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COVID-19 in the State of São Paulo, Brazil: Epidemiological Analysis and Ongoing Challenges

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ABSTRACT

Introduction: The COVID-19 pandemic, which began in early 2020, became a challenge for healthcare systems, especially in Brazil and the state of São Paulo. Non-pharmaceutical interventions, such as lockdowns and face masks, helped reduce transmission when combined with testing and tracing but were not sufficient alone to prevent high case numbers and deaths. On 5 May 2023, due to the sustained decline in severe cases and deaths, and an increase in global immunity through vaccination and prior infection, the World Health Organization (WHO) declared that COVID-19 no longer constituted a Public Health Emergency of International Concern (PHEIC). Consistent with the WHO's position, and the emergence of new SARS-CoV-2 variants continues to highlight the need for ongoing vaccination efforts. Additionally, post-acute sequelae of SARS-CoV-2 infection—commonly referred to as long COVID—have affected a significant portion of the infected population, adding to the burden on public health systems. **Methods:** Given this complex scenario, the present study investigates a comparative epidemiological analysis of COVID-19 in São Paulo state across three key phases: pre-vaccination, mass vaccination, and the post-PHEIC period. **Results:** Public data indicated that although immunization campaigns contributed to reduced cases, hospitalizations, and deaths, COVID-19 still caused more deaths than most infectious diseases during the analyzed period. The persistence of the pandemic occurred concurrently with declining vaccination coverage following the PHEIC declaration. **Conclusion:** To address this ongoing public health challenge, ongoing policies are needed, including continued sustained vaccination efforts, variant surveillance, public awareness campaigns, and long-term health system strengthening.

INTRODUCTION

The coronavirus disease 2019 (COVID-19), caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was officially declared a pandemic by the World Health Organization (WHO) in March 2020 [1], posing significant challenges to healthcare systems on a global scale [2]. This public health crisis led to severe hospital overload, with a drastic increase in hospitalizations and deaths [3]. Brazil faced severe consequences, particularly in the state of São Paulo—the most populous and the most affected state in absolute terms [4]. São Paulo's complex socioeconomic landscape, marked by significant inequality, informal labor, and densely populated urban areas, further influenced the dynamics of disease spread and population adherence to public health measures [5]. This socioeconomic context contributed to the challenges faced in mitigating transmission during critical phases of the pandemic.

The adoption of preventive measures against COVID-19, such as social distancing, wearing face masks, and lockdowns, played an essential role in slowing the spread of SARS-CoV-2, especially during the early stages of the pandemic [6]. These interventions helped reduce transmission rates and temporarily relieved pressure on healthcare systems, allowing governments to implement responses [7]. However, the overall effectiveness of these measures was often hindered by inconsistent adherence,

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socioeconomic constraints, political discord, and unequal healthcare infrastructure across regions [8]. As a result, despite their proven value, these strategies alone were not sufficient to prevent high case and mortality rates, particularly among low-income, other vulnerable populations. in resource-limited settings [9].

Therefore, the rapid development of vaccines against SARS-CoV-2 and their large-scale distribution to the Brazilian population in the early months of 2021 was essential in combating the pandemic, significantly contributing to the reduction of severe cases and deaths [10]. Vaccination was associated with the transition from the critical phase of the pandemic to improved control, reaffirming its importance in mitigating outbreaks and preventing the collapse of healthcare systems [11,12].

On 5 May 2023, the World Health Organization declared that COVID-19 no longer constituted a Public Health Emergency of International Concern (PHEIC) [1]. This decision was based on a sustained global decline in severe cases and deaths, high levels of population immunity, reduced healthcare strain, and improved health system capacity. However, the WHO emphasized that this did not mean the pandemic was over and urged countries to maintain surveillance, preparedness, and vaccination efforts [1], focusing on sustained global equity.

