

# Vaccination status and clinical outcome of COVID-19 in hospitalized patients

## Situação vacinal e desfecho clínico da COVID-19 em pacientes hospitalizados

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### ABSTRACT

**Objective:** to analyze the relationship between the vaccination status of patients hospitalized for COVID-19 and clinical outcomes. **Methods:** retrospective cohort study conducted at a referral hospital for COVID-19, including 305 patients  $\geq 5$  years of age admitted to wards and/or intensive care units with a diagnosis of COVID-19. Hospitalization data were collected from electronic medical records, and vaccination status data were obtained from the VacíVida system. The analysis was performed using Poisson regression models. **Results:** the comparison between patients who did not receive any vaccine doses and those who received a booster dose showed a relative risk of 1.46 ( $p = 0.160$ ), suggesting an increased risk of death among the unvaccinated; however, this was not statistically significant. The comparison between unvaccinated individuals and those with an incomplete vaccination schedule revealed a relative risk of 2.42 ( $p = 0.350$ ). **Conclusion:** it was observed that most patients who died or required intensive care did not have a complete vaccination schedule, which points to a possible trend toward worse outcomes among unvaccinated individuals. **Contributions to practice:** the findings underscore the importance of vaccination and active surveillance of clinical factors associated with severity to inform management in patients with COVID-19.

**Descriptors:** COVID-19; COVID-19 Vaccines; Hospitalization; Outcome Expectations.

### RESUMO

**Objetivo:** analisar a relação entre a situação vacinal de pacientes internados pela COVID-19 e os desfechos clínicos. **Métodos:** coorte retrospectiva realizada em um hospital de referência para a COVID-19, incluindo 305 pacientes  $\geq 5$  anos de idade internados em enfermarias e/ou unidades de terapia intensiva com diagnóstico da COVID-19. Dados de internação foram coletados em prontuários eletrônicos e dados da situação vacinal obtidos no sistema VacíVida. A análise foi realizada por modelos de regressão de Poisson. **Resultados:** a comparação entre pacientes sem nenhuma dose da vacina e aqueles que receberam dose de reforço apresentou risco relativo de 1,46 ( $p=0,160$ ), sugerindo um aumento no risco de óbito entre os não vacinados, ainda que sem significância estatística. A comparação entre indivíduos sem vacinação e aqueles com esquema incompleto apresentou risco relativo de 2,42 ( $p=0,350$ ). **Conclusão:** observou-se que a maioria dos pacientes que evoluíram para óbito ou necessitaram de cuidados intensivos não possuíam esquema vacinal completo, o que aponta para uma possível tendência a piores desfechos entre indivíduos não vacinados. **Contribuições para a prática:** os achados reforçam a importância da vacinação e vigilância ativa sobre fatores clínicos de gravidade para orientar condutas em pacientes com COVID-19. **Descritores:** COVID-19; Vacinas contra COVID-19; Hospitalização; Expectativas de Desfechos.

## Introduction

The novel coronavirus disease (COVID-19), caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), has had a profound impact on global public health, resulting in high morbidity and mortality, as well as severe economic and health crises. The rapid spread of the virus led to the declaration of a pandemic by the World Health Organization (WHO) in March 2020, necessitating health measures to contain transmission<sup>(1)</sup>.

At the beginning of the pandemic, diagnostic tests were essential for the rapid identification of infected individuals and the adoption of preventive and control measures<sup>(1)</sup>. In addition, the pandemic has driven the development of vaccines and technologies, resulting in more than 70 vaccines being submitted for clinical trials in the first year. Innovative technologies, such as messenger RNA (mRNA) and non-replicating adenovirus vaccines, were rapidly developed and approved, representing one of the most significant advances in the fight against the pandemic<sup>(2)</sup>.

In Brazil, vaccination against COVID-19 began on January 17, 2021, with a priority given to health-care professionals and the elderly. The National Immunization Program (PNI, acronym in Portuguese) incorporated various immunobiological, including CoronaVac, AstraZeneca, Pfizer, and Janssen, ensuring broad vaccine coverage<sup>(3)</sup>.

