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Influenza vaccination in older adults during the COVID-19 pandemic: a population-based study in 133 Brazilian cities

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Abstract *Routine immunization during pandemics can be harmed. This study estimated the influenza vaccination coverage in older adults during the COVID-19 through the EPICOVID-19, a population-based study conducted in 133 cities from the 26 Brazilian states and Federal District. We selected 25 census tracts per city, with probability proportional to the tract's size, ten households by census tract, and one random individual interviewed. A total of 8,265 older adults (≥60 years old) were interviewed and asked whether they had been vaccinated against flu in 2020. Vaccination coverage was 82.3% (95% CI: 80.1-84.2) with no difference by gender, age, and region; higher vaccination coverage was observed among the wealthiest (84.7% versus 80.1% in the poorest) and among the more educated (87.3% versus 83.2% less educated); lower coverage among indigenous (56.9% versus > 80% among other ethnic groups). A positive association was identified with the number of comorbidities among men but not among women. Most of the population was vaccinated (97.5%) in the public health system. The private network was chosen mainly in the South by the wealthiest and more educated. Vaccination coverage was seven percentage points lower than the government target (90%), and inequalities should be reversed in future campaigns.*

Key words *Vaccination coverage, Influenza virus, Elderly, Coronavirus infections*

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Introduction

Influenza is a viral infectious respiratory disease, with high morbimortality, especially in some risk groups such as older adults, children, and people with chronic diseases[1]. In Brazil, the influenza vaccine has been incorporated into the National Immunization Program (PNI) since 1999 to reduce hospitalizations, complications, and deaths[2,3]. Although the vaccine's effectiveness is heterogeneous[4-6], the World Health Organization (WHO)[2] and the Brazilian Ministry of Health[7] recommend an annual vaccination, prioritizing certain groups, including the older adults aged 60 years and over[8]. The PNI vaccination coverage goal has been to reach 90% of this target population[9] since 2017. However, some population-based studies in the country show lower coverage, ranging from 70 to 78%, in the last ten years[10-13].

Given the COVID-19 pandemic, the Ministry of Health adopted a new strategy for the flu vaccine in 2020, anticipating the vaccination start to the end of March and extending free vaccination to other population groups, such as adults aged 55-59 years and professionals such as port workers, drivers, public transport collectors, truck drivers and professionals from the security and rescue forces[14].

Although the influenza vaccine is not effective against the coronavirus, it can help health professionals exclude the COVID-19 diagnosis and reduce the demand for health services[14], as the symptoms may be similar.

It should be reminded that the population may be concerned with adherence to vaccination. On the one hand, the recommendation is to remain in isolation and avoid crowding. On the other hand, the population is called to be vaccinated against influenza, which can expose individuals to a high risk of SARS-CoV-2 contagion. As pointed out in the Andrade's paper[15], other reasons must be considered besides non-adherence to vaccination due to the pandemic, such as fear of vaccine side effects, lack of knowledge regarding its benefits, considering oneself naturally immune to the flu, medical contraindication, and difficulties to visit the health post.

In 2020, we faced an atypical epidemiological scenario in the country. The population and health authorities had to reorganize several primary health care activities and implement new strategies without an adequate assessment of the changes that had occurred since the urgency was to fight the pandemic. The national and population-based EPICOVID-19 study assessed the new epidemiological scenario in 2020.

This paper aimed to estimate the influenza vaccine coverage during the COVID-19 pandemic in older adults aged 60 years and over and its association with sociodemographic variables and comorbidities and the share of vaccination through a private provider in the fourth phase of the EPICOVID-19 study.