Despite the significant reduction in hospitalizations and deaths, COVID-19 remains a global concern with ongoing local implications in regions like São Paulo. The emergence of new variants and the potential waning of immunity over time underscore the need for ongoing prevention efforts and continued vaccination promotion [13]. Preventing infections helps mitigate one of the pandemic's most concerning consequences: long COVID—a condition affecting millions of people with prolonged symptoms such as extreme fatigue, respiratory difficulties, cognitive impairments, and mental health issues [14]. Severe symptoms can persist in post-COVID-19 patients [15]. While prevalence estimates vary widely based on factors such as vaccination status, infection severity, and the specific viral variant, recent global data suggest that between 6% and 20% of individuals who contract SARS-CoV-2 may develop long-term symptoms consistent with post-COVID-19 condition [16].

In this context, this study aimed to analyze the current state of the pandemic following the WHO's declaration of the end of COVID-19 as a global emergency, using public epidemiologic data from the state of São Paulo. Additionally, the study sought to evaluate the impact of vaccination on reducing hospitalizations and deaths due to COVID-19.

METHODS

Study design and data sources. This study adopted a descriptive and quantitative approach to explore the epidemiological state of the COVID-19 pandemic retrospectively. Although the WHO has declared that COVID-19 is no longer a public health emergency of international concern, it is essential to assess whether SARS-CoV-2 is truly under control. To this end, data on confirmed positive cases, hospitalizations, and deaths due to COVID-19 in the state of São Paulo were analyzed, based on records from the Fundação Sistema Estadual de Análise de Dados (Fundação SEADE - https://coronavirus.seade.gov.br/; interface in Portuguese).

Definition of study periods. The analysis was conducted across three distinct periods:

1. From the beginning of the pandemic until the expansion of vaccination eligibility to the general adult population in São Paulo;

2. From the expansion of vaccination eligibility until the WHO's declaration ending the PHEIC;

3. From the WHO declaration ending the PHEIC until 8 December 2024.

The Period 1 spans from 26 February 2020, when the first COVID-19 case was confirmed in São Paulo state, to 15 June 2021, when vaccination in the state of São Paulo was expanded to include the general adult population beyond high-risk groups. This timeframe encompasses the initial phases of the pandemic, characterized by the first wave of infections and the subsequent, more severe peak in early 2021, which was predominantly driven by the Gamma (P.1) variant in Brazil. The Period 2 begins on 16 June 2021, marking the start of broader vaccine distribution and increased access for the general adult population, and continues until 5 May 2023, when the WHO declared the end of COVID-19 as a PHEIC. Finally, the Period 3 extends from 5 May 2023, reflecting the stabilization of hospitalization and mortality rates following widespread immunization, until 8 December 2024, when these study's analyses were concluded.

According to legislation implemented on 22 April 2022 (Ministry of Health Ordinance No. 913) [17], Brazilian hospitals were no longer required to report the number of COVID-19 hospitalizations in 2024. Thus, the Period 3 of hospitalization analysis only had records from the year 2023.

Statistical analysis. Data analyses were conducted using the weekly number of COVID-19 cases, hospitalizations, and deaths during the three predefined periods. These intervals were strategically selected to reflect distinct phases of the COVID-19 pandemic, including major shifts in epidemiological patterns in the state of São Paulo. Particular attention was given to the post-WHO declaration period. The SEADE platform presents graphical data visualizations generated using Microsoft Power BI, based on weekly records. Graphs presenting cumulative and weekly data on COVID-19 cases, hospitalizations, and mortality were accessed on December 8, 2024, from SEADE website (https://coronavirus.seade.gov.br), while raw data were downloaded as comma-separated values (CSV) files from

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the GitHub repository (https://github.com/seade-R/dados-covid-sp).

