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ARTICLE

COVID-19 vaccination and case fatality rates: a case report in a Brazilian municipality

Vacinação contra a COVID-19 e taxas de letalidade: relato de caso em uma cidade brasileira

Vacunación contra el COVID-19 y tasas de letalidad: reporte de caso en una ciudad brasileña

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Abstract

Vaccination campaigns played a crucial role in reducing the incidence of COVID-19. However, a scant number of studies evaluated the impact of vaccination on case fatality rates (CFRs), including in Brazil. Our study aimed to compare CFRs according to vaccination status among subjects living in Arapongas (Paraná State, Brazil), considering the age composition of the population. Several strategies adopted by the Arapongas City Hall to minimize the spread of the virus were also elaborated upon. We accessed the 2021 database of the Arapongas Municipal Health Department, in which a total of 16,437 confirmed cases and 425 deaths were reported. The CFR was calculated as the ratio between COVID-19 deaths and the number of confirmed cases. Differences in age composition between unvaccinated and fully vaccinated individuals were observed in our study. Considering that CFR is a crude indicator and is highly sensitive to the age composition of the population, we adopted the average age distribution of confirmed cases among the three vaccination statuses (unvaccinated, partially, and fully) as a standard age distribution. The age-standardized CFR for unvaccinated and fully vaccinated groups were 4.55% and 2.42%, respectively. Fully vaccinated individuals showed lower age-specific CFRs in all age groups above 60 years than unvaccinated populations. Our findings strengthen the role of vaccination as a critical measure for preventing deaths among infected people and is particularly important to the ongoing reassessment of public health interventions and policies.

COVID-19; Vaccination; Mortality

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Background

The COVID-19 pandemic has had a substantial impact on public health systems worldwide. Without an effective treatment and vaccine against SARS-CoV-2, various individual and community measures have been taken to minimize serious illness and deaths while containing the spread of the virus [1].

Vaccines were a turning point for the pandemic. With accelerated trials, the first COVID-19 vaccine efficacy results were delivered less than a year after the first publication of the viral genome sequencing [2,3]. In Brazil, vaccination campaigns against COVID-19 began on January 17, 2021, with a phased program prioritizing age groups, health professionals, institutionalized people, and indigenous populations [4]. Brazil ranks fourth globally in the absolute number of people fully vaccinated against COVID-19 [5], with 85.8% of the population being fully vaccinated [6]. After implementing this measure, severe illnesses and deaths have been continuously declining, despite not following a linear pathway [7]. Indeed, the longer it takes to contain the virus, the longer new viral variants have time to emerge and spread, which could lead to a resurgence of cases.

Recent studies highlighted that Brazilian vaccination campaigns played a relevant role in reducing the incidence of COVID-19 among health professionals [8,9] and in severe cases and deaths among older adults [10,11,12]. More recently, a study also demonstrated that vaccination for COVID-19 was significantly associated with reduced case fatality rates (CFRs) across all age groups in a municipality in Southern Brazil [13]. Although vaccinated individuals may still get infected, they develop milder symptoms and have a lower death risk than unvaccinated subjects [14]. Thus, vaccination has empirically shown its effectiveness.

The success of vaccination depends on numerous factors, including efficacy and safety, availability, and public acceptance and compliance. To this end, few studies in Brazil have shown that vaccine hesitancy is directly related to efficacy and potential adverse side effects [15,16]. Thus, further local studies showing vaccine efficacy in reducing fatality rates may decrease the population's vaccine hesitancy. This improved knowledge will allow the ongoing reassessment of public health interventions and policies based on local characteristics, maximizing their effectiveness.

CFR is an essential index that helps to understand the epidemiological characteristics of the COVID-19 outbreak [17]. It is defined as the ratio between the number of confirmed deaths from a disease and the number of reported cases in a given time. Certain points require caution and awareness when investigating the impact of COVID-19 vaccines on CFR. It is highly recognized that CFR is a metric sensitive to demographic factors (age-structure of diagnosed infection cases and age-specific fatality rates), delays in reported cases, and testing policies [18,19,20]. Another study also showed that the CFR depends not only on the effectiveness of vaccines in reducing deaths among the vaccinated but also on detecting infections among both vaccinated and unvaccinated individuals [21]. If the same testing strategy is maintained before and after the beginning of vaccination campaigns, a decline in CFR may indicate that vaccines are preventing deaths [21].