Methods

EPICOVID-19[16] is a study consisting of serial serological surveys designed to monitor the coronavirus pandemic trend in Brazil. The survey was conducted in 133 sentinel cities in 26 Brazilian states and the Federal District. These cities are the most populous in each of the 133 intermediate Brazilian regions as per the Brazilian Institute of Geography and Statistics (IBGE) distribution. Twenty-five census tracts were sampled in each city with probability proportional to the size, and IBGE provided a random list of 10 households. In each household, one of the residents was randomly selected to perform the rapid test to detect antibodies against SARS-CoV-2 and answer a questionnaire. In the fourth phase of the study, carried out in the August 27-30, 2020 period, information on influenza vaccination was collected, an outcome analyzed in this study. Participants who answered "yes" to the question "Have you had the flu vaccine this year?" were considered vaccinated for influenza. This study's vaccine data is restricted to older adults aged 60 years and over. Vaccination coverage was calculated as the number of older adults who reported having been vaccinated against influenza in 2020 divided by the total number of individuals. As EPICOVID-19 was a population-based survey, the term vaccination coverage was used as a synonym for prevalence[17,18].

The following characteristics of the individuals were assessed: participant's gender, age collected in complete years (later categorized as 60-69, 70-79, ≥ 80 years), self-reported skin color (white, brown, black, yellow, and indigenous), region of the country (North, Northeast, Southeast, South, and Midwest), Wealth Index (in quintiles), education (less than elementary, elementary, high school/incomplete higher education, and higher education and over) and the number of comorbidities (none, one, two, and three or more). The Wealth Index was created through a principal component analysis from

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a list of assets and ownership at the household level, similar to the National Economic Indicator (IEN)[19]. The first component was extracted, and the households were sorted and divided into quintiles. The first quintile represented the 20% poorest households in the distribution, and the last quintile the wealthiest 20%. The self-reported medical diagnosis of the following comorbidities was investigated: hypertension or high blood pressure; diabetes; asthma or bronchitis; cancer; chronic kidney disease; heart disease; and another morbidity not formerly mentioned.

Descriptive analyses were performed for the variables considered, and vaccination coverage was estimated per the older adults' characteristics. Differences between proportions were verified using the chi-square test or linear trend test, considering a significance level of 5%. Crude and adjusted coverage ratios were used with the respective 95% confidence intervals, using Poisson regression models with robust variance to verify the associations between comorbidities and influenza vaccination. The Mantel-Haenszel test was used to test if there was effect modification by gender and comorbidity variables, in the crude Poisson regression model, with a significance level of 10%. The following variables were included in the adjustment: region of the country, age in categories, skin color, Wealth Index, and schooling.

The National Research Ethics Committee (CONEP) approved the EPICOVID-19 study under N° 30721520.7.1001.5313. In the case of minors or people with disabilities, all participants or guardians signed an informed consent form. Additional information about EPICOVID-19 can be found in previous publications[20-22].

The overall response rate for EPICOVID-19 was 55% due to logistical difficulties during the pandemic isolation period. No people were found at the residence in 22% of the households, and another 23% of the residents refused to perform the test to detect COVID-19 antibodies. Losses and refusals were replaced by neighbors to reach the desired total of 33,250 people interviewed in 133 cities, of which 8,265 (24.9%) were aged 60 or over.

Results

The characteristics and vaccination coverage for influenza among older adults are shown in Table 1. Coverage in the 133 cities in the country was 82.3% (95% CI 80.1-84.2). Results by city are not shown, as the median number of older adults interviewed was only 62 per city. Two-thirds were women, 43.3% were white, about 30% lived in the Northeast, and a similar proportion in the Southeast; one-third lived in poor households, and more than half of the sample had less than primary elementary school level.

There was no statistical evidence of differences in coverage by gender, age, or country region (Table 1). Regarding skin color, it is noteworthy that vaccination coverage was 56.9% in indigenous peoples compared to coverage above 80% in other ethnic groups, but without statistical significance. Statistically significant differences were observed for coverage per Wealth Index ($p < 0.001$) and schooling ($p=0.041$). The Wealth Index variable was positively associated with coverage, ranging from 80.1% in the poorest quintile to 84.7% in the wealthiest quintile. As for schooling, the two extreme groups had the highest coverage; individuals who did not complete elementary school had 83.2% coverage, while those with higher education had coverage of 87.3%. Concerning the skin color variable, the p-value was equal to 0.056, while the coverage among the 140 indigenous people was only 56.9%, much lower than the other groups with coverage above 80%.