The Shapiro-Wilk test [18] was applied to assess the normality of the weekly distributions of cases, deaths, and hospitalizations for each period, using the SciPy library in Python. The results showed that only the distribution of cases in Period 1 did not significantly deviate from normality (P = 0.177), while all other variables and periods exhibited significant deviations (P < 0.05), indicating non-normal distributions and justifying the use of non-parametric statistical methods. Given the significant deviation from normality in most distributions and the large differences in standard deviations suggesting heterogeneity of variances across the periods (Table 1), non-parametric methods were deemed most appropriate. Consequently, comparisons across the three periods were performed using the Kruskal–Wallis test [19] with the scikit-posthocs library, followed by Dunn's post-hoc test with Bonferroni correction [20] implemented in the scikit-posthocs library, both conducted in Python.

Descriptive complementary analyses were conducted to further elucidate the current state of the COVID-19 pandemic in the state of São Paulo. Vaccination coverage data were extracted using the Vacinômetro platform (a Brazilian Ministry of Health COVID-19 vaccination monitoring system) (https://www.gov.br/saude/pt-br/composicao/seidigi/demas/covid19). An analysis of vaccination coverage rates was performed based on a time series depicting the monthly vaccination rate in the state of São Paulo, from early 2021, when vaccines were administered to healthcare professionals and older adults, until the end of 2024.

In addition, the number of COVID-19-related deaths was compared to those caused by the most prevalent infectious diseases in the state, such as pneumonia, dengue, HIV/AIDS, tuberculosis, viral hepatitis, and influenza. The available data span from the beginning of the vaccination campaign (when healthcare professionals and vulnerable populations were prioritized) through the mass vaccination phase. Mortality data for viral diseases were obtained from the Mortality Information System (SIM; https://opendatasus.saude.gov.br/dataset/sim). Since the SIM database provides information up to August 2024, the most recent twelve months of available data—covering the period from August 2023 to August 2024—were analyzed.

To compare the mortality rates of COVID-19 with other infectious diseases within the same period and population, pairwise proportion tests were conducted using the z-test for proportions, implemented in the *statsmodels* library in Python. Comparisons were made between COVID-19 and each of the other diseases (viral pneumonia, dengue, AIDS, tuberculosis, hepatitis, and influenza), with Bonferroni correction applied for multiple comparisons. This approach allowed us to determine whether COVID-19 mortality was statistically different (higher or lower) than that of the other diseases, considering an adjusted significance level.

RESULTS

Accumulated number of SARS-CoV-2 infections

The analysis of public data on the COVID-19 pandemic in the state of São Paulo revealed that the initial months were characterized by a sharp increase in confirmed cases, hospitalizations, and deaths (Figure 1). During the first analyzed period, which spanned over fifteen months, approximately 3.57 million SARS-CoV-2 infections were recorded; the weekly mean was 54,138 cases (Figure 1A and Table 1). The highest peak within this period occurred in the second week of April 2021, with approximately 116,000 new cases (during the Gamma variant wave) (Figure 1B).

Table 1. Weekly descriptive statistics of COVID-19 cases, hospitalizations, and deaths in São Paulo state across three key epidemiological periods: pre-vaccination (Period 1), mass vaccination (Period 2), and post-PHEIC (Period 3)

Type	Period	Total	Weekly mean	SD	95% CI lower	95% CI upper	*P*-value
Cases	1	3,573,145	54,138	31,857	46,307	61,970	$P < 0.001$
	2	3,016,068	30,776	25,379	25,687	35,864	
	3	325,113	3,870	3,063	3,205	4,535	
Hospitalizations	1	470,550	7,129	7502	5,285	8,973	$P < 0.001$
	2	328,460	3,351	3218	2,706	3,996	
	3	23,664	281	384	198	365	
Deaths	1	121,960	1,847	1,346	1,516	2,179	$P < 0.001$
	2	58,031	592	745	442	741	
	3	4,253	50	37	42	58	

P-value comparing the weekly distributions across all three periods. Pairwise comparisons are detailed in Table 2.

