Vaccine coverage and effectiveness against laboratory-confirmed symptomatic and severe Covid-19 in indigenous people in Brazil: a cohort study

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Abstract

Background

Indigenous people have historically suffered devastating impacts from epidemics and continue to have lower access to healthcare and be especially vulnerable to respiratory infectious. We estimated the coverage and effectiveness of Covid-19 vaccines against laboratory-confirmed Covid-19 cases among indigenous people in Brazil.

Methods

We linked nationwide Covid-19 vaccination data with flu-like surveillance records and studied a cohort of vaccinated indigenous people aged ≥ 5 years between 18th Jan 2021 and 1st Mar 2022. We considered individuals unexposed from the date they received the first dose of vaccine until the 13th day of vaccination, partially vaccinated from the 14th day after the first dose until the 13th day after receiving the second dose, and fully vaccinated onwards. We estimated the Covid-19 vaccination coverage and used Poisson regression to calculate the relative risks (RR) and vaccine effectiveness (VE) of CoronaVac, ChAdOx1, and BNT162b2 against Covid-19 laboratory-confirmed cases incidence, mortality, hospitalisation, and hospital-progression to Intensive Care Unit (ICU) or death. VE was estimated as (1-RR)*100, comparing unexposed to partially or fully vaccinated.

Results

By 1st Mar 2022, 48·7% (35·0–62·3) of eligible indigenous people vs 74·8% (57·9–91·8) overall Brazilians had been fully vaccinated for Covid-19. VE for the three Covid-19 vaccines combined was 53% (95%CI:44–60%) for symptomatic cases, 53% (95%CI:-56-86%) for mortality and 41% (95%CI:-35-75%) for hospitalisation. Among hospitalised patients, VE was 87% (95%CI:27–98%) for progression to ICU and 96% (95%CI: 90–99%) for death.

Conclusions

Lower coverage but similar Covid-19 VE among indigenous people than overall Brazilians suggest the need to expand access, timely vaccination, and urgently offer booster doses to achieve a great level of protection among this group.

Background

Indigenous peoples have historically suffered the devastating impacts of epidemics of infectious diseases that have resulted in drastic reductions in their population over the centuries[1, 2]. The high risk of infectious diseases, including acute respiratory infections[3–6], is largely attributed to poverty,

precarious sanitation, and limited access to health care. In Brazil [7, 8], this is further exacerbated by the long history of exposure to discrimination, violence, environmental degradation, and territorial restriction[2, 3, 9], which perpetuate respiratory infection as a major health issue for indigenous populations[3–6].

The Covid-19 pandemic has disproportionally impacted socially disadvantaged population groups in Brazil, including indigenous peoples[10–13]. In the first trimester of the pandemic, there was a rapid increase in the risk of sustained transmission of Covid-19 in areas with an indigenous presence[11]. Two national household surveys of seroprevalence of antibodies against SARS-CoV-2 in 133 cities showed an 87% higher adjusted prevalence among indigenous subjects compared to whites[10]. In addition, in the first year of the pandemic, mortality among indigenous people was 16.7% higher than that observed in the general Brazilian population[12]. Age-specific mortality rates[14] as well as hospital case fatality rates in all age groups, were also higher in indigenous subjects compared to other colour/race categories registered in Brazilian health information systems[13, 14]. The social vulnerability and the severe impact of the pandemic on the indigenous peoples resulted in the inclusion of the population covered by the Brazilian Indigenous Health Care Subsystem (IHS) as one of the priority groups for vaccination against Covid-19 [15, 16].

Although two of the main vaccines available in Brazil, ChAdOx-1 (previously Vaxzevria/Fiocruz or Oxford-AstraZeneca) and CoronaVac/Butantan, proved to be effective (i.e., > 50%) in protecting against SARS-CoV-2 symptomatic infection and severity, lower vaccine effectiveness (VE) was seeing in some population strata, such as the elderly[17]. VE is also likely to change according to intersecting factors, such as the type of vaccine and vaccination schedule, comorbidities, risk of exposure, time after vaccination, and circulation of specific variants[18]. To our knowledge, no investigation has been carried out so far about VE against Covid-19 in the Indigenous populations in Brazil. In this study, we estimated the coverage of Covid-19 vaccines and evaluated VE against infection, hospitalisation, admission to ICU, and death related to SARS-CoV-2 in the indigenous population in Brazil. We provide crucial evidence to be taken into consideration in health policies aimed at mitigating ethnic-racial gaps in health in the country.

Methods

Study design and setting

We followed a cohort of Covid-19 vaccinated indigenous individuals living in municipalities that overlap with the Special Indigenous Health Districts *(Distritos Sanitários Especiais Indígenas*, DSEIs), which provide primary health care to indigenous living in villages.

