (50.7)	1796 (50.6)
Self-reported race[†], n (%)'				
White/Branca	13,415 (76.1)	19,796 (74.9)	9051 (81.7)	2882 (81.2)
Brown/Pardo	3,192 (18.1)	4,983 (18.9)	1747 (15.8)	538 (15.2)
Black/Preta	785 (4.5)	1,258 (4.8)	242 (2.2)	97 (2.7)
Yellow/ Amarela	226 (1.3)	390 (1.5)	35 (0.3)	32 (0.9)
Indigenous/Indigena	4 (0.0)	6 (0.0)	-	-
Residence in "Grande São Paulo" Health Region, n (%)	12,381 (70.3)	16,538 (62.6)	3242 (29.3)	1441 (40.6)
Comorbidities				
Reported number[‡], n (%)				
None	10,027 (56.9)	12,668 (47.9)	6078 (54.9)	910 (25.6)
One or two	6,984 (39.6)	12,548 (47.5)	4557 (41.1)	2273 (64.0)
Three or more	611 (3.5)	1,217 (4.6)	440 (4.0)	366 (10.3)
Cardiovascular disease , n (%)	5,293 (30.0)	10,079 (38.1)	3367 (30.4)	1986 (56.0)
Diabetes, n (%)	3,233 (18.3)	6,533 (24.7)	2183 (19.7)	1313 (37.0)
Prior SARS-CoV-2 exposure[**]				

Previous symptomatic events notified to the surveillance systems**, n (%)	685 (3.9)	354 (1.3)	8 (0.1)	8 (0.2)
Positive SARS-CoV-2 test result [††], n (%)	66 (0.4)	13 (0.0)	0 (0.0)	1 (0.0)
Interval between symptoms onset and RT-PCR testing, median (p25-p75), days	3 [2-5]	4 [2-6]	3 [1-5]	4 [2-6]
Hospitalisations, n (%)	4,524/17,484 (25.9)	12,987/26,221 (49.5)	645/2,035 (31.7)	1,939/2,025 (95.8)
Deaths, n (%)	1,594/16,710 (9.5)	7,054/24,508 (28.8)	255/1,940 (13.1)	2,052/2,052 (100)
Interval between symptoms onset and hospitalization, median (p25-p75), days	3 [2-6]	7 [4-10]	4 [2-7]	7 [4-10]
Interval between symptoms onset and deaths, median (p25-p75), days	8 [4-13]	14 [9-21]	8 [4-15]	15 [10-22]
Vaccination status				
Not vaccinated, n (%)	11,986 (68.0)	17,233 (65.2)	7022 (63.4)	2373 (66.9)
Single dose, within 0-13 days, n (%)	1,446 (8.2)	2,976 (11.3)	1430 (12.9)	455 (12.8)
Single dose, ≥14 days, n (%)	1,797 (10.2)	3,312 (12.5)	1305 (11.8)	414 (11.7)
Two doses, within 0-13 days, n (%)	1,041 (5.9)	1,533 (5.8)	648 (5.9)	159 (4.5)
Two doses, ≥14 days, n (%)	1,352 (7.7)	1,379 (5.2)	670 (6.0)	148 (4.2)
Interval between first and second dose, mean (SD), days	25 (6)	30 (12)	25 (7)	23 (5)
Interval between first dose and RT-PCR testing, mean (SD), days	28 (19)	23 (16)	23 (17)	21 (16)
Interval between second dose and RT-PCR testing, mean (SD), days	20 (15)	17 (14)	18 (15)	18 (14)

*Continuous variables are displayed as mean (SD); categorical variables are displayed as n (%).

^These numbers refer to RT-PCR tests and represent 43,774 individuals for the eligible cases and controls and 8,581 individuals in the matched cases and controls.

[†]Race/skin colour as defined by the Brazilian national census bureau (Instituto Nacional de Geografia e Estatísticas).

[‡]Comorbidities included: cardiovascular, renal, neurological, haematological, or hepatic comorbidities, diabetes, chronic respiratory disorder, obesity, or immunosuppression.

[**]Prior to the start of the study on 17 January, 2021 and after systematic surveillance was implemented on 1 February, 2020.

** Reported illness with COVID-19 associated symptoms in the eSUS and SIVEP-Gripe databases.

[††] Defined as a positive SARS-CoV-2 RT-PCR or antigen detection test result.

Supplementary Table 5. **Sensitivity analysis for the bias indicator period expanding from 0-13 days to 0-6 and 7-13 days after first dose**