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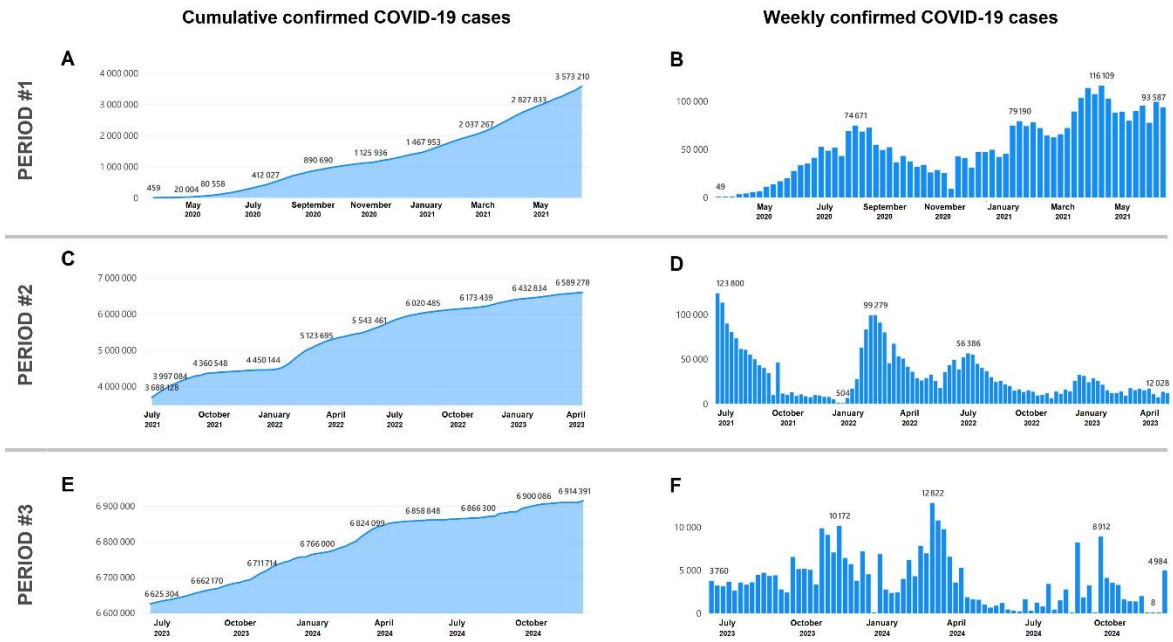

Fig. 1. Time series of confirmed COVID-19 cases across different periods: from the beginning of the pandemic until the day before mass vaccination distribution (A and B); from the start of mass vaccination until the WHO declared the end of COVID-19 as a Public Health Emergency of International Concern (PHEIC) (C and D); and from the WHO declaration to 8 December 2024 (E and F).

At the beginning of the vaccination campaign, marking the start of the second analysis period, the rate of new cases remained significantly high, reaching another major peak of 120,000 new cases between 20 and 27 June 2021 (Figure 1D). However, as vaccination coverage increased, this rate began to decline. Despite the high accumulated number of cases during the Period 2 (approximately 3 million cases), the weekly average fell to 30,776 cases (Figure 1C and Table 1).

The WHO's decision to declare the end of the COVID-19 pandemic as a Public Health Emergency of International Concern marked the beginning of the third analysis period. By the end of 2024, the state of São Paulo had accumulated approximately 6.91 million cases, but with 325,000 new cases during the Period 3 (Figure 1E and Table 1). Although this number remains high, there was a significant slowdown (approximately 87% reduction in weekly average compared to Period 2) in the growth of SARS-CoV-2 infections. While the first two periods recorded over 54,000 and 30,000 weekly cases respectively, the Period 3 was characterized by a low weekly case rate with a mean of 3,870. However, an increase in cases was observed in March 2024, with 12,000 new infections recorded in the first week of that month (Figure 1F). A comparison of case numbers across the three periods (Table 1) revealed a statistically significant difference ($P < 0.001$). Pairwise comparisons between the groups revealed significant differences in most cases (Table 2), with the exception of hospitalizations between Period 1 and Period 2.