In Brazil, Covid-19 vaccination was started on the 18th of January 2021 by the National Immunization Program (PNI) of the Brazilian Ministry of Health. It initially relied on the CoronaVac-Sinovac/Butantan, the first vaccine in the country, and ChAdOx-1 vaccine. Later, Brazil implemented vaccination with BNT162b2 (Pfizer/BioNTech) and Ad26.COV2.S (Janssen). Covid-19 vaccination followed a pre-specified

calendar, including in the campaign's first phase elderly, healthcare professionals, and indigenous individuals attended by the DSEIs of the IHS. This population mostly comprises subjects living in Indigenous Lands in rural areas. It also includes a smaller proportion of indigenous subjects residing in Indigenous Lands in urban areas or outside indigenous lands, both in urban and rural areas. In September 2021, the government initiated the vaccination of adolescents aged 12 to 18 years, and in January 2022, of children from 5 to 11 years.

Data sources

We used data from (i) individuals vaccinated for Covid-19 from the Information System of Brazilian National Vaccination Programme (SI-PNI), and SARS-CoV-2 using (ii) laboratory-confirmed cases of symptomatic Influenza-like Illness (ILI) notified in the Brazilian Influenza-like surveillance information system (*e-SUS-Notifica*) and (iii) laboratory-confirmed cases of Severe Acute Respiratory Infection (SARI) notified in the Flu Epidemiologic Surveillance System (SIVEP-Gripe), from Brazil's Unified Health System. Datasets were extracted on 1st March 2021, and made available by the Brazilian Ministry of Health. The information technology bureau of the Brazilian Ministry of Health provided pseudo-anonymised data with a common unique identifier that was used to link individual-level records from the three databases (more details about linkage procedures are available at https://vigivac.fiocruz.br/).

From the SI-PNI dataset, we extracted information on individuals' age, sex, municipality of residence, the date of the first and second doses, and type of vaccine received. From e-SUS-Notifica (ILI cases) and SIVEP-Gripe (SARI cases) databases, we extracted information on age, sex, date of first symptoms, notification date, date of admission to hospital and Intensive Care Unit (ICU), and outcomes of interest: hospitalisation, ICU admission or death. In addition, we used the municipality-level material deprivation index (Brazilian Deprivation Index - *Índice Brasileiro de Privação*, IBP) as a *proxy* of the municipal socioeconomic context of where the indigenous community is located.

Study population

We identified indigenous individuals five years of age and older who were vaccinated between 18th January 2021 and 1st March 2022. For the vaccine effectiveness (VE) estimation, we excluded (i) individuals who received vaccines other than CoronaVac, ChAdOx-1, or BNT162b2, (ii) individuals who received two heterologous doses of any vaccine, (iii) individuals with ILI or SARI within 90 days before starting vaccination, and (iv) individuals with two doses within < 14 days.

Intervention and outcomes

We followed individuals from the date of receipt of the first dose until the date they presented each of the outcomes (i.e., symptomatic Covid-19 laboratory confirmed by PCR or antigen test, hospitalisation, admission to ICU or death for Covid-19), or until 1st March of 2022, date of the end of the study, whichever came first. For individuals who received the third dose, we also restricted their follow-up to the date of receipt of that dose. As this study comprised a cohort of vaccinated individuals, we considered individuals as (i) unexposed from the date they received the first dose of vaccine until the 13th day of

vaccination; (ii) partially vaccinated from the 14th day after the first dose until the 13th day after receiving the second dose; or (iii) fully vaccinated from the 14th day after the second dose onwards.

ILI cases were defined by fever and cough or sore throat. SARI cases were defined by fever, cough, shortness of breath, or difficulty breathing, and hospitalisation or, for those not hospitalised who were notified of death for Covid-19. Laboratory confirmed ILI or SARI included those with a positive PCR or antigen test for COVID following the first 10 days of the start of the symptoms. We considered the primary outcome (i) case of ILI or SARI due to laboratory-confirmed Covid-19, and secondary outcomes (ii) hospitalisation for Covid-19, (iii) death for Covid-19, and (iv) admission to the Intensive Care Unit (ICU) and (v) death for Covid-19 in hospitalised patients.

Statistical analysis

We estimated vaccination coverage for indigenous people living in municipalities overlapping with the DSEI territories, by age, sex, region of residence, and IBP. To do this, we first had to estimate the indigenous demographic distribution for the year 2020. In Brazil, the official socio-demographic data result from the decennial Demographic Censuses and population counts that have been carried out since 1940 by the Brazilian Institute of Geography and Statistics (IBGE)(Brazilian Institute of Geography and Statistics [IBGE], 2022). Since the most recent official estimate of the indigenous population in Brazil is from the 2010 Demographic Census, we developed a strategy to estimate the indigenous population in 2020 for further calculation of Covid-19 vaccine coverage.