	Bias indicator 0-13 days after first dose				**Bias indicator 0-6 / 7-13 days after first dose**		
	OR (95% CI)^	**VE (95% CI)^**	**p-value^**		**OR (95% CI)^**	**VE (95% CI)^**	**p-value^**
Symptomatic COVID-19 (n=55,519)							
Single dose, within 0-13 days vs. unvaccinated*	1.01 (0.93-1.09)	-0.8% (-9.4-7.2)	0.86	Single dose, within 0-6 days vs. unvaccinated*	0.88 (0.79-0.99)	11.6% (1.5-20.7)	0.03
				Single dose, within 7-13 days vs. unvaccinated*	1.13 (1.02-1.25)	-12.9% (-25--2)	0.02
COVID-19 associated hospitalisations (n=30,308)							
Single dose, within 0-13 days vs. unvaccinated*	0.93 (0.84-1.04)	6.6% (-4.3-16.3)	0.23	Single dose, within 0-6 days vs. unvaccinated*	0.76 (0.66-0.89)	23.7% (11.4-34.3)	<0.001
				Single dose, within 7-13 days vs. unvaccinated*	1.10 (0.96-1.26)	-10.1% (-25.9-3.7)	0.16
COVID-19 associated deaths (n=14,624)							
Single dose, within 0-13 days vs. unvaccinated*	0.87 (0.74-1.02)	13.1% (-1.5-25.6)	0.08	Single dose, within 0-6 days vs. unvaccinated*	0.75 (0.61-0.93)	24.6% (7-38.9)	0.008
				Single dose, within 7-13 days vs. unvaccinated*	0.98 (0.81-1.18)	2.4% (-18-19.3)	0.80

*At date of index sample collection for cases and controls.

^ Models adjusted by age (linear term for symptomatic and restricted cubic spline for hospitalisation and deaths) and number of comorbidities (None, One or Two, Three or more)

Supplementary Table 6. **Adjusted effectiveness of CoronaVac during the period ≥14 days after the second CoronaVac dose for subgroups of adults ≥70 years of age.**

Outcome	OR (95% CI)	VE (95% CI)	p-value for interaction
Symptomatic COVID-19 (n=55,519)			
70-74 (n=29,824)	0.41 (0.30-0.56)	59.0% (43.7-70.2)	0.007
75-79 (n=14,853)	0.44 (0.34-0.57)	56.2% (43.0-66.3)	
80+ (n=10,842)	0.67 (0.55-0.83)	32.7% (17.0-45.5)	
Hospitalisations (n=30,308)			
70-74 (n=14,402)	0.22 (0.13-0.38)	77.6% (62.5-86.7)	<0.001
75-79 (n=8,428)	0.33 (0.23-0.48)	66.6% (51.8-76.9)	
80+ (n=7,478)	0.61 (0.48-0.79)	38.9% (21.4-52.5)	
Deaths (n=14,624)			
70-74 (n=6,408)	0.16 (0.06-0.41)	83.9% (59.2-93.7)	0.001
75-79 (n=4,193)	0.22 (0.12-0.41)	78.0% (58.8-88.3)	
80+ (n=4,023)	0.56 (0.39-0.80)	44.0% (20.3-60.6)	

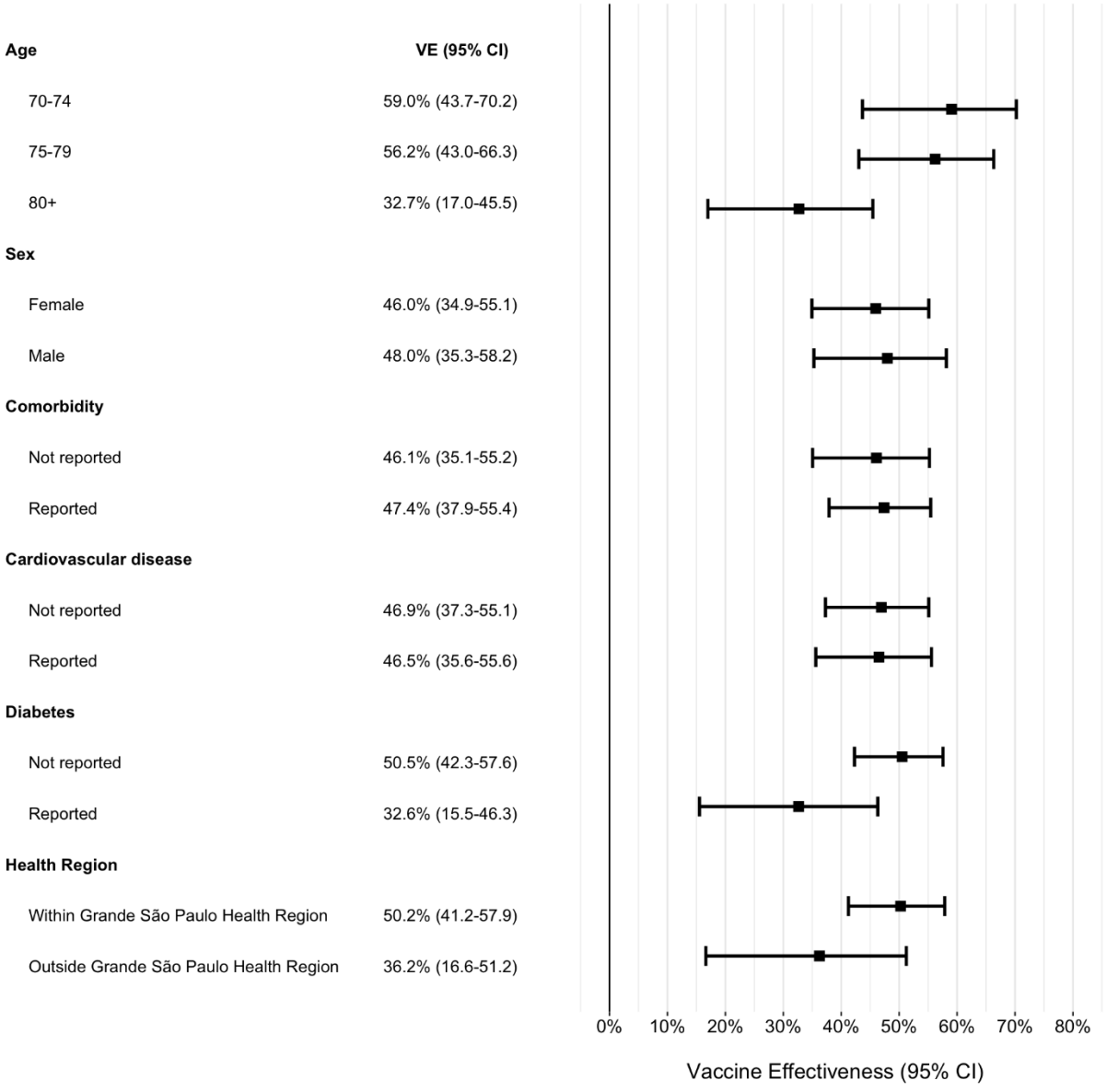
Estimates of vaccine effectiveness were obtained from a conditional logistic regression model that included covariates of age and the number of comorbidities and incorporated an interaction term between the category of interest and the period ≥14 days after the second CoronaVac dose.