Table 2. Pairwise comparison of weekly COVID-19 cases, hospitalizations, and deaths by period (Dunn's Post-Hoc test with Bonferroni correction)

Metric	Period 1 vs. Period 2	Period 1 vs. Period 3	Period 2 vs. Period 3
Cases	$P = 0.0066$	$P < 0.0001$	$P < 0.0001$
Hospitalizations	$P = 0.15$	$P < 0.0001$	$P < 0.0001$
Deaths	$P < 0.0001$	$P < 0.0001$	$P < 0.0001$

Accumulated number of COVID-19 hospitalizations

The number of COVID-19 hospitalizations in the state of São Paulo began to be recorded in the SEADE database in the last week of April 2020 (Figure 2). In that initial week, 7,643 hospitalizations were reported (Figure 2A). The highest hospitalization peak prior to the start of vaccination occurred between March and April 2021, reaching a weekly peak of approximately 23,000 hospitalizations, reflecting the growing pressure on the healthcare system as the pandemic intensified. In the week immediately preceding the onset of mass vaccination, just over 19,000 hospitalizations were recorded (Figure 2A). Over the entire Period 1, a total of 470,550 individuals were hospitalized, with a weekly average of 7,129 cases (Table 1).

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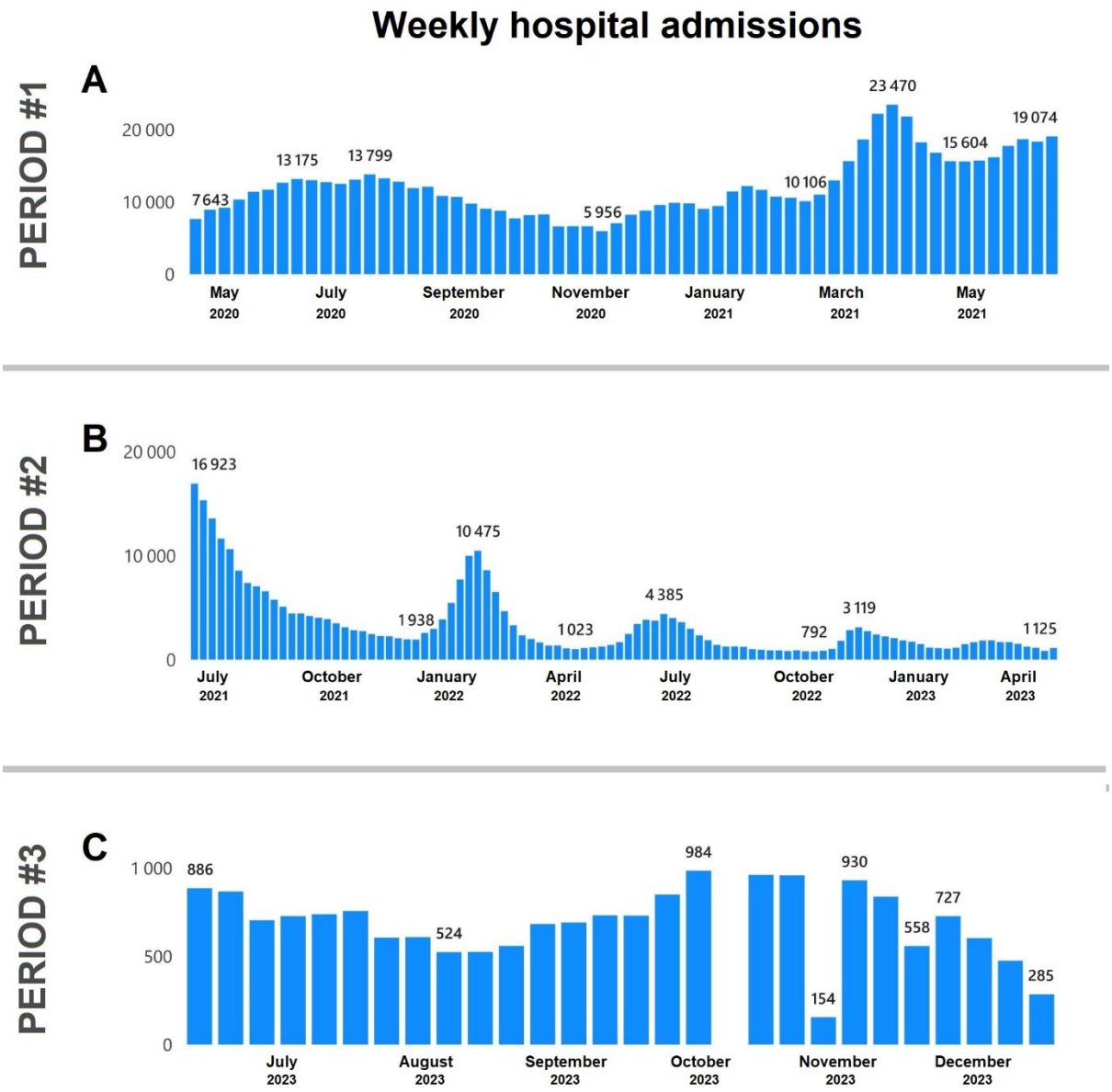