In this study, we contrast the behavior of the CFR between vaccinated and unvaccinated individuals in a municipality in Southern Brazil to understand the role of COVID-19 vaccination as a vital public health measure to prevent COVID-related deaths. We also discuss the primary public health interventions adopted by the municipal authorities to minimize the spread of the disease in the municipality. The underlying hypothesis from our work is that vaccinated individuals have lower fatality rates than those unvaccinated in all age groups. This study contributes to the discussion on how local policymakers should accurately measure vaccine effectiveness in reducing fatalities, considering the influence of demographic factors on these values to develop appropriate strategies for the ongoing reassessment of local public health interventions.

Methods

Study design and setting

This is an ecological study conducted in Arapongas, located in the north of the state of Paraná (Figure 1), with an estimated population of 126,545 inhabitants in 2021 [22]. Arapongas has a 382,215km^2 and

population density of 272.49 inhabitants/km². Arapongas belongs to the 16th Health District among the 22 districts from Paraná; these are territorial divisions of political-administrative nature to make health actions more agile and efficient.

Participants

This study included all individuals within the Arapongas Municipal Health Department database with a confirmed COVID-19 diagnosis. The time interval considered comprises cases and deaths after the start of vaccination, on January 20, 2021, until December 31, 2021. A total of 16,437 confirmed cases and 425 deaths were reported during this period. The COVID-19 case definition followed the World Health Organization (WHO) criteria: an individual with a positive Nucleic Acid Amplification Test (NAAT) or a positive SARS-CoV-2 antigen rapid diagnostic test and meeting the probable or suspect case definition criteria [23].

The study was approved by the Research Ethics Committee of the State University of Londrina (reference n. 44128621.3.0000.5231).

Variables

Sociodemographic variables included age (years), sex (male, female), and vaccination status. Confirmed cases and deaths were grouped into unvaccinated, partially vaccinated, and fully vaccinated according to the vaccination status reported at the time of the COVID-19 notification. Complete vaccination status encompassed all individuals with ≥ 14 days after the second dose (for 2-dose vaccines) or a single dose (for the Janssen vaccine). Incompletely vaccinated were defined as those individuals who received only one dose (in the case of 2-dose vaccines) or were less than 14 days after the second dose or after a single-dose vaccine (Janssen).

Case fatality rates definition

The CFR measures the proportion of individuals with a specific condition who died from that condition during the reference period; it is therefore a measure of severity among detected cases [24]. In this article, CFR metric refers to the ratio of COVID-19 deaths (D) divided by the number of confirmed cases (N): CFR = D/N.

Statistical analysis

CFRs were calculated according to the vaccination status to compare immunization effectiveness. Since CFR is a crude rate, differences in age distributions of confirmed cases among subgroups with different vaccination statuses may strongly affect the results [13]. To make reliable comparisons between CFRs, the average age distribution of confirmed cases among the vaccination statuses was adopted as a standard age distribution. The age-standardized CFR is given by:

$$Age\ standardized\ CFR = \sum_{i=1}^{\infty} C_i \left(\frac{P_i^{Unvaccinated} + P_i^{Incomplete} + P_i^{Complete}}{3} \right)$$

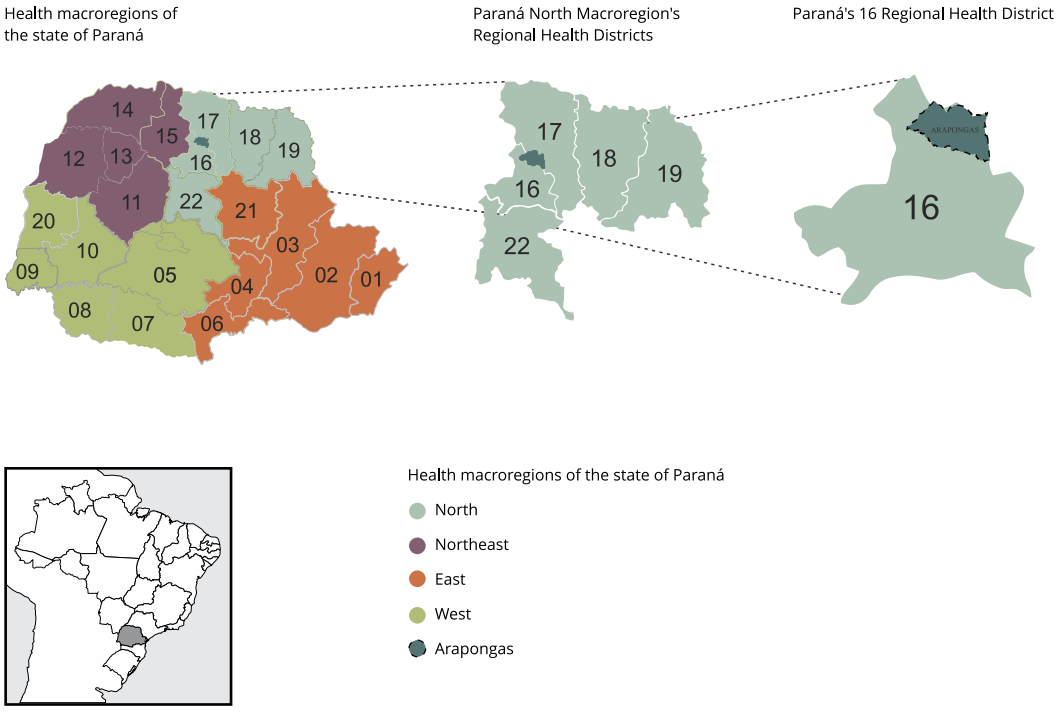
where C_i represents the age-specific CFRs and P_i is the proportion of cases in each age group among the vaccination statuses.