As vaccination campaigns progressed around the world, it became clear that approved vaccines were able to induce immunity with a high degree of effectiveness, ensuring protection against severe forms of COVID-19. Vaccination is estimated to have prevented approximately 19.8 million deaths worldwide<sup>(4)</sup>.

During the evolution of the pandemic, numerous variants were identified, and a reduction in the immunity conferred by two doses of the vaccine was observed, necessitating the administration of booster doses to maintain protection against hospitalizations and deaths<sup>(5)</sup>. Although the WHO has declared the end of the Public Health Emergency of International

Concern in 2023, marking a transition from a pandemic stage to endemicity of the disease, the importance of vaccination in minimizing outbreaks and their impacts, especially among vulnerable populations, remains reinforced<sup>(6)</sup>.

During critical periods of the pandemic, health systems faced significant limitations, including service overload, shortages of intensive care unit (ICU) beds, and variations in care response capacity, which directly impacted clinical outcomes<sup>(1,7)</sup>. In this context, it is essential to understand how factors such as age, presence of comorbidities, severity of clinical condition, and vaccination status influence the need for ICU admission, use of mechanical ventilation, and progression to death, especially in public referral hospitals.

Therefore, vaccination against COVID-19 has been a crucial factor in controlling the pandemic<sup>(4,7)</sup>. However, there is a lack of studies analyzing the association between vaccination status against the disease and clinical outcomes in patients hospitalized for an extended period, particularly during the critical periods of the pandemic and after the health emergency was brought under control. Given the above, this study sought to answer the following research question: What is the relationship between vaccination status against COVID-19 and clinical outcomes (such as ICU admission, use of mechanical ventilation, and death) among patients hospitalized for COVID-19 in a public hospital in the interior of São Paulo? Thus, this study aimed to analyze the relationship between the vaccination status of patients hospitalized for COVID-19 and clinical outcomes.

## Methods

### Study design and setting

This is a retrospective cohort study that followed the recommendations of the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines. It was conducted at Santa Casa de Misericórdia de São Carlos, and access to hospi-

tal records was granted from October 2023 to March 2024. The hospital was a referral center for the treatment of COVID-19 for an estimated population of 390,000 inhabitants from the six cities that make up the Coração Region (São Carlos, Dourado, Ibaté, Ribeirão Bonito, Descalvado, and Porto Ferreira) of the Regional Health Department III. Santa Casa provides care to patients from the Brazilian Unified Health System (SUS), as well as those with health insurance and private patients, and is considered a reference center for medium and high complexity cases.

## Participants

The study population consisted of individuals aged five years or older admitted via the SUS to wards and/or intensive care units (ICUs) with a diagnosis of COVID-19 (ICD- B34.2) between February 26, 2021, the date vaccination began in the municipality, and December 31, 2023. Medical records that lacked the necessary information for analysis, such as the full name required to verify vaccination status, were excluded. During the period analyzed, 305 patients were hospitalized for COVID-19.

## Variables

The variables collected included age, sex, presence of comorbidities, type of hospitalization (ward or ICU), use of invasive mechanical ventilation, length of hospitalization, signs and symptoms, and clinical outcome (discharge, transfer, or death). The number of doses administered and the immunobiological received were considered.

## Data source

Clinical data were collected from electronic medical records and recorded in Microsoft Excel spreadsheets. Vaccination status was verified using the VaciVida platform of the São Paulo State Government, with prior authorization from the municipal Epidemiological Surveillance Department. To analyze

immunization levels, participants were classified into four categories: no dose, incomplete schedule, complete schedule, and complete schedule with booster. The classification of the vaccination schedule followed the guidelines of the technical document for the COVID-19 Vaccination Campaign in the state of São Paulo<sup>(8)</sup>, considering information on the availability of doses for different age groups and priority groups between 2021 and 2023. The classification considered the patient's date of admission, correlated with information from the technical document on the availability of immunizers and the intervals between doses of CoronaVac, Pfizer, AstraZeneca, and Janssen.