Fig. 2. Time series of the number of hospitalizations due to COVID-19 across different periods: from the beginning of the pandemic until the day before mass vaccination distribution (A); from the start of mass vaccination until the WHO declared COVID-19 no longer a Public Health Emergency of International Concern (B); and from the WHO declaration to 8 December 2023 (C).

In the second analysis period (Figure 2B), a significant decline in hospitalizations was observed, consistent with the effectiveness of the vaccines. The weekly average of hospitalizations (3,351) fell to less than half that of the Period 1 (Table 1). However, despite this decrease (Figure 2B), new significant peaks in hospitalizations occurred in São Paulo State during the vaccination campaign, while COVID-19 was still considered a global health emergency by the WHO.

In the Period 3, following the WHO declaration (Figure 2C), hospitalization rates continued to decline. The weekly average of hospitalizations declined to 281 (Table 1). However, according to current legislation [17], there were no updated hospitalization records in the SEADE database, with available data extending only until 2023.

Comparing the number of hospitalizations across the three periods, a statistically significant difference was observed ($P < 0.001$). The post-hoc analysis revealed no significant difference between Period 1 and Period 2 ($P = 0.15$), while both periods differed significantly from Period 3 ($P < 0.0001$ for both comparisons) (Table 2).

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Accumulated number of deaths caused by COVID-19

By the end of March 2020, during the initial weeks of the pandemic's lethal impact in the state, a cumulative total of 260 deaths had been recorded. Within sixty days, this cumulative death figure surged to 7,500 (Figure 3A). Overall, the first analysis period accounted for 121,960 deaths (Table 1). The second week of April 2021 marked the deadliest period of the pandemic in São Paulo, with 5,892 deaths recorded (Figure 3B). The weekly average in the Period 1 was 1,847 deaths from COVID-19 (Table 1).