Vaccination coverage by sociodemographic variables and region and stratified by gender are shown in Figure 1. Women had coverage slightly higher than men in most of the categories of the studied variables. However, an overlap of confidence intervals for men and women is observed in almost all categories. Regarding the geographic region, there was a change in the effect with gender ($p=0.04$); among men, the most significant coverage was in the Southeast (84.9%) and North (83.4%), while the most significant coverage was in the Midwest (84.4%) and Southeast (84.3%) among women.

Table 2 shows the results of vaccination coverage against influenza for older adults and stratified by the number of comorbidities reported. There was no statistically significant difference for the adjusted coverage ratio ($p=0.278$) concerning women. In men, higher coverage was observed among those with two (PR=1.14; 95% CI: 1.02-1.19) and three or more comorbidities (PR=1.19; 95% CI: 1.07-1.31) and was 19% higher in the latter than the group without this condition ($p=0.007$).

Figure 2 shows the percentage of obtaining the vaccine from a private health provider by sociodemographic variables. Almost all (97.5%) the older adults obtained the vaccine in the pub-

Table 1. Characteristics of the sample of older adults and influenza vaccination coverage. EPICOVID-19 Study, Brazil.

Variable	Category	N	%	Vaccination coverage (%)	95% CI	P-value
Region of the country	North	984	11.9	79.1	74.6 - 83.0	0.129
	Northeast	2510	30.3	80.5	77.7 - 83.1	
	Southeast	2452	29.6	84.5	80.3 - 87.9	
	South	1518	18.3	79.9	76.8 - 82.6	
	Midwest	828	10.0	81.1	75.5 - 85.7	
Gender	Male	3053	36.8	81.7	78.0 - 84.8	0.658
	Female	5239	63.2	82.6	79.9 - 85.0	
Age	60-69	4557	55.0	82.0	79.1 - 84.5	0.123*
	70-79	2671	32.2	83.2	79.4 - 86.5	
	80+	1064	12.8	81.3	74.5 - 86.6	
Skin color	White	3423	43.3	82.1	78.6 - 85.1	0.056
	Brown	3041	38.4	83.1	79.8 - 86.0	
	Black	1059	13.4	80.5	73.7 - 85.9	
	Yellow	246	3.1	87.1	78.3 - 92.6	
	Indigenous	140	1.8	56.9	30.6 - 79.8	
Wealth Index (quintiles)	Poorest	2566	30.9	80.1	76.0 - 83.6	<0.001*
	2nd	1693	20.4	81.1	75.5 - 85.6	
	3rd	1346	16.2	81.2	74.8 - 86.2	
	4th	1434	17.3	85.3	80.7 - 88.9	
	Wealthiest	1253	15.1	84.7	79.7 - 88.7	
Schooling	Less than Elementary School	4178	51.6	83.2	80.1 - 85.8	0.041
	Elementary School	1441	17.8	77.1	70.3 - 82.8	
	High School	1650	20.4	82.1	77.8 - 85.8	
	Higher Education	823	10.2	87.3	83.1 - 90.6	
Total		8265	100	82.3	80.1 - 84.2	

CI = Confidence interval. P-values of the chi-square test for heterogeneity. * Linear trend chi-square test

Source: Own elaboration based on data from the EPICOVID-19 Study, Brazil.

lic network. There was no difference in percentages regarding gender and age groups (p>0.05) among those who acquired it through a private provider. However, 7.7% of older adults in the South obtained the vaccine in the private network, five times that observed in the Southeast (1.4%). The most educated (7.5%) and those belonging to the highest wealth quintile (5.3%) had the highest percentage of vaccination in the private network.

Discussion

Flu vaccine coverage in older adults during the COVID-19 pandemic in the sentinel cities of the EPICOVID-19 study was 82.3% (95% CI: 80.1-84.2). No differences were observed by gender, age, or region of the country, but higher coverage was identified between more affluent and more educated individuals. Among indigenous people, coverage was lower than among other ethnic groups but without statistical significance. A direct association was observed between coverage and number of comorbidities among men, but not among women, even adjusting for confounding factors. Most of the population obtained the vaccine from the public network (97.5%), and among those who obtained it through the private network, the highest percentage was in the South, among the most educated and wealthiest.