First, we estimated the number of indigenous people for 2020 living in municipalities that overlap with the DSEIs territories (480/5,570) by age and sex strata. For reasons related to statistical confidentiality, the number of subjects enumerated in the National Census, which also applies to the indigenous population, is not provided in data outputs when they are from 1 and 6 individuals. To circumvent this possible inaccuracy in the size population, we obtained the number of indigenous people aged five or more in 2010 by calculating the difference between the total population in this age range minus the total non-indigenous population in the same age range for each municipality. Then, for each municipality, we estimated the size of the indigenous population in 2020 by multiplying the percentage of the indigenous population in 2010 in each age and sex strata by the overall 2020 population estimates provided by IBGE. Finally, we calculated vaccine coverage for partial and full vaccination as the number of individuals who received either (i) one dose of CoronaVac, ChAdOx-1, or BNT162b2 (partial), or (ii) one dose of Ad26.COV2.S or two doses of CoronaVac, ChAdOx-1 or BNT162b2; and divided this by the number of indigenous individuals estimated for 2020, within each stratum of age and sex, later grouped by region of residence and municipal deprivation level. We used as a numerator the total number of doses before applying exclusion criteria i.e., considering individuals receiving Janssen or a mixed calendar, presence of symptoms before the vaccine, and inconsistencies in time between doses (Fig. 1).

In order to evaluate VE against each outcome, we performed Poisson regression using the follow-up time as the offset to calculate the relative risks (RR) and 95% Confidence Intervals (95%CI) for individuals partially or fully vaccinated, relative to non-exposed individuals. We performed the analysis for any of the

three combined vaccination schemes (CoronaVac, ChAdOx-1, or BNT162b2) and exclusively for CoronaVac. Vaccine effectiveness for Ad26.COV2.S was not performed as the profile of partial or fully immunized would be different from the remaining vaccines. In our analysis, we considered that each individual contributed first as unexposed and later as partially or fully vaccinated, and we included cluster robust standard errors to account for individuals contributing to multiple rows. The analysis was adjusted for age, sex, region of residence, IBP, and the month of the first dose. Age was used as a continuous variable given the sample size. Models evaluating VE for Covid-19 mortality, hospitalisation, and hospital-based admission to ICU or death were only adjusted for age or age and sex to avoid over-adjustment. VE was estimated as (1-RR)*100.

In addition, to estimate if VE changed by year after the introduction to the Omicron variant in Brazil, we estimated VE restricting it to individuals who received the first dose up to 31st Dec 2020 and followed the individuals up to the same date.

All analyses were performed in STATA 16.0.

Results

Using the data on 389,753 eligible indigenous people (Fig. 1), the overall vaccine coverages were 65·0% and 48·7%, respectively, for partial or full vaccination (Table 1). Coverage of over 90% was achieved only for partial vaccination in adults in all age strata over 20 years old. The highest percentage of full vaccination was achieved among those aged 50 to 59 years (77·2%). Among people aged 10–19 years, partial and full vaccination coverages were 40·7% and 21·3%, respectively, and below 3% in children 5–9 years (Table 1).

Table 1

Vaccine coverage among people aged 5 or more overall and among indigenous living in municipalities overlapping DSEIs territories (target of priority for vaccination) according to sex, age, region, and deprivation index quintiles in Brazil up to 1st March 2022.

Characteristic	Coverage partial vaccination[a] (% and 95% CI)		Coverage full vaccination[b] (% and 95% CI)	
	Overall (Brazil)	Indigenous living in municipalities overlapping with the DSEIs	Overall (Brazil)	Indigenous living in municipalities overlapping with the DSEIs
Overall	87·6 (69·3-106·0)	65·0 (49·2–80·8)	74·8 (57·9–91·8)	48·7 (35·0–62·3)
Sex				
Woman	89·3 (70·8-107·9)	65·6 (49·7–81·5)	77·5 (60·3–94·8)	49·6 (35·8–63·4)
Men	85·8 (67·6-103·9)	64·4 (48·7–80·2)	72·0 (55·4–88·6)	47·8 (34·2–61·3)
Age (years)				
5–9	40·7 (28·2–53·2)	2·6 (-0·6 – 5·8)	2·0 (-0·8 – 4·8)	0·0 (-0·3 – 0·3)
10–19	81·5 (63·8–99·2)	40·7 (28·2–53·2)	51·6 (37·5–65·7)	21·3 (12·2–30·3)
20–49	89·6 (71·1-108·2)	96·9 (77·6-116·2)	81·8 (64·1–99·5)	77·2 (60·0–94·4)
50–59	97·1 (77·8-116·4)	101·1 (81·4-120·8)	92·3 (73·5-111·2)	83·1 (65·3-101·0)
> 60	102·5 (82·6-122·3)	90·8(72·1-109·4)	97·3 (78·0-116·7)	74·7 (57·7–91·6)
Region				
North	84·6 (66·6-102·6)	56·9 (42·1–71·6)	73·7 (56·9–90·5)	40·3 (27·8–52·7)

[a]Partial vaccination - one dose of ChAdOx-1, CoronaVac or BNT162b2.