To compare the proportions of cases and deaths among groups (unvaccinated, partially, and fully vaccinated subjects), pairwise comparisons between pairs of proportions (Z-tests) with correction for multiple testing were performed.

All analyses were conducted in R software program (http://www.r-project.org).

Figure 1

Regional Health Districts in the state of Paraná, Brazil.



Results

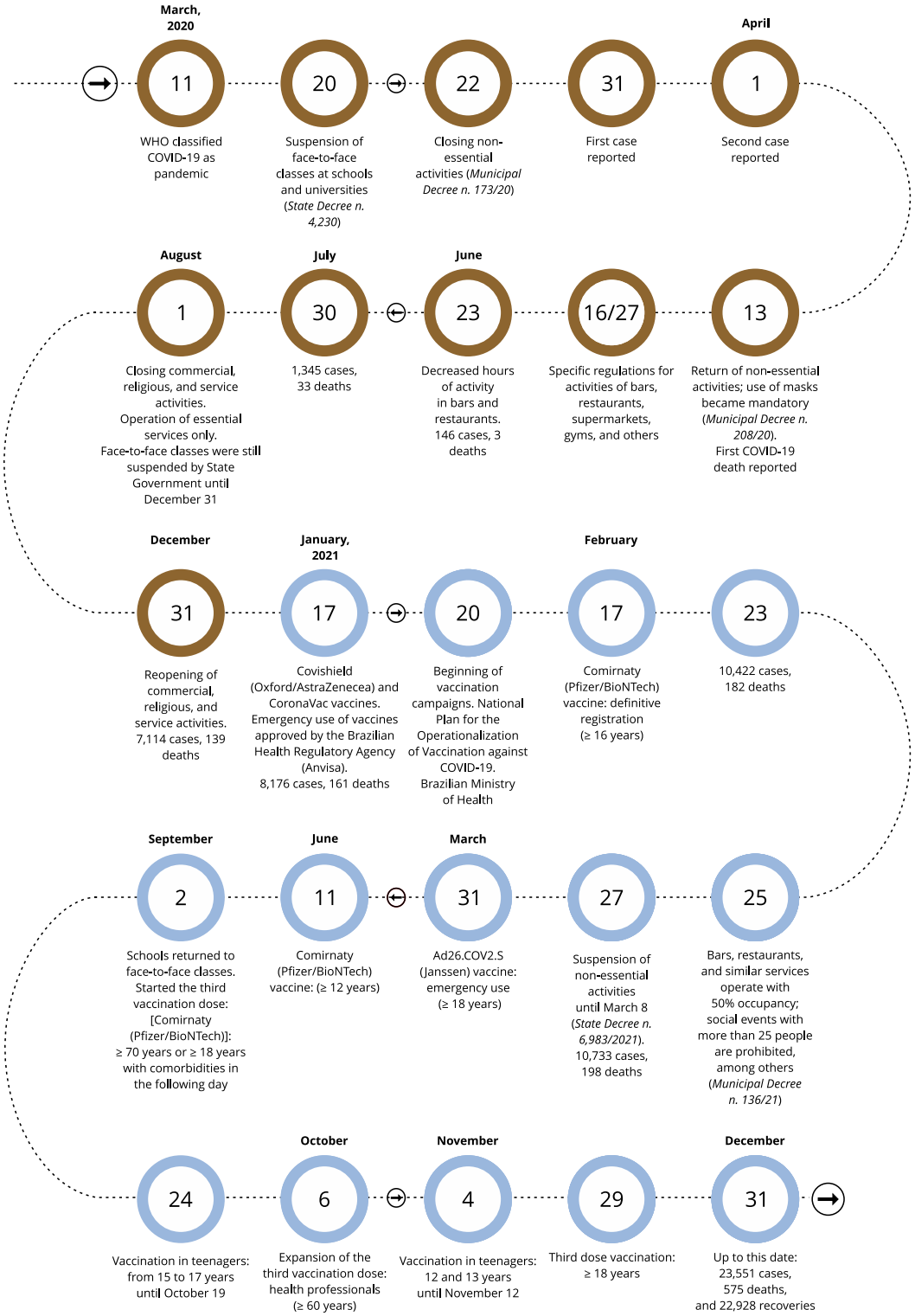
Figure 2 shows the leading public health measures at municipal and state levels through decrees and other actions adopted to minimize the spread of the disease between 2020 and 2021. The numbers of confirmed cases and deaths were made available periodically, and the Arapongas Municipal Health Department maintained a close dialogue with researchers from higher education institutions with high regional impact, such as the State University of Londrina. Moreover, local guidelines were made available to the Arapongas population as part of the strategy to combat the disease.