Supplementary Table 7**. Adjusted effectiveness of CoronaVac against symptomatic COVID-19 ≥14 days after the second dose, in subgroups of adults ≥70 years of age.**

Subgroup	Adjusted OR (95% CI)	Adjusted VE (95% CI)	p-value for interaction
Age			
70-74 (n=29,824)	0.41 (0.30-0.56)	59.0% (43.7-70.2)	0.007
75-79 (n=14,853)	0.44 (0.34-0.57)	56.2% (43.0-66.3)	
80+ (n=10,842)	0.67 (0.55-0.83)	32.7% (17.0-45.5)	
Sex			
Females (n=30,990)	0.54 (0.449-0.651)	46.0% (34.9-55.1)	0.37
Males (n=24,529)	0.52 (0.418-0.647)	48.0% (35.3-58.2)	
Comorbidities			
No reported (n=29,847)	0.54 (0.45-0.65)	46.1% (35.1-55.2)	0.85
Reported (n=25,672)	0.53 (0.45-0.62)	47.4% (37.9-55.4)	
Cardiovascular disease			
No reported (n=37,474)	0.53 (0.45-0.63)	46.9% (37.3-55.1)	0.93
Reported (n=18,045)	0.54 (0.44-0.64)	46.5% (35.6-55.6)	
Diabetes			
No reported (n=43,672)	0.50 (0.42-0.58)	50.5% (42.3-57.6)	0.008
Reported (n=11,847)	0.67 (0.54-0.85)	32.6% (15.5-46.3)	
Health regional area			
“Grande São Paulo” (n=35,038)	0.50 (0.42-0.59)	50.2% (41.2-57.9)	0.31
Not “Grande São Paulo” (n=20,481)	0.64 (0.49-0.83)	36.2% (16.6-51.2)	

All models are adjusted by age (continuous) and number of comorbidities, and include an interaction term between the subgroup of interest and vaccinations with 2 doses, ≥14 days after second vaccine dose.

Supplementary Figure 4**. Adjusted effectiveness of CoronaVac against symptomatic COVID-19 ≥14 days after the second CoronaVac dose for other subgroups of adults ≥70 years of age.**



Estimates of vaccine effectiveness were obtained from a conditional logistic regression model that included covariates of age (continuous) and the number of comorbidities and incorporated an interaction term between the category of interest and the period ≥14 days after the second CoronaVac dose.

Supplementary Table 8. Detailed description of **effectiveness of CoronaVac against the composite outcome hospitalisations or deaths in adults ≥70 years of age**

	Unadjusted Analysis			Adjusted Analysis^		
COVID-19 associated hospitalizations or deaths (n=30,944)	**OR (95% CI)**	**VE (95% CI)**	**p-value**	**OR (95% CI)**	**VE (95% CI)**	**p-value**
Single dose, within 0-13 days vs. unvaccinated*	0.98 (0.88-1.09)	2.1% (-8.6-11.8)	0.69	0.93 (0.84-1.04)	6.7% (-4-16.3)	0.21
Single dose, ≥14 days vs. unvaccinated*	0.87 (0.77-0.9 8)	13.3% (2.2-23.1)	0.02	0.83 (0.73-0.94)	17.5% (6.5-27.3)	0.003
Two doses, within 0-13 days vs. unvaccinated*	0.65 (0.56-0.76)	34.8% (23.7-44.3)	<0.001	0.61 (0.52-0.72)	39.2% (28.3-48.4)	<0.001
Two doses, ≥14 days vs. unvaccinated*	0.48 (0.40-0.57)	51.9% (42.8-59.6)	<0.001	0.45 (0.37-0.54)	55.4% (46.5-62.8)	<0.001

^Adjusted for age (continuous) and the number of comorbidities.