## Statistical method

Statistical analysis was conducted using absolute frequencies and percentages for qualitative variables and measures of central tendency and dispersion, such as mean, standard deviation, minimum value, median, and maximum value, for quantitative variables. The primary outcome analyzed was hospital discharge or death. To estimate the crude relative risk, we used a simple and multiple Poisson regression model with robust variance, adjusted for age, sex, and the presence of comorbidities<sup>(9)</sup>. All analyses were performed using SAS 9.4 software, adopting a significant level of 5%.

## Ethical aspects

The study was approved by the Research Ethics Committee of *Santa Casa de Misericórdia de São Carlos* under opinion No. 6,309,369/2023 (Certificate of Ethical Review 68054423.1.3001.8148) and by the Research Ethics Committee of the *Universidade Federal de São Carlos* under opinion No. 6,139,767/2023 (Certificate of Ethical Review 68054423.1.0000.5504).

## Results

During the study period, 305 patients were admitted through the SUS, most of whom were white

(67.7%), male (63.6%), and had a mean age of 55.2 years. Regarding the type of admission, ICU admission predominated (71%), and the average age of patients admitted to the ICU was 55.3 years. Among patients who died, the average age was 64.2 years.

Regarding comorbidities, most patients had at least one pre-existing condition (75.4%), and among patients who died, almost all had comorbidities (89.9%). The most frequent conditions were systemic

arterial hypertension (48.8%), diabetes mellitus (24.3%), and obesity (21.3%). It was observed that most patients admitted to the different sectors had a positive RT-PCR test, and the most prevalent signs and symptoms included oxygen saturation of less than 95% in both the ICU (90.9%) and the ward (71.4%), as well as between deaths (86.3%) and ICU or death (90.6%) (Table 1).

**Table 1** – Health conditions, type of diagnostic test, and symptoms of patients hospitalized for COVID-19 from February 26, 2021, to December 31, 2023 (n=305). São Carlos, SP, Brazil, 2024

Variáveis	Enfermaria n (%)	UTI* n (%)	Óbito n (%)	UTI ou Óbito n (%)	Total n (%)
Comorbidades					
Não	35 (29,7)	46 (21,5)	8 (10,1)	47 (21,4)	74 (24,6)
Sim	83 (70,3)	168 (78,5)	71 (89,9)	173 (78,6)	227 (75,4)
Missing <sup>†</sup> = 4					
Doenças cardiovasculares					
Não	103 (87,3)	188 (87,8)	60 (75,9)	193 (87,7)	264 (87,7)
Sim	15 (12,7)	26 (12,2)	19 (24,1)	27 (12,3)	37 (12,3)
Missing = 4					
Diabetes mellitus					
Não	93 (78,8)	160 (74,8)	55 (69,6)	165 (75,0)	228 (75,7)
Sim	25 (21,2)	54 (25,2)	24 (30,4)	55 (25,0)	73 (24,3)
Missing = 4					
Hipertensão arterial sistêmica					
Não	61 (51,7)	109 (50,9)	30 (38,0)	111 (50,4)	154 (51,2)
Sim	57 (48,3)	105 (49,1)	49 (62,0)	109 (49,6)	147 (48,8)
Missing = 4					
Obesidade					
Não	95 (80,5)	167 (78,0)	62 (78,5)	172 (78,2)	237 (78,7)
Sim	23 (19,5)	47 (22,0)	17 (21,5)	48 (21,8)	64 (21,3)
Missing = 4					
Pneumopatias crônicas graves					
Não	110 (93,2)	197 (92,1)	68 (86,1)	200 (90,9)	279 (92,7)
Sim	8 (6,8)	17 (7,9)	11 (13,9)	20 (9,1)	22 (7,3)
Missing = 4					
Tipo do teste					
Antígeno	32 (36,4)	41 (28,5)	18 (35,3)	42 (28,4)	63 (30,3)
Reação em cadeia da polimerase	56 (63,6)	103 (71,5)	33 (64,7)	106 (71,6)	145 (69,7)
Missing = 97					
Fadiga					
Não	96 (85,7)	180 (88,2)	65 (94,2)	183 (87,6)	251 (87,5)
Sim	16 (14,3)	24 (11,8)	4 (5,8)	26 (12,4)	36 (12,5)
Missing = 18					
Dispneia					
Não	66 (59,5)	74 (36,1)	32 (45,7)	77 (36,7)	124 (43,2)
Sim	45 (40,5)	131 (63,9)	38 (54,3)	133 (63,3)	163 (56,8)
Missing = 18					
Febre					
Não	78 (69,6)	116 (57,1)	41 (59,4)	118 (56,7)	174 (60,8)
Sim	34 (30,4)	87 (42,9)	28 (40,6)	90 (43,3)	112 (39,2)
Missing = 19					
Saturação <95%					
Não	32 (28,6)	19 (9,1)	10 (13,7)	20 (9,4)	45 (15,5)
Sim	80 (71,4)	189 (90,9)	63 (86,3)	193 (90,6)	246 (84,5)
Missing = 14					
Tosse					
Não	67 (59,8)	112 (54,9)	41 (59,4)	113 (54,1)	162 (56,5)
Sim	45 (40,2)	92 (45,1)	28 (40,6)	96 (45,9)	125 (43,5)
Missing = 18					