In 2021, COVID-19 vaccination campaigns began in the municipality, following the Brazilian National Immunization Program, which established priority groups to be vaccinated. Vaccination was conducted in a phased schedule according to the guidelines established by the Brazilian Ministry of Health. Up to December 31, 2021, 23,551 and 575 confirmed cases and deaths had occurred in Arapongas, respectively (Figure 2).

Figure 3 shows the distribution of COVID-19 cases and deaths stratified by age, sex, and vaccination status. We observed significant differences in age compositions among vaccination statuses. The fully vaccinated population had a greater number of older adults, contrasting with unvaccinated and partially vaccinated groups. The unvaccinated group had the highest proportion of individuals aged under 60 years for both sexes, resulting in a younger age composition than that observed among the other groups. In the fully vaccinated subgroup, deaths occurred only among older adults (60+ years),

Figure 2

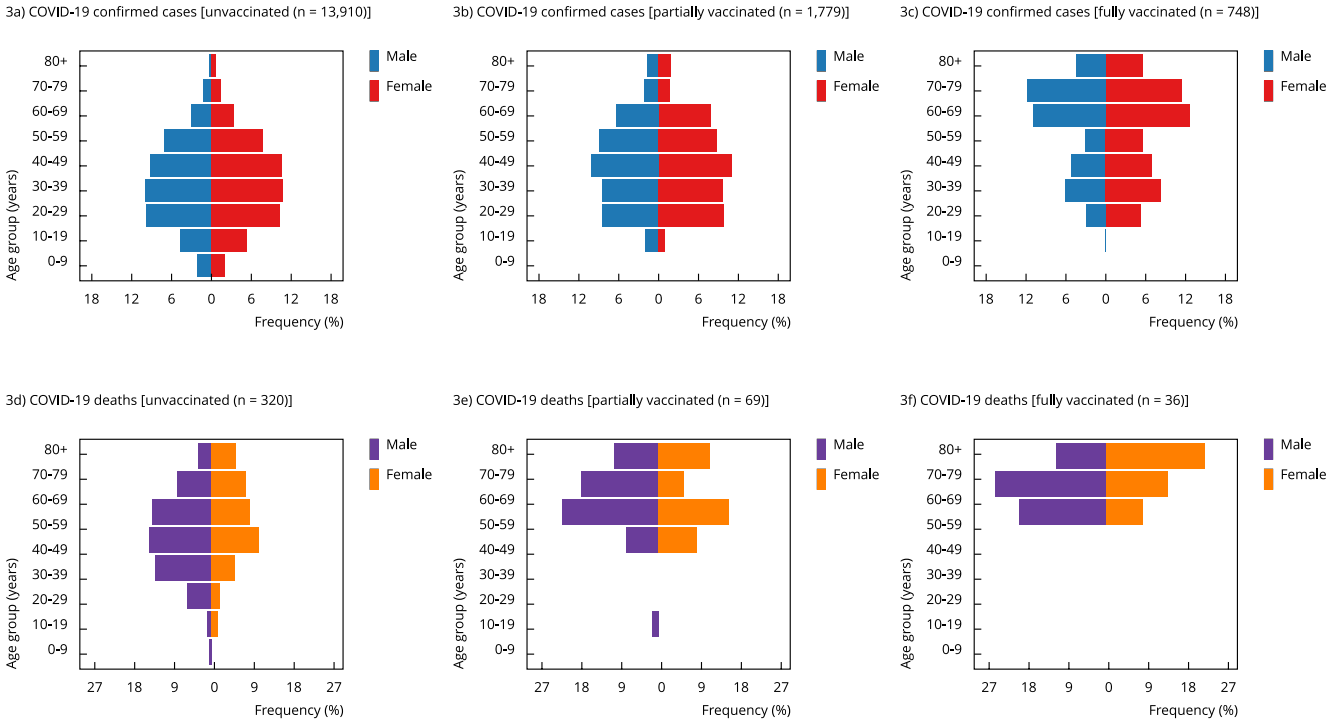
Timeline of the main public health measures adopted during the COVID-19 pandemic (2020-2021) in Arapongas, state of Paraná, Brazil.