[b]Full vaccination - two doses of ChAdOx-1, CoronaVac, or BNT162b2; or one dose of Jannsen.

Northeast	85·5 (67·4-103·7)	80·4 (62·8–97·9)	70·3 (53·8–86·7)	66·4 (50·5–82·4)
Southeast	76·3 (59·2–93·5)	47·9 (34·3–61·4)	60·8 (45·5–76·1)	41·0 (28·5–53·6)
South	89·8 (71·2-108·4)	68·9 (52·6–85·1)	77·9 (60·6–95·2)	43·0 (30·1–55·8)
Central-West	89·9 (71·3-108·5)	73·0 (56·3–89·8)	80·8 (63·2–98·4)	56·3 (41·6–71·0)
IBP quintiles				
1 (less deprived)	90·3 (71·7-108·9)	16·7 (8·7–24·7)	80·2 (62·6–97·8)	9·1 (3·2–15·1)
2	89·6 (71·0-108·1)	30·7 (19·8–41·5)	77·9 (60·6–95·2)	23·3 (13·8–32·8)
3	87·5 (69·2-105·8)	95·2 (76·1-114·3)	75·5 (58·5–92·6)	71·6 (55·0–88·2)
4	87·0 (68·7-105·3)	81·8 (64·1–99·6)	73·8 (56·9–90·6)	59·7 (44·6–74·8)
5 (more deprived)	82·0 (64·3–99·8)	62·2 (46·7–77·6)	66·3 (50·3–82·2)	46·9 (33·5–60·3)
[a]Partial vaccination - one dose of ChAdOx-1, CoronaVac or BNT162b2.				
[b]Full vaccination - two doses of ChAdOx-1, CoronaVac, or BNT162b2; or one dose of Jannsen.				

VE was estimated among 370,092 indigenous subjects who remained in the study after applying the exclusion criteria (Fig. 1). The most frequent vaccine received was CoronaVac (322,102 doses; 87·0%), followed by BNT162b2 (43,795 doses; 11·8%) and ChAdOx-1 (4,266 doses; 1·2%). Seventy-five percent (262,081/370,092) received a second dose of the vaccine (Table 2). Older indigenous individuals and those living in the Southeast or Northeast or in more deprived municipalities were more likely to have received the second dose.

Table 2
Data for indigenous people who received at least one dose of Covid-19 vaccine according to whether they received one or two doses of ChAdOx-1, CoronaVac, or BNT162b2.

Covariates	**1 dose**	**2 doses**	**Total**	**p-value**
	n = 108,011	**n = 262,081**	**n = 370,092**	
	N (row%)	**N (row%)**	**N**	
Sex				< 0·001
Woman	52,279 (28·6)	130,742 (71·4)	18,3021	··
Men	55,732 (29·8)	131,339 (70·2)	18,7071	··
Age				< 0·001
5 to 9 years	2,612 (99·3)	18 (0·7)	2,630	··
10 to 19 years	45,961 (69·5)	20,173 (30·5)	66,134	··
20 to 49 years	47,237 (20·5)	183,417 (79·5)	230,654	··
50 to 59 years	5,701 (17·6)	26,642 (82·4)	32,343	··
60 or more	6,500 (17·0)	31,831 (83·0)	38,331	··
Region				< 0·001
North	51,416 (32·0)	109,141 (68·0)	160,557	··
Northeast	22,348 (22·7)	76,022 (77·3)	98,370	··
Southeast	3,200 (21·3)	11,835 (78·7)	15,035	··
South	13,347 (41·7)	18,696 (58·3)	32,043	··
Central-West	17,700 (27·6)	46,387 (72·4)	64,087	··
Deprivation index (IBP quintiles)				< 0·001
1 (less deprived)	685 (52·5)	619 (47·5)	1,304	··
2	1,712 (32·5)	3,561 (67·5)	5,273	··
3	4,943 (30·4)	11,306 (69·6)	16,249	··
4	25,968 (32·2)	54,786 (67·8)	80,754	··
5 (more deprived)	74,703 (28·0)	191,809 (72·0)	266,512	··

There were 1951 Covid-19 cases during the study period. 105 of them were hospitalised (5·4%), of which 37 were further admitted to ICU (35·2%), and 35 died (1·8% of all symptomatic and 33·3% of hospitalised cases). Age-adjusted effectiveness of the 1st dose of jointly CoronaVac, ChAdOx-1, or BNT162b2 schemes (partial vaccination) against Covid-19 incident cases was 55% (95%CI:46–63%), and 47%

(95%CI: 37–55%) after the second dose (full vaccination) (Table 3). After adjusting for sex, time of vaccination, region, and municipal deprivation index (IBP), VE against laboratory-confirmed incident cases was 51% (95%CI:41–60) for partial vaccination and 53% (95%CI:44–60) for full vaccination. After the second dose, age and sex-adjusted VE was 53% (95%CI:-56-86%) against mortality and 41% (95%CI:-35-75) against hospitalisation. Among hospitalised patients, the age-adjusted VE was 87% (95%CI:14–98) for progression to ICU and 96% (95%CI:90–99) for progression to death. We obtained similar point estimates when restricting the analysis to indigenous people vaccinated with CoronaVac (Table 3) and by restricting the analysis to 361,900 (97·8%) indigenous people vaccinated with the first dose in 2021 and followed up to the end of that year (Table S2).