\*ICU: intensive care unit; <sup>†</sup>Missing: referring to missing data due to incomplete annotation in medical records

The data indicated that most patients admitted to the ward had no previous history of hospitalization, 99 (83.2%). Among patients admitted to the ICU, 94 (43.3%) were referred by emergency care units, and 67 (30.9%) were referred by the hospital's ward. Among those who died, 39 (47.6%) came from emergency care units, and when considering the outcome of ICU admission or death, this percentage was 95 (42.6%).

Regarding the previous ICU admission, it was found that most patients admitted to Ward 112 (94.1%) and those admitted to the ICU (97.2%) had not previously been admitted to this unit. Regarding the type of hospitalization, 186 (85.7%) patients were admitted directly to the ICU, with a mortality rate of 16 (19.5%). In this group, the outcome was ICU or death in 40 (17.9%) cases. Of the patients admitted to the hospital ICU, 31 (26%) also spent time in the ward; 73 (89%) patients admitted to the ICU died, and when considering the outcome of ICU or death, this percentage was 214 (96%).

Among patients admitted to the hospital, 40 (13.1%) required invasive mechanical ventilation (IMV) before admission, i.e., at the service of origin. Among those who died, 25 (30.5%) used IMV before admission to the hospital. In the hospital setting, most patients admitted to the ICU required IMV, 114 (53.3%), with this need observed in 61 (76.25%) of those who died. Considering the outcome of ICU discharge or death, 116 (52.7%) patients used IMV.

The average length of stay in the ward was 5.92 days among patients admitted exclusively to that unit, 5.06 days for those who also spent time in the ICU, and 6.5 days among those who died. For the outcome of ICU or death, the average was 6.15 days. In the ICU, the average length of stay was 9.7 days for patients who passed through the ward, 11.3 days for those admitted directly to the ICU, and 10.47 days for those who died. For the outcome of ICU or death, the average was 11.07 days.

The total length of stay was 10.2 days on average, with 8.37 days in the ward and 11.81 days in the ICU. Patients who died remained hospitalized for an

average of 10.46 days, while for the outcome of ICU or death, the average length of stay was 11.68 days. The average time on IMV was 11.78 days in the ICU and 10.66 days among patients who died. At the ICU or death outcome, the average time on IMV was 11.66 days (Table 2).

**Table 2** – Length of hospital stay in days and duration of invasive mechanical ventilation among patients hospitalized for COVID-19 from February 26, 2021, to December 31, 2023 (n=305). São Carlos, SP, Brazil, 2024