WHO: World Health Organization.

Figure 3

Distribution of COVID-19 confirmed cases and deaths by age, sex, and vaccination status in Arapongas, state of Paraná, Brazil (2021).



while in the unvaccinated subgroup, deaths predominated in the 20-59 age group but occurred in all age ranges. Deaths occurred more frequently in men than in women, while the frequency of confirmed cases was more proportional between the sexes (Figure 3).

Table 1 depicts confirmed cases of COVID-19, deaths, and CFRs (per 100) according to vaccination status and age. The overall CFR of the studied population was 2.59. When considering the age-standardized CFR, a complete vaccination status had the lowest value; the measure for complete vaccination status (CFR = 2.42%) is about twice as low as the CFR of unvaccinated and incomplete vaccination statuses (4.55%). Individuals with complete vaccination also showed lower age-specific CFRs in all age groups above 60 years than unvaccinated populations (Table 1). Figure 4 shows (a) unadjusted CFR; (b) age-standardized CFR; and (c) CFR in each age range, showing that these rates are always lower in the vaccinated population in groups (b) and (c), reinforcing the importance of age adjustments.

According to vaccination status, the proportions of cases and deaths are followed by letters in Table 1. The same letters for the same age group indicate no significant differences among groups, while different letters indicate statistically significant differences (Table 1).

Table 1

COVID-19 confirmed cases, deaths, and case fatality rates (CFRs; per 100 cases) by vaccination status and age groups in Arapongas, Paraná State, Brazil, 2021.

Age group (years)	Unvaccinated					Partially vaccinated *				
	Cases		Deaths		CFR (%) **	Cases		Deaths		CFR (%) **
	n	%	n	%		n	%	n	%	
0-11	719	5.17 a	0	0.00 a	0.00	0	0.00 b	0	0.00 a	-
12-17	828	5.95 a	1	0.31 a	0.12	13	0.73 b	0	0.00 a	0.00
18-29	3,230	23.22 a	9	2.81 a	0.28	367	20.63 b	1	1.45 b	0.27
30-39	2,887	20.75 a	24	7.50 a	0.83	323	18.16 b	0	0.00 b	0.00
40-49	2,759	19.83 a	58	18.13 a	2.10	376	21.14 a	0	0.00 b	0.00
50-59	2,074	14.91 a	79	24.69 a	3.81	317	17.82 b	11	15.94 a	3.47
60-69	906	6.51 a	71	22.19 a	7.84	252	14.17 b	26	37.68 b	10.32
70-79	363	2.61 a	50	15.63 a	13.77	68	3.82 b	16	23.19 ab	23.53
80+	144	1.04 a	28	8.75 a	19.44	63	3.54 b	15	21.74 b	23.81
Total	13,910	100.00	320	100.00	2.30	1,779	100.0	69	100.00	3.88
Age-standardized CFR					4.55					5.51

Age group (years)	Fully vaccinated ***					Total				
	Cases		Deaths		CFR (%) **	Cases		Deaths		CFR (%) **
	n	%	n	%		n	%	n	%	
0-11	0	0.00 b	0	0.00 a	-	719	4.37	0	0.00	0.00
12-17	0	0.00 c	0	0.00 a	-	841	5.12	1	0.24	0.12
18-29	62	8.29 c	0	0.00 c	0.00	3,659	22.26	10	2.35	0.27
30-39	107	14.30 c	0	0.00 b	0.00	3,317	20.18	24	5.69	0.72
40-49	91	12.17 b	0	0.00 b	0.00	3,226	19.63	58	13.65	1.80
50-59	65	8.69 c	0	0.00 b	0.00	2,456	14.94	90	21.18	3.66
60-69	176	23.53 c	10	27.78 ab	5.68	1,334	8.12	107	25.18	8.02
70-79	173	23.13 c	14	38.89 b	8.09	604	3.67	80	18.82	13.25
80+	74	9.89 c	12	33.33 b	16.22	281	1.71	55	12.94	19.57
Total	748	100.00	36	100.00	4.81	16,437	100.00	425	100.00	2.59
Age-standardized CFR					2.42					

* Partially vaccinated: who received only one dose (in the case of 2-dose vaccine) or were less than 14 days after the second dose or after a single-dose vaccine (Janssen);