Supplementary Table 9. **General characteristics of the matched sample according to main and sensitivity analyses.**

	Main Analysis (1:5, unbalanced, with replacement)		**Sensitivity Analysis 1 (1:1 without replacement)**		**Sensitivity Analysis 2 (1:1 with replacement)**		**Sensitivity Analysis 3 (1:2 with replacement)**	
Characteristics*	**Controls (n=42,236)**	**Cases (n=13,283)**	**Controls (n=7,950)**	**Cases (n=7,950)**	**Controls (n=13,283)**	**Cases (n=13,283)**	**Controls (n=18,804)**	**Cases (n=9,402)**
Demographics								
Age, mean (SD), years	75.69 (5.44)	75.90 (5.64)	76.15 (5.8)	76.15 (5.8)	75.92 (5.67)	75.90 (5.64)	75.77 (5.56)	75.78 (5.52)
Age categories, n (%)								
70-79 years	34134 (80.8)	10543 (79.4)	6,150 (77.4)	6,150 (77.4)	10543 (79.4)	10543 (79.4)	15064 (80.1)	7532 (80.1)
80-89 years	7045 (16.7)	2311 (17.4)	1,510 (19.0)	1,510 (19.0)	2311 (17.4)	2311 (17.4)	3200 (17.0)	1600 (17.0)
≥90 years	1057 (2.5)	429 (3.2)	290 (3.6)	290 (3.6)	429 (3.2)	429 (3.2)	540 (2.9)	270 (2.9)
Male sex, n (%)	18610 (44.1)	5919 (44.6)	3,276 (41.2)	3,276 (41.2)	5919 (44.6)	5919 (44.6)	8258 (43.9)	4129 (43.9)
Self-reported race[†], n (%)[ˈ]								
White/Branca	34603 (81.9)	10803 (81.3)	6,420 (80.8)	6,420 (80.8)	10803 (81.3)	10803 (81.3)	15460 (82.2)	7730 (82.2)
Brown/Pardo	6797 (16.1)	2115 (15.9)	1,301 (16.4)	1,301 (16.4)	2115 (15.9)	2115 (15.9)	2970 (15.8)	1485 (15.8)
Black/Preta	727 (1.7)	287 (2.2)	191 (2.4)	191 (2.4)	287 (2.2)	287 (2.2)	338 (1.8)	169 (1.8)
Yellow/ Amarela	109 (0.3)	78 (0.6)	38 (0.5)	38 (0.5)	78 (0.6)	78 (0.6)	36 (0.2)	18 (0.2)
Indigenous/Indigena	-	-	-	-	-	-	-	-
Residence in “Grande São Paulo” Health Region, n (%)	14368 (34.0)	6113 (46.0)	4,259 (53.6)	4,259 (53.6)	6113 (46.0)	6113 (46.0)	6752 (35.9)	3376 (35.9)
Comorbidities								
Reported number[‡], n (%)								
None	23961 (56.7)	5886 (44.3)	4,510 (56.7)	3,564 (44.8)	7574 (57.0)	5886 (44.3)	10621 (56.5)	4090 (43.5)
One or two	16626 (39.4)	6713 (50.5)	3,151 (39.6)	3,994 (50.2)	5267 (39.7)	6713 (50.5)	7453 (39.6)	4781 (50.9)
Three or more	1649 (3.9)	684 (5.1)	289 (3.6)	392 (4.9)	442 (3.3)	684 (5.1)	730 (3.9)	531 (5.6)
Cardiovascular disease , n (%)	12563 (29.7)	5482 (41.3)	2,375 (29.9)	3,252 (40.9)	3861 (29.1)	5482 (41.3)	5646 (30.0)	3955 (42.1)
Diabetes, n (%)	8269 (19.6)	3578 (26.9)	1,314 (19.0)	2,092 (26.3)	2518 (19.0)	3578 (26.9)	3655 (19.4)	2601 (27.7)
Prior SARS-CoV-2 exposure[**]								
Previous symptomatic events notified to the surveillance systems**, n (%)	47 (0.1)	37 (0.3)	35 (0.4)	35 (0.4)	37 (0.3)	37 (0.3)	14 (0.1)	7 (0.1)