Variables	n (%)	Mean (Standard Deviation)	Median (Minimum; Maximum)
<b>Length of stay in ward (days)</b>			
Ward			
Yes	119 (39.0)	5.92 (5.71)	5 (1; 41)
No	—	—	—
Intensive Care Unit			
Yes	31 (10.2)	5.06 (5.25)	3 (1; 24)
No	88 (28.8)	6.23 (5.87)	5 (1; 41)
Death			
Yes	16 (5.2)	6.5 (10.11)	3 (1; 41)
No	103 (33.8)	5.83 (4.76)	5 (1; 24)
Intensive Care Unit or death			
Yes	40 (13.1)	6.15 (7.62)	3.5 (1; 41)
No	79 (25.9)	5.81 (4.51)	5 (1; 24)
<b>Length of ICU* stay (days)</b>			
Ward			
Yes	30 (9.8)	9.7 (8.17)	9 (1; 38)
No	186 (61.0)	11.37 (11.92)	7 (1; 65)
Intensive Care Unit			
Yes	216 (70.8)	11.13 (11.47)	7 (1; 65)
No	—	—	—
Death			
Yes	72 (23.6)	10.47 (9.27)	7 (1; 37)
No	144 (47.2)	11.47 (12.44)	7 (1; 65)
Intensive Care Unit or death			
Yes	213 (69.8)	11.07 (11.47)	7 (1; 65)
No	3 (1.0)	15.67 (12.5)	10 (7; 30)
<b>Total length of stay (days)</b>			
Ward			
Yes	119 (39.0)	8.37 (8.36)	6 (1; 43)
No	186 (61.0)	11.37 (11.92)	7 (1; 65)
Intensive Care Unit			
Yes	217 (71.1)	11.81 (11.83)	7 (1; 65)
No	88 (28.9)	6.23 (5.87)	5 (1; 41)
Death			
Yes	82 (26.9)	10.46 (9.57)	7 (1; 41)
No	223 (73.1)	10.1 (11.18)	6 (1; 65)
Intensive Care Unit or death			
Yes	223 (73.1)	11.68 (11.85)	7 (1; 65)
No	82 (26.9)	6.17 (5.18)	5 (1; 30)
Total hospitalizations	305 (100.0)	10.2 (10.76)	6 (1; 65)
<b>Invasive mechanical ventilation time (days)</b>			
Ward			
Yes	18 (5.9)	8.11 (6.88)	6 (1; 29)
No	104 (34.1)	12.27 (10.44)	9 (1; 62)
Intensive Care Unit			
Yes	119 (39.0)	11.78 (10.11)	9 (1; 62)
No	3 (1.0)	6.67 (8.96)	2 (1; 17)
Death			
Yes	65 (21.3)	10.66 (9.61)	6 (1; 37)
No	57 (18.7)	12.79 (10.57)	9 (1; 62)
Intensive Care Unit or death			
Yes	122 (40.0)	11.66 (10.08)	9 (1; 62)
No	—	—	—

\*ICU: Intensive Care Unit

The results indicated that 40 (33.6%) patients admitted to the ward had a complete vaccination schedule, while 65 (54.6%) had not received any doses of the COVID-19 vaccine. Among patients

admitted to the ICU, 115 (53%) had not received a vaccination. Among the deceased, 37 (45.1%) had not received any doses of the vaccine (Table 3).

**Table 3** – Type of immunization of patients hospitalized for COVID-19 in wards and ICUs from 26 February 2021 to 31 December 2023. São Carlos, SP, Brazil, 2024

Immunization scheme	Ward		ICU*		Death		ICU or Death	
	No n (%)	Yes n (%)	No n (%)	Yes n (%)	No n (%)	Yes n (%)	No n (%)	Yes n (%)
With reinforcement	21 (11.3)	13 (10.9)	12 (13.6)	22 (10.2)	21 (9.4)	13 (15.9)	11 (13.4)	23 (10.3)
Complete	61 (32.8)	40 (33.6)	25 (28.4)	76(35.0)	70 (31.4)	31 (37.8)	23 (28.1)	78 (35.0)
Incomplete	4 (2.1)	1 (0.9)	1 (1.2)	4 (1.8)	4 (1.8)	1 (1.2)	1 (1.2)	4 (1.8)
None	100 (53.8)	65 (54.6)	50 (56.8)	115 (53.0)	128 (57.4)	37 (45.1)	47 (57.3)	118(52.9)

\*ICU: Intensive Care Unit

Regarding clinical outcomes, 99 (83.2%) patients admitted to wards and 140 (64.5%) of those admitted to the ICU were discharged from the hospital. Regarding deaths, 16 (13.4%) patients admitted to wards and 73 (33.6%) of those in the ICU died. Among unvaccinated patients, 37 (22.4%) died, and 118 (71.5%) had an outcome of ICU admission or death.