Table 3

Relative risks (RR) and vaccine effectiveness (VE) of Covid-19 vaccines on symptomatic, hospitalised, UCI admitted, and death Covid-19 cases using the cohort of vaccinated indigenous people living in indigenous communities in Brazil.

	Adjusted by age[a]		Adjusted by age and other covariates[b]	
N = 370,092	**RR (95%CI)**	**VE (%) (95%CI)**	**RR (95%CI)**	**VE (%) (95%CI)**
Covid-19 incidence				
CoronaVac/AZ/Pfizer				
1st dose (< 14 days)	1	..	1	..
1st dose (> = 14 days)	0·45 (0·37 – 0·54)	55 (46–63)	0·49 (0·40 – 0·59)	51 (41–60)
2nd dose (> = 14 days)	0·53 (0·45 – 0·63)	47 (37–55)	0·47 (0·40 – 0·56)	53 (44–60)
CoronaVac				
1st dose (< 14 days)	1	..	1	..
1st dose (> = 14 days)	0·43 (0·36 – 0·52)	57 (48–64)	0·47 (0·39 – 0·57)	53 (43–61)
2nd dose (> = 14 days)	0·48 (0·41 – 0·58)	52 (42–59)	0·46 (0·39 – 0·55)	54 (45–61)
Covid-19 mortality				
CoronaVac/AZ/Pfizer				
1st dose (< 14 days)	1	..	1	..
1st dose (> = 14 days)	0·26 (0·06 – 1·08)	74 (-8-94)	0·26 (0·06 – 1·08)	74 (-9-94)
2nd dose (> = 14 days)	0·47 (0·14 – 1·6)	53 (-60-86)	0·47 (0·14 – 1·56)	53 (-56-86)
CoronaVac				

[a]Relative risks (RR) estimated using Poisson regression adjusted by age (continuous).

[b]Relative risks (RR) estimated using Poisson regression adjusted. RR for laboratory-confirmed cases was adjusted by age (continuous), sex, region, the month of the 1st dose vaccination, and municipal deprivation index (IBP); RR for mortality, hospitalisation, progression to ICU, and death were adjusted by age (continuous) and sex.

[c]Among the 105 hospitalised cases.

1st dose (< 14 days)	1	..	1	..
1st dose (> = 14 days)	0·26 (0·06 – 1·09)	74 (-9-94)	0·26 (0·06 – 1·09)	74 (-9-94)
2nd dose (> = 14 days)	0·46 (0·14 – 1·53)	54 (-53-86)	0·46 (0·14 – 1·53)	54 (-53-86)
Covid-19 hospitalisation				
CoronaVac/AZ/Pfizer				
1st dose (< 14 days)	1	..	1	..
1st dose (> = 14 days)	0·82 (0·34 – 1·96)	18 (-96-66)	0·82 (0·34 – 1·96)	18 (-96-66)
2nd dose (> = 14 days)	0·59 (0·25 – 1·35)	42 (-35-75)	0·59 (0·25 – 1·35)	41 (-35-75)
CoronaVac				
1st dose (< 14 days)	1	..	1	..
1st dose (> = 14 days)	0·99 (0·39 – 2·55)	1 (-155-61)	0·99 (0·39 – 2·55)	1 (-155-61)
2nd dose (> = 14 days)	0·68 (0·27 – 1·69)	32 (-69-73)	0·68 (0·27 – 1·69)	32 (-69-73)
Covid-19 progression to ICU[3]				
CoronaVac/AZ/Pfizer				
1st dose (< 14 days)	1	..	1	..
1st dose (> = 14 days)	0·15 (0·02 – 0·98)	85 (2–98)	0·15 (0·02 – 0·93)	85 (2–98)
2nd dose (> = 14 days)	0·13 (0·02 – 0·86)	87 (14–98)	0·14 (0·02 – 0·81)	87 (14–98)
Coronavac				
1st dose (< 14 days)	1	..	1	..

[a]Relative risks (RR) estimated using Poisson regression adjusted by age (continuous).

[b]Relative risks (RR) estimated using Poisson regression adjusted. RR for laboratory-confirmed cases was adjusted by age (continuous), sex, region, the month of the 1st dose vaccination, and municipal deprivation index (IBP); RR for mortality, hospitalisation, progression to ICU, and death were adjusted by age (continuous) and sex.