Positive SARS-CoV-2 test result [††], n (%)	1 (0.0)	4 (0.0)	1 (0.0)	4 (0.1)	1 (0.0)	4 (0.0)	-	-
Interval between symptoms onset and RT-PCR testing, median (p25-p75), days	3 [1-5]	4 [2-6]	3 [1-5]	4 [2-6]	3 [2- 5]	4 [2- 6]	3 [1-5]	4 [2-6]
Hospitalisations, n (%)	11,020/41,980 (26.3)	7,043/13,175 (53.5)	2,065/7,889 (26.2)	4,039/7,883 (51.2)	3,488/13,196 (26.4)	7,043/13,175 (53.5)	4,923/18,704 (26.3)	5,171/9,330 (55.4)
Deaths, n (%)	4,072/40,134 (10.1)	3,549/12,251 (29.0)	729/7,557 (9.6)	2,052/7,359 (27.9)	1,301/12,630 (10.3)	3,549/12,251 (29.0)	1,790/17,873 (10.0)	2,491/8,607 (28.9)
Interval between symptoms onset and hospitalization, median (p25-p75), days	4 [2-7]	7[4-10]	3 [2-6]	7 [4-10]	3 [2-6]	7 [4- 10]	4 [2-7]	7 [4-11]
Interval between symptoms onset and deaths, median (p25-p75), days	8 [4-16]	15 [10-22]	8 [4-15]	15 [10-22]	8 [4- 16]	15 [10- 22]	8 [4- 16]	16 [10- 23]
Vaccination status								
Not vaccinated, n (%)	27994 (66.3)	8989 (67.7)	5,485 (69.0)	5,561 (69.9)	8817 (66.4)	8989 (67.7)	12586 (66.9)	6378 (67.8)
Single dose, within 0-13 days, n (%)	4873 (11.5)	1565 (11.8)	747 (9.4)	762 (9.6)	1515 (11.4)	1565 (11.8)	2106 (11.2)	1138 (12.1)
Single dose, ≥14 days, n (%)	4631 (11.0)	1489 (11.2)	843 (10.6)	851 (10.7)	1457 (11.0)	1489 (11.2)	2005 (10.7)	1003 (10.7)
Two doses, within 0-13 days, n (%)	2445 (5.8)	700 (5.3)	437 (5.5)	421 (5.3)	782 (5.9)	700 (5.3)	1063 (5.7)	493 (5.2)
Two doses, ≥14 days, n (%)	2293 (5.4)	540 (4.1)	438 (5.5)	355 (4.5)	712 (5.4)	540 (4.1)	1044 (5.6)	390 (4.1)
Interval between first and second dose, mean (SD), days	25 (6)	30 (12)	25 (6)	29 (11)	25 (6)	30 (12)	25 (7)	30 (12)
Interval between first dose and RT-PCR testing, mean (SD), days	22 (17)	21 (16)	24 (17)	23 (16)	23 (16)	21 (16)	23 (17)	21 (16)
Interval between second dose and RT-PCR testing, mean (SD), days	17 (14)	16 (14)	18 (15)	17 (14)	17 (14)	16 (14)	17 (14)	17 (14)

*Continuous variables are displayed as mean (SD); categorical variables are displayed as n (%).
[†]Race/skin colour as defined by the Brazilian national census bureau (Instituto Nacional de Geografia e Estatísticas).
[‡]Comorbidities included: cardiovascular, renal, neurological, haematological, or hepatic comorbidities, diabetes, chronic respiratory disorder, obesity, or immunosuppression.
[**]Prior to the start of the study on 17 January, 2021 and after systematic surveillance was implemented on 1 February, 2020.
** Reported illness with COVID-19 associated symptoms in the eSUS and SIVEP-Gripe databases.
[††] Defined as a positive SARS-CoV-2 RT-PCR or antigen detection test result.

Supplementary Table 10. **Summary of effectiveness of CoronaVac against symptomatic COVID-19 of the main analysis and three sensitivity analyses for the matching procedure**

	Main analysis (1:5, unbalanced, with replacement)	**Sensitivity Analysis 1 (1:1 without replacement)**	**Sensitivity Analysis 2 (1:1 with replacement)**	**Sensitivity Analysis 3 (1:2 with replacement)**
Characteristics				
Matching	Age 5 years, sex, self-reported race, municipality, ±3 days of RT-PCR test	Age 5 years, sex, self-reported race, municipality, ±3 days of RT-PCR test	Age 5 years, sex, self-reported race, municipality, ±3 days of RT-PCR test	Age 5 years, sex, self-reported race, municipality, ±3 days of RT-PCR test
Cases:Controls	1:5	1:1	1:1	1:2
Replace	Yes	No	Yes	Yes
N total	55,519	15,900	26,566	28,206
N cases included	13,283 (50%)	7,950 (30%)	13,283 (50%)	9,402 (36%)
N individuals	13,283 as cases / 8,912 as controls	7,950 as cases / 7,912 as controls	13,283 as cases / 6,936 as controls	9,402 as cases / 6,330 as controls
N pairs	1:1 control (n=3,881) 1:2 controls (n=1,963) 1:3 controls (n=1,044) 1:4 controls (n=678) 1:5 controls (n=5,717)	1:1 control (n=7,950)	1:1 control (n=13,283)	1:2 controls (n=9,402)
N discordant pairs	2,934	1,999	3,749	2,172
N discordant pairs second dose x unvaccinated	264	143	258	187
Adjusted VE, Symptomatic disease				
Single dose, within 0-13 days vs. unvaccinated	-0.8% (-9.4-7.2)	2.5% (-12.2-15.3)	2% (-8.3-11.4)	-4.9% (-16-5.2)
Single dose, ≥14 days vs. unvaccinated	12.5% (3.7-20.6)	10.5% (-4.4-23.3)	12.8% (2.1-22.4)	13.9% (2.8-23.7)
Two doses, within 0-13 days vs. unvaccinated	24.7% (14.7-33.4)	18.2% (0.0-33.2)	29.6% (18.4-39.3)	25.2% (13-35.7)
Two doses, ≥14 days vs. unvaccinated	46.8% (38.7-53.8)	41.6% (26.9-53.3)	48.6% (38.9-56.8)	47.8% (38.2-56)
Age subgroups, Two doses, ≥14 days vs. unvaccinated				
70-74	59.0% (43.7-70.2)	61.8% (34.8-77.7)	64.9% (49.4-75.7)	59.9% (42.0-72.3)
75-79	56.2% (43.0-66.3)	48.9% (23.3-66.0)	53.6% (35.9-66.4)	55.5% (38.9-67.6)
80+	32.7% (17.0-45.5)	28.0% (0.60-47.9)	33.9% (15.0-48.6)	35.0% (16.0-49.7)
p-value for interaction	0.007	0.050	0.022	0.021