** The CFR is the ratio between confirmed deaths and confirmed cases;

*** Fully vaccinated: who received the second dose (or single-dose vaccine) for at least 14 days before.

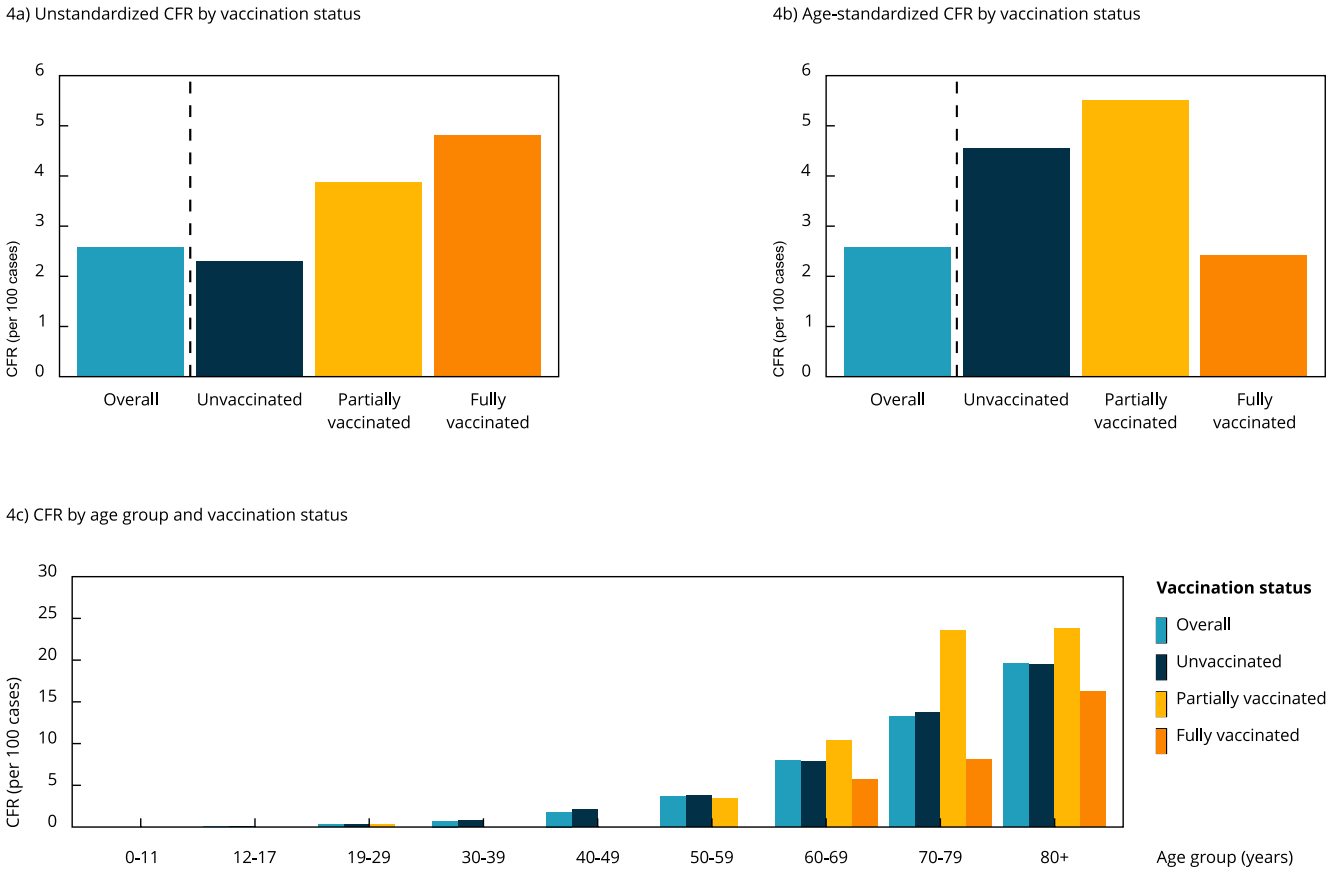
Note: comparison of the proportions of cases and deaths according to vaccination status are followed by letters: the same letters for the same age group indicate no significant differences between groups (p-value ≥ 0.05), different letters show statistically significant differences (p-value < 0.05).

Discussion

This study evaluated the behavior of CFRs among vaccinated and unvaccinated individuals in a municipality in Southern Brazil to understand the role of COVID-19 vaccination as a vital public health measure in preventing COVID-related deaths. Our results showed that age composition directly impacts the analysis of CFRs among subgroups of vaccination status. We also showed that complete vaccination is associated with lower COVID-19 fatality rates than the other vaccination status, regardless of age.