[c]Among the 105 hospitalised cases.

1st dose (> = 14 days)	0·13 (0·02 – 0·86)	87 (14–98)	0·13 (0·03 – 0·79)	87 (14–98)
2nd dose (> = 14 days)	0·12 (0·02 – 0·75)	88 (25–98)	0·12 (0·02 – 0·68)	88 (25–98)
Covid-19 death among hospitalised patients[c]				
CoronaVac/AZ/Pfizer				
1st dose (< 14 days)	1	··	1	··
1st dose (> = 14 days)	0·02 (0·01 – 0·08)	98 (92–99)	0·02 (0·01 – 0·8)	98 (92–99)
2nd dose (> = 14 days)	0·04 (0·01 – 0·10)	96 (90–99)	0·04 (0·01 – 0·1)	96 (90–99)
CoronaVac				
1st dose (< 14 days)	1	··	1	··
1st dose (> = 14 days)	0·02 (0·01 – 0·07)	98 (93–99)	0·02 (0·01 – 0·07)	98 (93–99)
2nd dose (> = 14 days)	0·04 (0·01 – 0·10)	96 (90–99)	0·04 (0·01 – 0·09)	96 (91–99)

[a]Relative risks (RR) estimated using Poisson regression adjusted by age (continuous).

[b]Relative risks (RR) estimated using Poisson regression adjusted. RR for laboratory-confirmed cases was adjusted by age (continuous), sex, region, the month of the 1st dose vaccination, and municipal deprivation index (IBP); RR for mortality, hospitalisation, progression to ICU, and death were adjusted by age (continuous) and sex.

[c]Among the 105 hospitalised cases.

Discussion

To our knowledge, this is the first study to evaluate vaccine effectiveness (VE) against Covid-19 in the Indigenous population in Brazil. Our results show that vaccination coverage is lower in the investigated indigenous population compared to the Brazilian general population. Receiving two doses of any of the three vaccines (Coronavac, ChAdOx1, or BNT162b2) was at least 50% effective against symptomatic laboratory-confirmed Covid-19 cases and over 80% effective against severe cases (i.e., progression to ICU and death).

A previous study calculated vaccine coverage of indigenous groups in Brazil, pointing out that vaccine coverage in the elderly was lower than in the general Brazilian population[19]. In our study, we also found lower coverage of partial or full vaccination against Covid-19 than in the general Brazilian population, with inadequate coverage (< 80%) for almost all strata of sex, region, socioeconomic index, and age. The

low coverage in the North region (40.3%) is particularly worrying, given that it is the region with the highest proportion of the indigenous population. Covid-19 vaccination coverage in Brazil has been marked by major structural socio-economic, environmental, and ethnic-racial inequities[20], with pronounced lower vaccination coverage than among the general Brazilian population in all but in the Northeast region of Brazil. Surprisingly, the indigenous vaccination coverage was similar between the North and South and Southeast regions, despite the two last regions being the most socio-economically developed and having the largest healthcare network in the country.

In Brazil, there were observed declining trends of the incidence and mortality caused by Covid-19 in indigenous people, supposed to have occurred due to the increased coverage of Covid-19 vaccines in that group during 2021. However, the study used aggregated data and did not provide a formal VE evaluation[19]. In the Colombian Amazon which borders Brazil, CoronaVac showed over 94% effectiveness against symptomatic Covid-19 in a majority indigenous population of a municipality of 7856 inhabitants with very large (> 99%) vaccine coverage[21]. On the other hand, a similar population based study using linked data have reported lower effectiveness of Pneumococcal conjugate vaccine against all-cause pneumonia hospitalizations in indigenous peoples compared to their counterparts[22].

High VE against symptomatic and severe Covid-19 cases among the general Brazilian population has been previously shown using the same linked data sources[13]. In addition, by analysing VE for Covid 19 in Brazil, a similar study also observed that VE of two doses of CoronaVac was 54% for symptomatic infection and 74% for death in Brazil's general population[17]. In our study, we found a similar VE for CoronaVac against symptomatic Covid-19 (54% in the indigenous population) but a lower VE against mortality (54%). The earlier study also analysed ChAdOx-1's VE, finding a higher magnitude of protection against all outcomes compared to the VE conferred by CoronaVac [17]. These findings may be relevant to explain the lower magnitude of VE in the indigenous population when analysing the effect of the combined vaccination schedules since they had a higher proportion (87·0%) of vaccination with CoronaVac. In addition, our study indicated no reductions in the hospitalisation of indigenous vaccinated subjects, which differs from the pronounced VE levels for CoronaVac (72%) and ChAdOx-1 (87%) against hospitalisation in the general Brazilian population[17]. Finally, in our study, there was also a non-significant protective effect of either vaccine schemes (CoronaVac, ChAdOx-1, or BNT162b2) against deaths from Covid-19, regardless of the condition of hospitalisation, while Cerqueira-Silva et al. (2022) found 74% and 90% effectiveness, respectively, of CoronaVac and ChAdOx-1 against deaths in the general population of the country.