Supplementary Table 11. Detailed description of **effectiveness of CoronaVac against symptomatic COVID-19, hospitalisations and deaths in adults ≥70 years of age in the Sensitivity Analysis 1, 1:1 without replacement**

	Unadjusted Analysis			Adjusted Analysis^		
Symptomatic COVID-19 (n=15,900)	**OR (95% CI)**	**VE (95% CI)**	**p-value**	**OR (95% CI)**	**VE (95% CI)**	**p-value**
Single dose, within 0-13 days vs. unvaccinated*	0.97 (0.85-1.12)	2.7% (-11.7-15.3)	0.70	0.98 (0.85-1.12)	2.5% (-12.2-15.3)	0.72
Single dose, ≥14 days vs. unvaccinated*	0.91 (0.78-1.05)	9.5% (-5.3-22.3)	0.20	0.90 (0.77-1.04)	10.5% (-4.4-23.3)	0.16
Two doses, within 0-13 days vs. unvaccinated*	0.81 (0.66-0.98)	19.5% (1.9-34.0)	0.03	0.82 (0.67-1.00)	18.2% (0.0-33.2)	0.05
Two doses, ≥14 days vs. unvaccinated*	0.60 (0.48-0.74)	40.5% (25.8-52.3)	<0.001	0.58 (0.47-0.73)	41.6% (26.9-53.3)	<0.001
COVID-19 **associated hospitalisations (n=8,078)**						
Single dose, within 0-13 days vs. unvaccinated*	0.89 (0.74-1.07)	11.3% (-7.0-26.4)	0.21	0.84 (0.68-1.02)	16.4% (-2.2-31.6)	0.08
Single dose, ≥14 days vs. unvaccinated*	0.85 (0.70-1.04)	14.6% (-4.2-30.0)	0.12	0.83 (0.66-1.01)	18.5% (-1.0-34.2)	0.06
Two doses, within 0-13 days vs. unvaccinated*	0.62 (0.47-0.81)	38.1% (18.8-52.8)	0.001	0.59 (0.44-0.79)	40.9% (20.7-55.9)	<0.001
Two doses, ≥14 days vs. unvaccinated*	0.47 (0.36-0.63)	52.7% (37.2-64.4)	<0.001	0.41 (0.30-0.56)	59% (44.2-69.8)	<0.001
COVID-19 **associated deaths (n=4,104)**						
Single dose, within 0-13 days vs. unvaccinated*	0.92 (0.72-1.18)	8.2% (-17.7-28.4)	0.50	0.93 (0.71-1.21)	7.4% (-21.3-29.2)	0.58
Single dose, ≥14 days vs. unvaccinated*	0.76 (0.57-1.00)	24.5% (0.0-43.0)	0.05	0.68 (0.50-0.93)	31.6% (7.1-49.7)	0.02
Two doses, within 0-13 days vs. unvaccinated*	0.40 (0.27-0.59)	60.4% (40.6-73.5)	<0.001	0.36 (0.23-0.55)	64.4% (44.6-77.1)	<0.001
Two doses, ≥14 days vs. unvaccinated*	0.34 (0.22-0.52)	66.2% (47.8-78.1)	<0.001	0.29 (0.18-0.46)	71.4% (53.7-82.3)	<0.001

*At date of index sample collection for cases and controls.

^ Models adjusted by age and number of comorbidities (None, One or Two, Three or more)

Supplementary Table 12. Detailed description of **effectiveness of CoronaVac against symptomatic COVID-19, hospitalisations and deaths in adults ≥70 years of age in the Sensitivity Analysis 2, 1:1 with replacement**