Considering the model adjusted for age, sex, presence of comorbidities, and total length of stay, no statistically significant differences were found concerning vaccination status, although some trends were observed. When comparing patients who did not receive any doses of the vaccine with those who received a booster dose, a relative risk of 1.46 (95% CI: 0.86–2.50; p = 0.160) was observed, suggesting an increased risk of death among the unvaccinated, although this difference was not statistically significant. The comparison between unvaccinated individuals and those with an incomplete vaccination schedule revealed a relative risk of 2.42 (95% CI: 0.38–15.25; p = 0.350). Finally, patients admitted to the ICU had a three times higher risk of death compared to those who did not require intensive care (95% CI: 1.74–5.88; p<0.010) (Table 4).

**Table 4** – Analysis model for clinical outcomes with vaccination status, considering patients hospitalized from February 26, 2021, to December 31, 2023. São Carlos, SP, Brazil, 2024

Comparisons	Adjusted model*		
	Relative risk	95% CI <sup>†</sup>	p-value <sup>‡</sup>
Outcome: Death			
None, vs Incomplete	2.42	0.38 – 15.25	0.350
None, vs Complete	1.34	0.88 – 2.04	0.170
None vs Reinforcement	1.46	0.86 – 2.50	0.160
Incomplete vs Complete	0.56	0.09 – 3.51	0.530
Incomplete vs Reinforcement	0.60	0.09 – 3.87	0.600
Complete vs Reinforced	1.09	0.65 – 1.82	0.740
ICU <sup>§</sup> : Yes, vs No	3.20	1.74 – 5.88	<0.010
Outcome: ICU or Death			
None, vs Incomplete	1.01	0.64 – 1.59	0.970
None vs Complete	1.01	0.87 – 1.19	0.870
None vs Reinforcement	1.17	0.89 – 1.53	0.270
Incomplete vs Complete	1.00	0.64 – 1.57	0.990
Incomplete vs Reinforcement	1.16	0.71 – 1.89	0.560
Complete vs Reinforced	1.15	0.90 – 1.48	0.270

\*Adjusted for age, gender, presence of comorbidities, and total length of stay; <sup>†</sup>CI: 95% confidence interval; <sup>‡</sup>Significant for p<0.05; <sup>§</sup>ICU: Intensive Care Unit

## Discussion

Among the demographic factors observed, there is a higher incidence of the disease in males, which is consistent with analyses conducted in other regions of Brazil and with international studies that indicate a male predominance<sup>(2,7,10)</sup>. In addition, men also have a higher frequency of admission to the ICU, which may be related to genetic and hormonal factors. Testosterone, for example, plays an immunosuppressive role and is associated with high levels of angiotensin-converting enzyme 2 (ACE-2), which favors infection and disease progression<sup>(11)</sup>. In addition, men's greater propensity for comorbidities, such as type 2 diabetes mellitus, hypertension, and cardiovascular disease, also increases their predisposition to severe infections<sup>(7)</sup>.

On the other hand, the lower incidence of morbidity and mortality in females may be related to the anti-inflammatory role of estrogen and its immunomodulatory action against COVID-19. Estradiol, specifically, plays a protective role by modulating pro-inflammatory signaling pathways, thereby hindering the virus's entry into cells<sup>(11-12)</sup>.

In addition to biological aspects, sociocultural factors also influenced the higher frequency of hospitalization in men, since there is a lower culture of self-care among this group. Characteristics traditionally associated with masculinity, such as strength and not expressing vulnerability, can lead to neglect in seeking health services<sup>(13)</sup>. These factors underscore the importance of initiatives targeting the male population to raise awareness about vaccination.