Figure 4

Unadjusted, by age group, and age-standardized case fatality rates (CFRs) according to vaccination status. State of Paraná, Brazil (2021).



Through January/2021, Arapongas had a higher number of deaths (472.7/100,000 inhabitants) compared with other municipalities in Paraná State, such as Londrina (408.9/100,000 inhabitants) and Curitiba (405.6/100,000 inhabitants). Notably, Arapongas followed state and national guidelines and contingency plans to mitigate community transmission of SARS-CoV-2 (Figure 2). Brazilian Unified National Health System (SUS) is decentralized, and local governments have the autonomy to implement their laws and public health interventions [16]. Thus, a series of measures were taken by the Arapongas Municipal Health Department to reduce community transmission of SARS-CoV-2 (Figure 2).

However, the outcomes of individual and community-based measures are difficult to measure as they depend on different scenarios. Even so, a recent study conducted in Rio de Janeiro, Brazil, showed that the combination of vaccination and non-pharmaceutical public health measures potentially reduced the number of hospitalizations by 380+ and 66+ thousand cases, respectively, compared with an alternative scenario with the absence of such policies [4]. Notably, the existing socioeconomic inequalities in Brazil may have also contributed to the course of the epidemic, affecting the adherence to individual- and community-based measures [25] and, potentially explaining the high number

of cases nationally. Considering that health information plays a fundamental role in the adherence of the local population to individual- and community-based measures the Arapongas Municipal Health Department published epidemiological bulletins on the local sanitary situation throughout the pandemic, soughing to periodically inform the population and the local press about the situation in the municipality during the pandemic.

The arrival of vaccines was a turning point for the city. Here, we demonstrated that a full vaccination status, especially among older adults, was associated with the lowest age-specific fatality rates compared with unvaccinated and partially vaccinated groups. This finding strengthens the role of vaccination as a critical measure for preventing deaths among infected people and aligns with previous findings from other studies. Liang et al. [26] evaluated the association between COVID-19 vaccine coverage with CFR on a global scale. The authors showed that a 10% increase in vaccine coverage was associated with a 7.6% reduction in the CFR (95%CI: -12.6; -2.7, p = 0.002) [26]. Indeed, this association was stronger in countries with more effective governments – defined by the authors as those with an intrinsic ability or preparedness to implement COVID-19 immunization programs and high-quality public services (-8.3%; 95%CI: -13.6; -3.1, p = 0.002). Another study showed that COVID-19 vaccination was significantly associated with reduced CFRs in all age groups in Londrina [13]. The authors also argued that age composition is a potential explanation for differences in overall CFRs among vaccinated and unvaccinated populations.

The role of age composition cannot be neglected when investigating disparities in fatality rates across populations and this factor has also been reinforced in other studies [18,27]. For example, in Arapongas, there were more older adults among those with complete vaccination than in the remaining two groups. As COVID-19-related mortality increases with age [28], it is expected that the CFR will be higher among the group with a higher proportion of older adults precisely because the CFR is a crude indicator and is highly sensitive to the age composition of the population [18]. Thus, in a hypothetical scenario, the unadjusted CFR was expected to be higher among the individuals with complete vaccination status, even if the age-specific risk of death was the same. For this reason, considering the effects that the population's age composition has on this measure is essential to avoid misinterpretation of the impact of vaccination on CFRs.

Moreover, there are several reasons for the higher COVID-19 mortality among older adults [29]. Notably, the observed higher fatality rates among vaccinated older adults may be associated with a reduced response to vaccination. Several studies have shown that most non-COVID-19 vaccines currently used are less immunogenic and effective in older adults than younger adults [30]. COVID-19 vaccines followed the same pattern. This evidence suggests that older adults need to be closely monitored and require additional vaccine doses to ensure stronger, long-lasting immunization [31].

Although our study is inherently essential since it contributes to the literature by evaluating the impact of vaccination on case fatality rates in a Brazilian municipality, we acknowledge the existence of some methodological limitations. First, the low number of cases and deaths in some age categories precluded us from employing other statistics to estimate CFRs for all age groups by vaccination status. Second, the CFR might be underestimated due to the time-lag bias associated with COVID-19 case diagnosis and reports in the municipality. Individuals who test are usually those most concerned about individual and collective health or belong to a specific segment of the general population, such as transport and health workers, for example. Also, asymptomatic cases of COVID-19, patients with mild symptoms, or individuals who are misdiagnosed could be left out of the denominator [32]. The underreporting of cases could lead to an inaccurate CFR estimation [33]. Although these factors are potential reporting biases in the study, we do not expect them to significantly impact the results or change the overall conclusions of the work. The last limitation refers to the impossibility of assessing other individuals' characteristics such as comorbidities and socioeconomic status by the database and incorporating them into the analysis due to the absence of such information. Despite these limitations, the evidence from this study is vital to the ongoing reassessment of public health interventions and policies.