	Unadjusted Analysis			Adjusted Analysis^		
Symptomatic COVID-19 (n=26,566)	**OR (95% CI)**	**VE (95% CI)**	**p-value**	**OR (95% CI)**	**VE (95% CI)**	**p-value**
Single dose, within 0-13 days vs. unvaccinated*	0.98 (0.89-1.08)	1.9% (-8.3-11.1)	0.71	0.98 (0.886-1.08)	2% (-8.3-11.4)	0.69
Single dose, ≥14 days vs. unvaccinated*	0.89 (0.79-0.99)	11.4% (0.8-21)	0.04	0.87 (0.78-0.98)	12.8% (2.1-22.4)	0.02
Two doses, within 0-13 days vs. unvaccinated*	0.71 (0.61-0.82)	29.2% (18.2-38.7)	<0.001	0.70 (0.61-0.82)	29.6% (18.4-39.3)	<0.001
Two doses, ≥14 days vs. unvaccinated*	0.52 (0.44-0.62)	48.1% (38.5-56.2)	<0.001	0.51 (0.43-0.61)	48.6% (38.9-56.8)	<0.001
COVID-19 associated hospitalisations (n=14,086)						
Single dose, within 0-13 days vs. unvaccinated*	0.95 (0.84-1.08)	4.9% (-8.1-16.4)	0.44	0.92 (0.80-1.06)	8.1% (-5.7-20)	0.24
Single dose, ≥14 days vs. unvaccinated*	0.93 (0.80-1.08)	7% (-7.8-19.8)	0.34	0.86 (0.73-1.01)	14.4% (-0.5-27.1)	0.06
Two doses, within 0-13 days vs. unvaccinated*	0.63 (0.52-0.76)	37.4% (24.2-48.3)	<0.001	0.57 (0.46-0.70)	43.5% (30.4-54.1)	<0.001
Two doses, ≥14 days vs. unvaccinated*	0.46 (0.37-0.57)	54.3% (43.1-63.2)	<0.001	0.39 (0.31-0.59)	60.6% (50.1-68.8)	<0.001
COVID-19 associated deaths (n=7,098)						
Single dose, within 0-13 days vs. unvaccinated*	0.85 (0.71-1.01)	15.3% (-1.1-29)	0.07	0.85 (0.70-1.03)	15.3% (-2.8-30.3)	0.092
Single dose, ≥14 days vs. unvaccinated*	0.77 (0.63-0.95)	22.9% (5.3-37.2)	0.01	0.67 (0.53-0.84)	33.1% (16.1-46.6)	0.001
Two doses, within 0-13 days vs. unvaccinated*	0.53 (0.40-0.70)	47.4% (30.5-60.2)	<0.001	0.45 (0.33-0.61)	55.2% (39.0-67.1)	<0.001
Two doses, ≥14 days vs. unvaccinated*	0.45 (0.33-0.62)	55% (38.3-67.2)	<0.001	0.39 (0.28-0.55)	61% (44.9-72.4)	<0.001

*At date of index sample collection for cases and controls.

^ Models adjusted by age and number of comorbidities (None, One or Two, Three or more)

Supplementary Table 13. Detailed description of **effectiveness of CoronaVac against symptomatic COVID-19, hospitalisations and deaths in adults ≥70 years of age in the Sensitivity Analysis 3, with replacement and 1:2 case-controls**

	Unadjusted Analysis			Adjusted Analysis^		
Symptomatic COVID-19 (n=28,206)	**OR (95% CI)**	**VE (95% CI)**	**p-value**	**OR (95% CI)**	**VE (95% CI)**	**p-value**
Single dose, within 0-13 days vs. unvaccinated*	1.06 (0.96-1.17)	-5.7% (-16.7-4.3)	0.28	1.05 (0.95-1.16)	-4.9% (-16-5.2)	0.36
Single dose, ≥14 days vs. unvaccinated*	0.88 (0.78-0.99)	12% (0.9-21.9)	0.04	0.86 (0.76-0.97)	13.9% (2.8-23.7)	0.02
Two doses, within 0-13 days vs. unvaccinated*	0.76 (0.65-0.88)	24.3% (12.2-34.8)	<0.001	0.75 (0.64-0.87)	25.2% (13-35.7)	<0.001
Two doses, ≥14 days vs. unvaccinated*	0.54 (0.46-0.64)	46.2% (36.3-54.5)	<0.001	0.52 (0.44-0.62)	47.8% (38.2-56)	<0.001
COVID-19 associated hospitalisations (n=10,342)						
Single dose, within 0-13 days vs. unvaccinated*	1.01 (0.89-1.15)	-1.4% (-15.2-10.7)	0.83	0.99 (0.86-1.13)	1.2% (-13.2-13.8)	0.86
Single dose, ≥14 days vs. unvaccinated*	0.87 (0.75-1.01)	13.3% (-0.8-25.4)	0.06	0.79 (0.68-0.93)	20.7% (6.9-32.5)	0.01
Two doses, within 0-13 days vs. unvaccinated*	0.65 (0.54-0.79)	35.1% (21.4-46.4)	<0.001	0.61 (0.50-0.75)	39.2% (25.5-50.4)	<0.001
Two doses, ≥14 days vs. unvaccinated*	0.51 (0.42-0.63)	48.8% (37.1-58.3)	<0.001	0.46 (0.37-0.57)	54% (42.7-63)	<0.001
COVID-19 associated deaths (n=4,982)						
Single dose, within 0-13 days vs. unvaccinated*	1.00 (0.83-1.19)	0.2% (-19.4-16.7)	0.98	1.00 (0.83-1.22)	-0.4% (-22-17.4)	0.97
Single dose, ≥14 days vs. unvaccinated*	0.85 (0.68-1.04)	15.5% (-4.4-31.7)	0.12	0.79 (0.63-0.99)	21.3% (1.1-37.3)	0.04
Two doses, within 0-13 days vs. unvaccinated*	0.67 (0.51-0.88)	33.2% (11.7-49.5)	0.005	0.64 (0.47-0.86)	36.3% (13.8-52.9)	0.003
Two doses, ≥14 days vs. unvaccinated*	0.47 (0.34-0.65)	52.7% (35-65.6)	<0.001	0.44 (0.31-0.61)	56.4% (38.8-69)	<0.001

*At date of index sample collection for cases and controls.