The federal government's goal for influenza vaccination coverage in older adults was 80% in the 2008-2016 period. However, population-based studies carried out in some municipalities in São Paulo and southern Brazil showed coverage ranging from 71%[18] to 78%[11-13]. Since 2017, this goal has changed to reach 90% of the

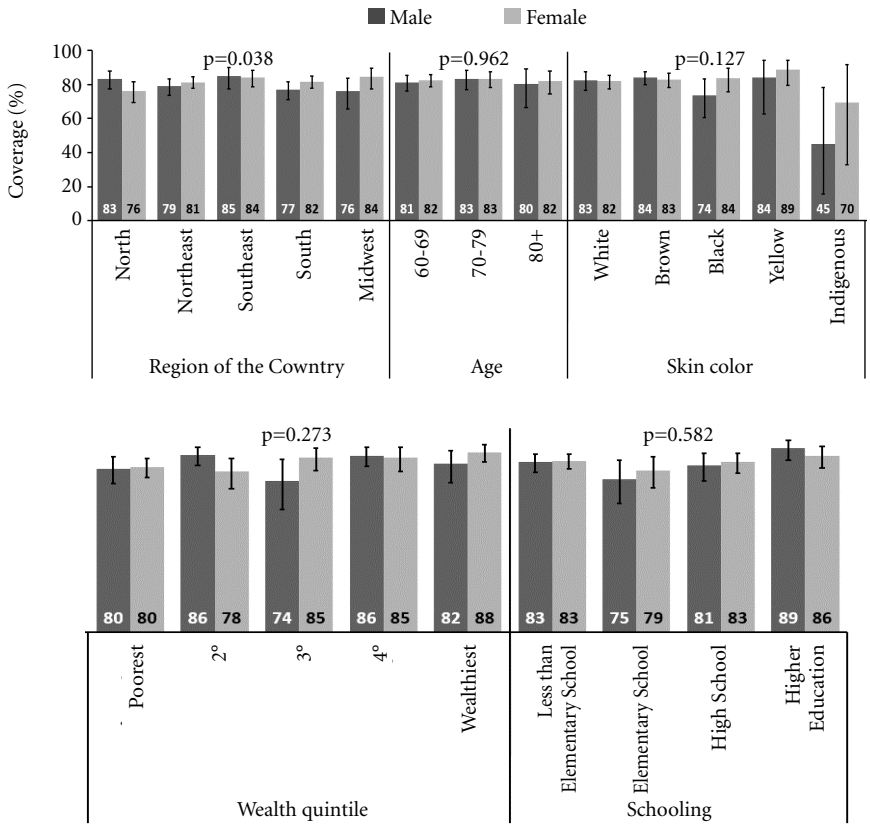

Figure 1. Vaccination coverage in older adults by sociodemographic characteristics, stratified by gender. EPICOVID-19 Study, Brazil (the bars represent the 95% confidence interval for proportions).

Note: presented p-value refers to the variable effect modification test with gender.

Source: Own elaboration based on data from the EPICOVID-19 Study, Brazil.

elderly population[9]. According to data from the Information System of the National Immunization Program (SI-PNI)[24], the ratio between administered doses and the estimated elderly population was stable at a level around 100% between 2016 and 2019, increasing by more than 20 percentage points from 2019 to 2020, when it reached 120.7%. It is essential to emphasize the need for continuous updating of census data given the aging speed of the Brazilian population. The high rates of vaccination coverage in recent years may be because the population used for the calculation is underestimated[25]. Regardless of the likely gap between the number of doses administered and the population estimate, the increase observed in 2020 can be related to the intensification of the national influenza vaccination campaign in health units and through the media. Despite every campaign carried out to get the elderly population vaccinated for influenza, our population survey results suggest that coverage in 2020 was seven percentage points below the 90% target. The coverage of 83% can be considered satisfactory because, given the pandemic, there was a strong recommendation for older adults – who are a group at higher risk for COVID-19 – to stay home, distancing themselves from friends, relatives, and neighbors and avoid social and religious events as a way to prevent the disease.