In interpreting our findings for indigenous populations, it is important to consider that 60·7% of the indigenous population in this study are located in the Central-West and North regions of Brazil. Indigenous territories in these regions are mostly situated in rural areas, with a scarcity of secondary and tertiary healthcare units in nearby towns. This results in major restrictions on access to specialised health care[15, 23]. During the peaks of the Covid-19 pandemic in 2020 and 2021, all regions in Brazil faced high demand for health care, and the collapse of the Brazilian Unified Health System occurred particularly in cities located in the more remote regions, such as the North. In addition, VE among the indigenous

population in Brazil is likely to be influenced by lower vaccination coverage, since high vaccination coverage in indigenous villages could have led to indirect protection of all the community. Another possible explanation is the high rates of Covid-19 in indigenous communities prior to vaccination.

It is important to mention some limitations of this study. Estimates of Covid-19 vaccination coverage depend on reliable population estimates. In the case of the indigenous population in Brazil, the most recent nationally representative demographic data was collected more than a decade ago, in the 2010 national census[24, 25]. A possible demographic source is the specific health information system of the IHS (known as SIASI - *Sistema de Informação da Atenção à Saúde Indígena*), but access to data in this system is not currently available to the general public, including researchers [26]. As an alternative, we estimated the 2020 indigenous population attended by IHS applying the 2010 Census proportions of the indigenous population to the 2020 demographic estimates for the general population residing in the municipalities that overlap with the DSEI territories of the IHS. According to government data on Covid-19[16], there were 657,758 indigenous individuals over 5 years of age considered in the priority group for vaccination. These estimates differ by around 10% from our estimates of 599,540 individuals in the same age group. This difference could be related to the fact that we did not rely on demographic projections because variation in the indigenous population size in the recent Brazilian national censuses has been suggested to be largely affected by ethnic/racial classification issues, and not solely by demographic dynamics[25]. This difference in the target population estimates might have led to an overestimated vaccine coverage, however, it did not impact the other findings of this study. We did not have sufficient power to evaluate waning and to stratify by calendar time, which would be necessary to investigate if VE among indigenous people is different from among non-indigenous groups. Also, as a small proportion of indigenous people had received the third dose by the time the data was extracted, we did not evaluate the VE of the third dose.

In addition, as data on Covid-19 vaccination in the indigenous population was only available from PNI, the only possible research design was a cohort study, taking vaccinated individuals (< 14 days of vaccination) as the control group. By using the cohort design, we certainly missed indigenous subjects living in urban areas not served by IHS, who have also been strongly affected by the pandemic but were not included as a priority group for vaccination. This implies restrictions on any generalization of our results beyond those indigenous living in municipalities overlapping with DSEI territories. Finally, IBP was estimated for the municipality, not for indigenous lands, and they probably differ even in the same municipality. Nevertheless, IPB still is an important indicator that could demonstrate differences in access to health services at a municipal level, and their financial capacity to deal with the pandemic locally.

Conclusions

Our results indicate low Covid-19 vaccine coverage among indigenous groups in Brazil, but with similar VE to non-indigenous counterparts. The observed heterogeneity in vaccination coverage leaves clusters of indigenous populations particularly susceptible to Covid-19. This highlights not only the challenges of vaccination in times of greater circulation of fake news and vaccination hesitancy[27] but also limitations

in the provision of primary care by the IHS. Low Covid-19 vaccination coverage in many indigenous communities composed of just a few hundred individuals might also threaten their cultural continuity, as Covid-19 affects older people most and it is they who are largely responsible for cross-generational cultural transmission in these societies[14, 15]. Therefore, strengthening the IHS and supporting strategies to reduce health access barriers and expand vaccination coverage against Covid-19, including booster doses, is key to preventing local outbreaks and reducing the unacceptable disproportionate impacts of Covid-19 on indigenous peoples.

Abbreviations

IHS: Indigenous Health Care Subsystem

DSEIs: Special Indigenous Health Districts *(Distritos Sanitários Especiais Indígenas*)

VE: vaccine effectiveness

ICU: Intensive Care Unit

PNI: National Immunization Program

SI-PNI: Information System of Brazilian National Vaccination Programme

ILI: Influenza-like Illness

SARI: Severe Acute Respiratory Infection

IBP: Brazilian Deprivation Index (*Índice Brasileiro de Privação)*

IBGE: Brazilian Institute of Geography and Statistics

Declarations

Ethical approval and consent to participate

The Brazilian National Commission on Research Ethics (CONEP) approved this study (n. 4.921.308). The study used an anonymised secondary dataset, which complies with the Brazilian General Personal Data Protection Law (LGPD). To receive and analyse the dataset, a term of responsibility for using the datasets was signed by the study coordinator (MB-N), and each member of the research team signed a confidentiality statement. All data were cleaned and analysed in a secure computing environment.