^ Models adjusted by age and number of comorbidities (None, One or Two, Three or more)

Supplementary Table 14. **Adjusted effectiveness of CoronaVac during the period ≥14 days after the second CoronaVac dose for subgroups of adults ≥70 years of age in the Sensitivity Analysis 1, without replacement and 1:1 case-controls (original analysis in the protocol)**

Outcome	OR (95% CI)	VE (95% CI)	p-value for interaction
Symptomatic cases (n=15,900)			
70-74 (n=8,178)	0.38 (0.22-0.65)	61.8% (34.8-77.7)	0.05
75-79 (n=4,122)	0.51 (0.34-0.77)	48.9% (23.3-66.0)	
80+ (n=3,600)	0.72 (0.52-0.99)	28.0% (0.60-47.9)	
Hospitalisations (n=8,078)			
70-74 (n=3,596)	0.20 (0.09-0.44)	80.1% (55.7-91.0)	0.04
75-79 (n=2,098)	0.31 (0.16-0.58)	69.5% (42.4-83.8)	
80+ (n=2,384)	0.57 (0.38-0.85)	43.4% (15.4-62.0)	
Deaths (n=4,104)			
70-74 (n=1,652)	0.14 (0.04-0.50)	86.0% (50.4-96.1)	0.19
75-79 (n=1,140)	0.13 (0.04-0.40)	87.1% (60.2-95.8)	
80+ (n=1,312)	0.50 (0.27-0.92)	49.9% (8.1-72.7)	

Estimates of vaccine effectiveness were obtained from a conditional logistic regression model that included covariates of age and the number of comorbidities and incorporated an interaction term between the category of interest and the period ≥14 days after the second CoronaVac dose.

Supplementary Table 15. **Adjusted effectiveness of CoronaVac during the period ≥14 days after the second CoronaVac dose for subgroups of adults ≥70 years of age in the Sensitivity Analysis 1, with replacement and 1:1 case-controls**

Outcome	OR (95% CI)	VE (95% CI)	p-value for interaction
Symptomatic COVID-19 (n=26,566)			
70-74 (n=14,048)	0.35 (0.24-0.51)	64.9% (49.4-75.7)	0.02
75-79 (n=7,038)	0.46 (0.34-0.64)	53.6% (35.9-66.4)	
80+ (n=5,480)	0.66 (0.51-0.85)	33.9% (15.0-48.6)	
Hospitalisations (n=14,086)			
70-74 (n=6,526)	0.18 (0.10-0.32)	82.1% (68.0-90.0)	<0.001
75-79 (n=3,856)	0.32 (0.20-0.52)	67.7% (47.9-79.9)	
80+ (n=3,704)	0.56 (0.41-0.77)	44.2% (23.5-59.2)	
Deaths (n=7,098)			
70-74 (n=3,034)	0.14 (0.05-0.38)	86.0% (61.9-94.8)	0.07
75-79 (n=2,010)	0.28 (0.13-0.63)	71.9% (37.2-87.5)	
80+ (n=2,054)	0.55 (0.36-0.84)	45.3% (15.9-64.4)	

Estimates of vaccine effectiveness were obtained from a conditional logistic regression model that included covariates of age and the number of comorbidities and incorporated an interaction term between the category of interest and the period ≥14 days after the second CoronaVac dose.

Supplementary Table 16. **Adjusted effectiveness of CoronaVac during the period ≥14 days after the second CoronaVac dose for subgroups of adults ≥70 years of age in the Sensitivity Analysis 2, with replacement and 1:2 case-controls**

Outcome	OR (95% CI)	VE (95% CI)	p-value for interaction
Symptomatic COVID-19 (n=28,206)			
70-74 (n=15,150)	0.40 (0.28-0.58)	59.9% (42.0-72.3)	0.02
75-79 (n=7,447)	0.45 (0.32-0.61)	55.5% (38.9-67.6)	
80+ (n=5,610)	0.65 (0.50-0.84)	35.0% (16.0-49.7)	
Hospitalisations (n=15,513)			
70-74 (n=7,323)	0.25 (0.14-0.44)	74.9% (56.4-85.6)	0.01
75-79 (n=4,248)	0.37 (0.24-0.56)	63.4% (43.8-76.1)	
80+ (n=3,942)	0.66 (0.48-0.89)	34.4% (10.9-51.7)	
Deaths (n=7,473)			
70-74 (n=3,267)	0.11 (0.03-0.50)	88.6% (49.6-97.4)	0.01
75-79 (n=2,094)	0.22 (0.10-0.47)	78.1% (52.7-89.8)	
80+ (n=2,112)	0.67 (0.43-1.03)	33.2% (-3.0-56.6)	

Estimates of vaccine effectiveness were obtained from a conditional logistic regression model that included covariates of age and the number of comorbidities and incorporated an interaction term between the category of interest and the period ≥14 days after the second CoronaVac dose.