Women generally seek health services the most, adopt preventive measures, and follow more health-related indications[26,27]. Our results showed a difference of 0.9 percentage points in

Table 2. Comorbidities, vaccination coverage, and crude and adjusted coverage ratios. EPICOVID-19 Study, Brazil.

Variable	N	%	Vaccination coverage (%)	P-value	Crude coverage ratio (95% CI)	P-value	Adjusted coverage ratio* (95% CI)	P-value
Comorbidities								
None	1848	22.9	79.5	<0.001	1	0.093	1	0.076
1	2702	33.5	81.2		1.02 (0.95; 1.10)		1.02 (0.95; 1.10)	
2	2122	26.3	85.9		1.08 (1.01; 1.15)		1.09 (1.02; 1.17)	
3+	1400	17.3	82.6		1.04 (0.96; 1.13)		1.04 (0.96; 1.08)	
Women								
Comorbidities								
None	1018	55.1	81.9	0.025	1	0.298	1	0.278
1	1699	62.9	82.0		1.00 (0.92; 1.09)		1.00 (0.92; 1.09)	
2	1407	66.3	86.2		1.05 (0.97; 1.14)		1.06 (0.98; 1.15)	
3+	973	69.5	80.0		0.98 (0.87; 1.09)		0.98 (0.88; 1.10)	
Men								
Comorbidities								
None	830	44.9	75.9	<0.001	1	0.019	1	0.007
1	1003	37.1	80.1		1.06 (0.94; 1.19)		1.06 (0.94; 1.19)	
2	715	33.7	85.4		1.13 (1.00; 1.27)		1.14 (1.02; 1.27)	
3+	427	30.5	88.3		1.16 (1.05; 1.29)		1.19 (1.07; 1.31)	

* Coverage ratio adjusted for region of the country, age, skin color, wealth quintiles and schooling level. [23]

Source: Own elaboration based on data from the EPICOVID-19 Study, Brazil.

favor of women, albeit without statistical significance. The lack of differences by gender is consistent with other Brazilian studies on the subject[12, 13, 15, 23]. We also did not observe differences between the three age groups of older adults, consistent with some studies[12,15,23], although other studies have found higher vaccine coverage in people in the older age group[13,28]. Given the COVID-19 pandemic's outlook, where one of the priority groups in the flu campaign were older adults aged 60 years or more, coverage was more evenly distributed in this group than in other studies carried out in times without pandemic.

Our results showed similar coverage regarding the country's regions, ranging from 79.1% in the North to 84.5% in the Southeast, while the SI-PNI[24] data suggest higher coverage in the cities of the Northeast. Evaluating a nationally representative sample of individuals aged 60 years and over, the study by Andrade[15] showed a vaccination coverage against influenza in the country of 72.6% (95% CI: 71.1-74.1), with different vaccine coverage by region (p<0.001), where the North and Northeast regions had the lowest coverage (71.2% and 66.6%, respectively) and the South had the highest coverage (78.7%). Among the reasons given by the population for not getting vaccinated, in Andrade's study, "not knowing that it was necessary to have the influenza vaccine" was among the top five reasons, with 7.4% in the North region, 4.4% in the Northeast and 2.1% in the South[15]. A sample of hypertensive older adults was analyzed in the 2013 National Health Survey and the highest vaccination coverage was in the Southeast and South, which was attributed to the better socioeconomic position with possibly greater access to health services and better counseling regarding vaccination[29]. Another aspect to be considered in immunization against influenza is the disease's seasonality in different regions of the country. The South has a pronounced seasonality, with the highest occurrence of influenza in the winter months, that is, in the period after the vaccination campaign, while the peak of the disease occurs more before the vaccination campaign[30] in the North. It may be that in the EPICOVID-19 study, during 2020, no significant differences were observed in the vaccination coverage by region due to the escalating vaccination campaign across the country and because the COVID-19 pandemic was the one that scared the population the most, and