Consent for publication

Not applicable

Availability of data and materials

The unidentified data underlying this article can be shared upon reasonable request to the authors and after ethical approval from Fiocruz.

Competing interests

We declare no competing interests.

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Author contributions

JMP, AMC, RVS, PS, ESP, OTR, TC-S, VB, JB-J, VAO, GLW, MLM, and MB-N contributed to the conception and design of the work. JB-J, VAO, and MB-N contributed to the acquisition of data. JMP, AMC, RVS, PS, ESP, OTR, and TC-S contributed to the analysis and interpretation of data, and the draft of the manuscript. All authors have revised the final version and approved the submitted version.

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Figures

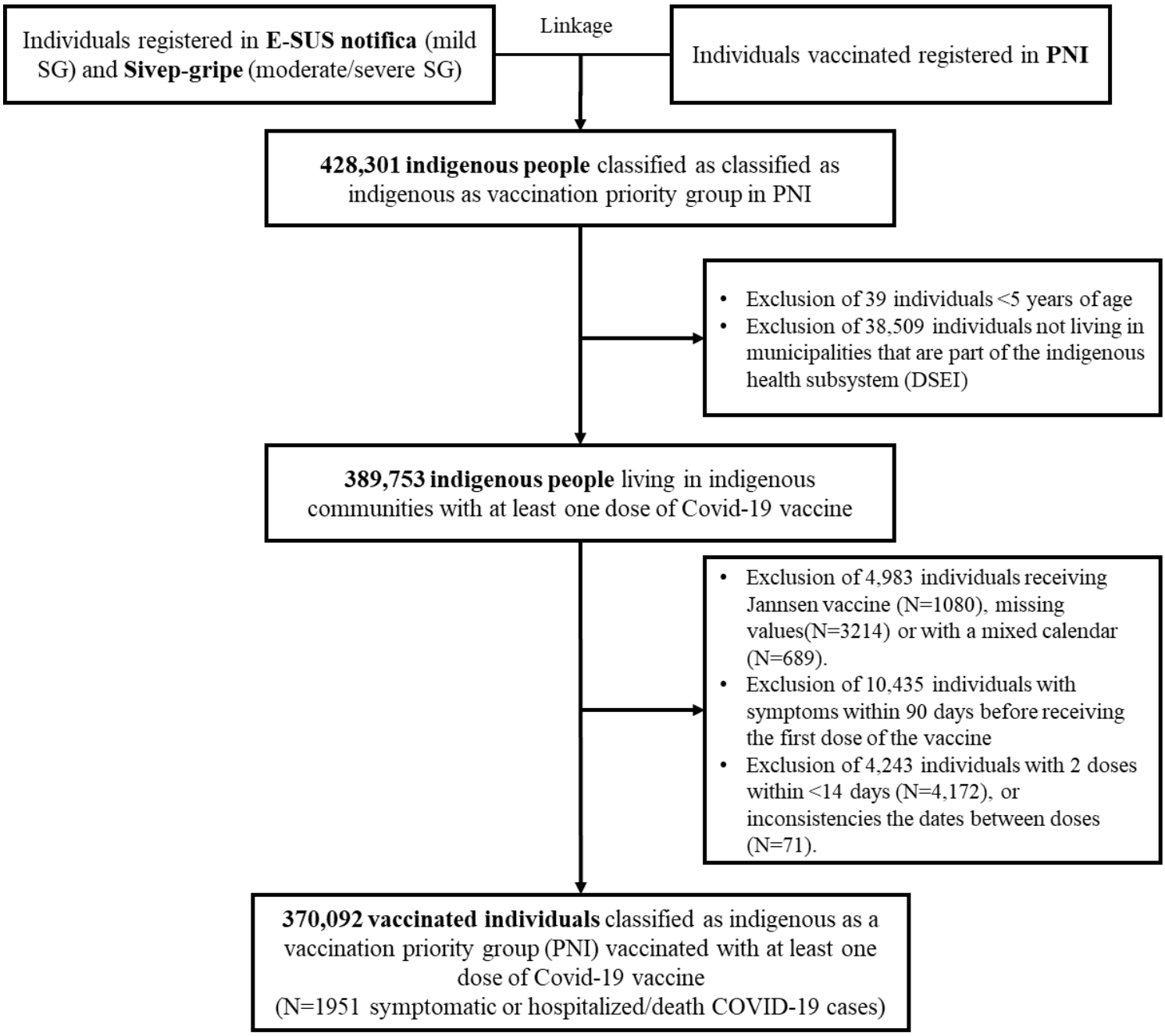

Figure 1

Flowchart of data selection of the cohort of indigenous people living on indigenous land and vaccinated with Covid-19 vaccines.

Supplementary Files

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