As for self-declared race, the higher frequency of hospitalization among white patients differs from some national findings, which indicate a higher incidence of hospitalizations among individuals of African descent<sup>(10)</sup>. Furthermore, it is worth noting that in the municipality investigated, the self-declared white population accounts for 67%, while the mixed-race population comprises 25%, and the Black population accounts for 7.1%<sup>(14)</sup>. In the international context,

there is a higher frequency of hospitalizations among whites, but also a direct relationship between higher COVID-19 mortality in lower-income populations and those belonging to minority groups. The disproportionate prevalence of morbidity and mortality among Black individuals may be associated with a higher incidence of chronic diseases, as well as structural inequalities, such as housing, transportation, employment, and access to health care<sup>(2)</sup>.

Age has also been identified as a significant vulnerability factor in the clinical progression of COVID-19. Even among non-elderly adults, the disease can present severe clinical evolution. The average age of hospitalized individuals was 55.2 years. Although cases involving children and adolescents were included, this group did not significantly impact the analysis of this result. The low frequency of hospitalizations in the pediatric population is justified by the fact that this group presents mild or asymptomatic cases of the disease and rarely requires hospitalization<sup>(15)</sup>.

However, among patients who died, the average age was significantly higher (64.2 years), which reinforces the risk of hospitalization and mortality from COVID-19 with advancing age<sup>(2)</sup>. In addition, aging is associated with immunological changes that reduce the body's ability to respond to viral infections, such as COVID-19, as well as a higher prevalence of chronic comorbidities that contribute to the worsening of the clinical condition<sup>(16-17)</sup>. It is noteworthy that most of the patients who died had at least one comorbidity. The analysis of comorbidities indicated a high prevalence of hypertension, diabetes mellitus, and obesity, all directly associated with worse clinical outcomes, with cardiovascular diseases having a significant impact on clinical outcomes<sup>(7,18)</sup>.

Regarding vaccination, the findings reinforce that most deaths occurred among unvaccinated patients or those with incomplete vaccination schedules. In a study conducted in Spain, a higher proportion of severe acute respiratory failure was found among unvaccinated patients admitted to the ICU, followed by those with complete vaccination. However, the study

found no statistically significant differences between the groups in terms of complications, ventilatory support time, or length of hospital stay, although it did identify higher mortality rates in unvaccinated patients<sup>(19)</sup>. However, it is essential to note that the lack of statistical significance in some studies, including the present one, does not necessarily reflect the absence of a protective effect of vaccination but may be related to sample size, heterogeneity between the groups analyzed, and the temporal variability of the pandemic, which influenced the profile of hospitalized patients and the predominant variants of SARS-CoV-2.

While some studies have not observed significant differences in the length of hospital stay and mortality between vaccinated, partially vaccinated, and unvaccinated patients<sup>(19-20)</sup>, others reinforce the effectiveness of vaccines in reducing hospitalizations due to COVID-19<sup>(21-22)</sup>. These studies demonstrate lower mortality rates in fully vaccinated patients compared to those who are unvaccinated or partially vaccinated. This pattern was also observed in our findings, pointing to a risk of death in unvaccinated patients, which highlights the protective impact of vaccination.

In the context of ICU admissions, the results indicated that patients admitted to this sector were three times more likely to die. This finding can be attributed to the severity of SUS patients admitted to the institution, many of whom remained in critical condition in emergency care units or field hospitals while waiting for beds in referral hospitals. This delay contributed to the worsening of the clinical condition, with severe manifestations such as respiratory failure at the time of admission<sup>(2)</sup>.

In this perspective, vaccination is associated with reduced use of ICU resources, such as IMV, and administering a booster dose of the vaccine increases survival in critical cases of COVID-19<sup>(23)</sup>. It has also been observed that the average duration of IMV use in the ICU is around 10 days<sup>(24)</sup>, which is corroborated by our findings.

Among the main factors associated with mortality in the ICU are the use of IMV, advanced age, and

critical condition upon admission, highlighting the importance of timely clinical management for the treatment of COVID-19<sup>(24)</sup>. IMV is indicated in patients with acute hypoxemic respiratory failure resulting from SARS-CoV-2 infection to ensure adequate gas exchange in the face of lung damage caused by the disease<sup>(25)</sup>. In critically ill adults with respiratory failure due to COVID-19, early initiation of IMV, compared to late initiation, is associated with reduced mortality<sup>(26)</sup>. Therefore, although IMV is a fundamental intervention, its effectiveness is closely related to early management, the quality of intensive care, and the response capacity of hospital units.