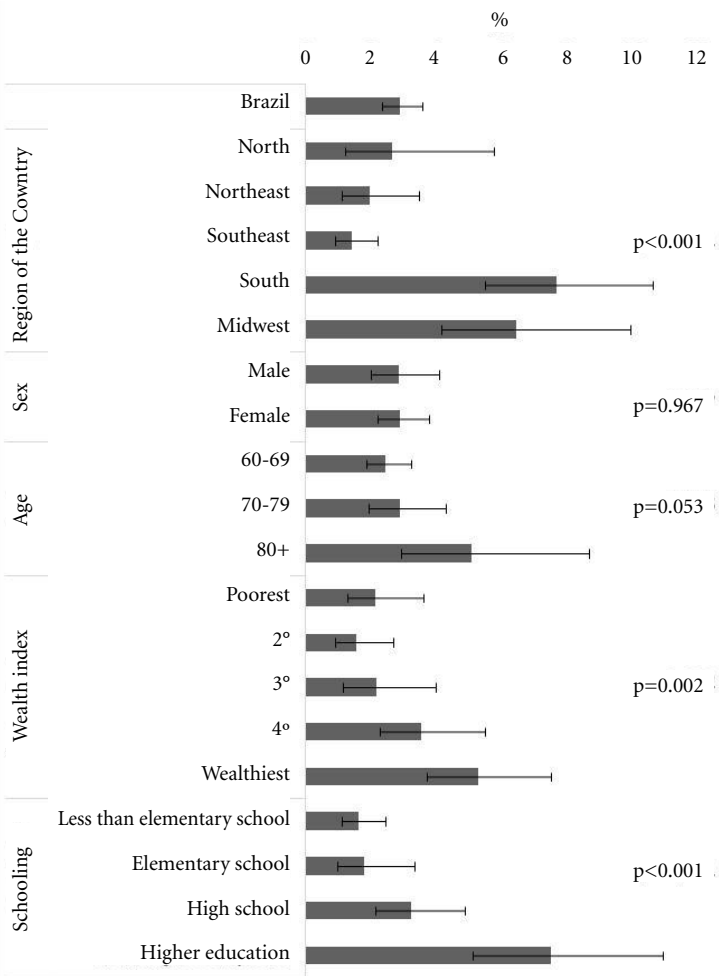

Figure 2. Acquisition of influenza vaccine from a private healthcare provider. EPICOVID-19 Study, Brazil (the bars represent the 95% confidence interval for proportions).

Source: Own elaboration based on data from the EPICOVID-19 Study, Brazil.

could even manifest itself with respiratory flu-like symptoms.

The relationship between immunization against influenza and socioeconomic conditions has been a controversial topic in the literature. Studies carried out in the state of São Paulo have shown higher coverage in the less educated[10,31] and a lack of association between coverage and schooling[28]. In another study with older adults in southern Brazil, Neves et al.[23] found a 20% higher prevalence of influenza vaccination among those with a higher economic level, with no significant association with schooling.

Notably, most studies show the presence and number of comorbidities as essential factors for adherence to influenza vaccination[11,12,23]. Our study identified higher vaccination coverage among men, who reported a more significant number of comorbidities, but not among women. The study by Bacurau[32] found differences with statistical significance in females for the comorbidities of asthma, arthritis or rheumatism, lung diseases or chronic obstructive pulmonary disease and renal failure, and only for stroke comorbidities in males. Hypertension, diabetes mellitus, and heart disease did not show statistical significance by gender. The Health Well-being and Aging Study (SABE, 2015) with a population-based sample of older adults in São Paulo did not show a statistically significant difference

for the number of comorbidities (p=0.642). The comorbidities assessed separately, such as arterial hypertension, diabetes mellitus, cardiovascular disease, chronic lung disease, and falls in the last 12 months, also did not show statistical significance. According to self-report, depression was the only comorbidity with lower coverage reaching statistical significance (p=0.031)[13].