Conclusions

The age composition of COVID-19 cases significantly affects group-wise estimates of case fatality rates. This evidence points to the need to standardize CFR by age before analyzing differences between groups. Nevertheless, individuals with a full vaccination status experience lower fatality rates than those with another vaccination status. This improved knowledge is beneficial for the continuous reassessment of public health interventions and policies in the fight against COVID-19 spread.

Contributors

M. Paludetto Junior contributed to the study concept, data curation, and review; and approved the final version. A. S. Olak contributed to the study concept, data curation, and review; and approved the final version. H. Passarelli-Araujo contributed to the study concept, writing, and review; and approved the final version. A. M. Susuki contributed to the study concept, data curation, and review; and approved the final version. M. Aschner contributed to the study concept, editing, and review; and approved the final version. H. Pott-Junior contributed to the study concept, writing, and review; and approved the final version. M. M. B. Paoliello contributed to the study concept, writing, and review; and approved the final version. M. R. Urbano contributed to the study concept, data curation, writing, and review; and approved the final version.

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Resumo

As campanhas de vacinação desempenharam um papel crucial na redução da incidência da COVID-19. No entanto, um número escasso de estudos avaliou o impacto da vacinação nas taxas de letalidade, inclusive no Brasil. Este estudo teve como objetivo comparar as taxas de letalidade de acordo com a situação vacinal dos residentes do Município de Arapongas (Paraná, Brasil), considerando a composição etária da população. Várias estratégias adotadas pela Prefeitura Municipal para minimizar a propagação do vírus também foram elaboradas. Acessou-se a base de dados de 2021 da Secretaria Municipal de Saúde de Arapongas, onde foram notificados 16.437 casos confirmados e 425 óbitos. A taxa de letalidade foi calculada como a razão entre as mortes por COVID-19 e o número de casos confirmados. Este estudo inédito observou diferenças na composição etária entre indivíduos não vacinados e totalmente vacinados. Considerando que a taxa de letalidade é um indicador bruto e altamente sensível à composição etária da população, adotou-se a distribuição etária média dos casos confirmados entre os três níveis vacinais (não vacinados, parcialmente vacinados e completamente vacinados) como distribuição etária padrão. A taxa de letalidade padronizada por idade para os não vacinados e completamente vacinados foi de 4,55% e 2,42%, respectivamente. Indivíduos completamente vacinados apresentaram menores taxas de letalidade específicas por idade em todas as faixas etárias acima de 60 anos em comparação às populações não vacinadas. Estes achados fortalecem o papel da vacinação como uma medida essencial para a prevenção de mortes entre pessoas infectadas e é de particular importância para a reavaliação contínua das intervenções e políticas de saúde pública.

COVID-19; Vacinação; Mortalidade

Resumen

Las campañas de vacunación juegan un papel clave en la reducción de la propagación del COVID-19. Sin embargo, pocos estudios evalúan el impacto de la vacunación en las tasas de letalidad, incluso en Brasil. Este estudio tuvo por objetivo comparar las tasas de letalidad según el estado de vacunación de los residentes de Arapongas (Paraná, Brasil) a partir de la composición por grupo de edad de la población. El Ayuntamiento Municipal aplicó varias estrategias para mitigar la propagación del virus. Se accedió a la base de datos de 2021 del Departamento de Salud de Arapongas, donde se reportaron 16.437 casos confirmados y 425 defunciones. Se calculó la tasa de letalidad como la relación entre las muertes por COVID-19 y el número de casos confirmados. Este estudio inédito evaluó las diferencias en la composición por grupo de edad entre individuos no vacunados y los individuos totalmente vacunados. Teniendo en cuenta que tasa de letalidad es un indicador bruto y muy sensible a la composición por grupo de edad de la población, se adoptó la distribución estándar por grupo de edad de los casos confirmados entre los tres niveles de vacunación (no vacunados, parcialmente vacunados y totalmente vacunados). La tasa de letalidad estandarizada por edad para los no vacunados y los totalmente vacunados fue del 4,55% y del 2,42%, respectivamente. Los individuos totalmente vacunados tenían más baja tasa de letalidad por grupo de edad en todos los grupos de edad superiores a los 60 años en comparación con las poblaciones no vacunadas. Estos hallazgos confirman el papel de la vacunación como una medida esencial de prevención de muertes entre los infectados y es importante para la reevaluación en curso de las intervenciones y políticas de salud pública.

COVID-19; Vacunación; Mortalidad

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