The survival time of patients hospitalized for COVID-19, considering the period from admission to outcome, has a median survival of 7 to 11 days, according to previous studies<sup>(27-28)</sup>. However, when comparing vaccinated and unvaccinated patients, it was found that the median was significantly higher among those who were fully vaccinated. Specifically, the median survival time was 30 days or longer among vaccinated individuals<sup>(22,28-29)</sup>. This finding suggests that vaccination, in addition to reducing the likelihood of hospitalization, may be associated with a slower or less abrupt clinical course, allowing for a longer therapeutic response time and progressive recovery.

The findings also highlighted the influence of ICU admission on clinical outcomes, with higher mortality rates observed among unvaccinated patients or those with incomplete vaccination schedules. There is consensus in the literature on the protective effect of vaccination against progression to death<sup>(19,21,23)</sup>. During the period of circulation of the Delta variant, from July to December 2021, most deaths occurred among unvaccinated or partially immunized individuals, a pattern that was repeated during the period of circulation of the Omicron variant, from January to February 2022<sup>(30)</sup>. The reduction in the protection conferred by vaccines over time, especially in the face of virus variants, raises the need for periodic vaccine boosters to maintain population immunity and reduce severe cases.

In this context, the demographic and clinical characterization of patients, combined with the analysis of outcomes, helps to identify the most vulnerable groups, such as men and individuals with comorbidities. These findings reinforce the severity associated with ICU admission, a key determinant of mortality, and highlight the association between the absence or incompleteness of the vaccination schedule and unfavorable outcomes.

Thus, the importance of broad and continuous vaccination campaigns is evident, as well as the need for efficient management during health crises, ensuring timely treatment of the disease. These results also underscore the importance of interventions that optimize hospital care and promote integrated public policies to strengthen prevention, expand vaccination, and reduce healthcare access inequalities, particularly within the Brazilian healthcare system.

### Study limitations

Among the study limitations, we highlight the incomplete information on symptoms and comorbidities due to the incomplete medical records. Additionally, data protection for patients with health insurance and private plans prevented the inclusion of information on these individuals when they were admitted to the ICU.

Another factor to consider is the temporal variation in the pandemic context, marked by different phases of the health crisis, including periods when ICU beds were unavailable and long wait times for beds.

These limitations may have compromised the statistical power of the analysis, limiting the ability to detect significant associations between variables, even when consistent trends were observed. This is particularly relevant in comparisons between different vaccination schedules, whose results showed high amplitudes in the confidence intervals.

Despite these limitations, the study has essential potential, as it is a comprehensive analysis based on data covering the critical and control periods of the

pandemic, which enabled the identification of relevant patterns related to clinical outcomes and vaccination status.

### Contributions to practice

These findings underscore the importance of continuous surveillance of clinical and epidemiological indicators of COVID-19 in hospitalized populations, highlighting the potential protective role of vaccination. Furthermore, the data obtained contributes to the planning of more effective public policies and care strategies, especially in the context of the Unified Health System and the planning of vaccination strategies, considering the endemic nature of COVID-19 and the potential for new outbreaks.

### Conclusion

We found that the clinical-epidemiological profile of patients hospitalized with COVID-19 was predominantly male, white, with an average age of over 55 years and a high burden of comorbidities, especially systemic arterial hypertension, diabetes mellitus and obesity.

It was observed that most patients who died or required intensive care did not have a complete vaccination schedule, which points to a possible trend toward worse outcomes among unvaccinated individuals.

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### Authors' contribution

Conception and design or analysis and interpretation of data; writing of the manuscript or critical revision of intellectual content: Poli P. Writing of the

manuscript or critical revision of intellectual content; Agreement to be responsible for all aspects of the manuscript related to the accuracy or integrity of any part of the manuscript being investigated and resolved appropriately: Magno GD. Writing of the manuscript or critical review of the intellectual content: final approval of the version to be published: Uehara SCSA.

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