Analyzing each of the comorbidities self-reported in the EPICOVID-19 survey and their number, stratified by gender, a higher prevalence was found in males for two or three or more comorbidities concerning systemic arterial hypertension, diabetes, cancer, heart, and kidney disease, compared to asthma and other unspecified diseases, in females. Therefore, the higher coverage of the vaccine in men may have occurred because they report more severe illnesses than women, which would lead to greater demand for health services and, consequently, greater immunization against influenza.

The national literature is unanimous regarding the public network being the primary source for obtaining the vaccine[23,31], as was also found in this study, in which less than 3% of the vaccines were purchased in the private sector. Brazil is among the countries that have implemented flu vaccination since 1999, with annual seasonal campaigns and free vaccination for priority groups[14]. Despite the WHO recommendation that all countries have national influenza immunization programs[33], not all of them follow this instruction, and it is not offered free of charge in some, with lower vaccine coverage[34].

In our study, the private sector was most frequently used in the South and, at the national level, among the more affluent older adults, reinforcing the importance of free and available vaccines.

Specifically, during the COVID-19 pandemic, world health authorities have warned the population about the possible risks of lack of vaccination for influenza and other vaccines[35-37]. Isolation measures adopted to mitigate the pandemic can negatively influence the search for the vaccine, especially in older adults, a population at higher risk for COVID-19. A pilot study in Australia[38] showed that strategies such as in-house influenza vaccination could be successfully adopted during a pandemic.

Some limitations of this study should be mentioned. The most important is the lack of confirmation of vaccination status through a card or proof of vaccination. However, some validation studies in the general population and specific groups show high sensitivity for self-report (around 97%)[39,40]. Considering this high sensitivity of self-report and the short time elapsed between the survey and vaccination, the occurrence of recall bias is unlikely, although it cannot be excluded. The EPICOVID-19 was restricted to urban areas, which does not allow us to assess vaccination coverage in rural areas, where 14.2% of elderly Brazilians reside[41]. Furthermore, the sentinel cities sampled tend to be larger, more developed, and better equipped with health services than other urban areas. White individuals were underrepresented in our sample compared to the national population, probably due to more refusals in certain places of residence. Furthermore, the average human development index (HDI) of the 133 cities included is higher than that of the 5,437 cities not included, which may have overestimated the vaccination coverage. The official data on vaccine coverage according to the HDI of the municipalities[24,42] revealed higher vaccine coverage against influenza per the HDI quintile (118% vaccine coverage in the highest HDI quintile and 109.9% coverage in the lowest HDI quintile).

On the other hand, the strengths of the EPICOVID-19 survey are the size of the study sample, the coverage of a large area of the country, and the information on vaccine coverage for influenza in a pandemic such as COVID-19, in which the epidemiological scenario is unique, with no other studies on the subject in the country.

Flu vaccination is a cost-effective program, which requires good adherence by the target population to achieve it. Despite the adequate flu vaccination coverage in older adults during COVID-19, some inequalities such as lower coverage among the less educated and less wealthy deserve special attention in future vaccination campaigns. We also highlight indigenous people with much less coverage than other ethnic groups, despite the lack of statistical significance. We should reflect on overcoming these inequalities and planning immunizations according to that moment's epidemiological profile. Vaccination campaigns are essential and seem to be contributing to better population adherence. However, among those most vulnerable, where coverage is lower, active search and home visits through community health workers or other health professionals should be considered to achieve universal coverage and promote healthy aging.

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Contributions

AMB Menezes was responsible for the conception, analysis, and writing of the paper. PC Hallal is the coordinator of the EPICOVID-19 study. CG Victora, FC Wehrmeister, and PD Oliveira helped in the analysis and discussion of the results. The following participated in the critical review of the paper: CG Victora, PC Hallal, MF Silveira, FC Wehrmeister, BL Horta, AJD Barros, FP Hartwig, PD Oliveira, LP Vidaletti, MA Mesenburg, N Jacques, FC Barros. Paper review: All authors participated in the final approval of the paper for publication and assumed public responsibility for all aspects of the research: All authors.

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