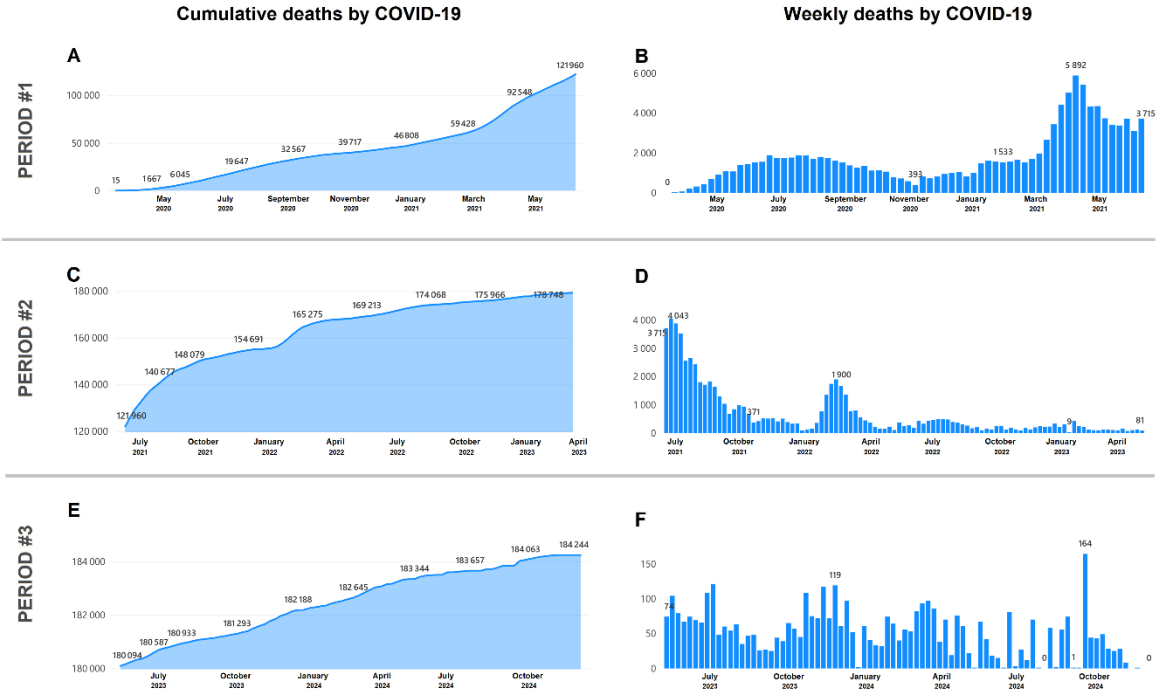

Fig. 3. Time series of COVID-19 deaths from the beginning of the pandemic until the day before the widespread rollout of vaccination (A and B); from the start of mass vaccination until the WHO declared COVID-19 no longer a PHEIC (C and D); and from the WHO declaration until 8 December 2024 (E and F).

In the Period 2, which marks the beginning of the vaccination rollout, a decline in the number of deaths was observed. Nevertheless, reflecting residual burden, over 58,000 people lost their lives to COVID-19 during this time (Figure 3C and Table 1). Even after the widespread distribution of vaccines, a mortality peak can be observed (Figure 3D). In January 2022, 1,900 deaths were recorded in a single week. Despite this, the vaccination campaign played a crucial role in significantly reducing mortality. The weekly average in the Period 2 was 592 deaths from COVID-19 (Table 1).

In the Period 3, following the WHO declaration, the cumulative number of deaths increased more slowly by 4,253; the weekly average was 50.

The comparison of COVID-19 mortality rates across the three periods ($P < 0.001$; Table 2) showed differences between all three groups, both when analyzed together and in pairwise comparisons ($P < 0.001$; Table 2).

COVID-19 immunization rates

At the beginning of the COVID-19 pandemic, the high mortality rate, social disruption, and economic impact of the health crisis generated a strong demand for vaccination, despite the initially limited availability of doses. At the peak of the campaign, in August 2021, 14 million doses of the original monovalent SARS-CoV-2 vaccines, designed to target the ancestral strain of the virus, were administered in the state of São Paulo (Figure 4). However, as vaccine access expanded and mortality and hospitalization rates declined, a decrease in public interest in vaccination was observed in many contexts, including urban areas of São Paulo. For example, in December 2022, 18 months after the start of mass vaccination in São Paulo, approximately 800,000 doses were administered. From 2023 onward, vaccine administration rates declined sharply; monthly doses administered consistently remained below one million doses per month, representing less than 10% of the August 2021 peak.

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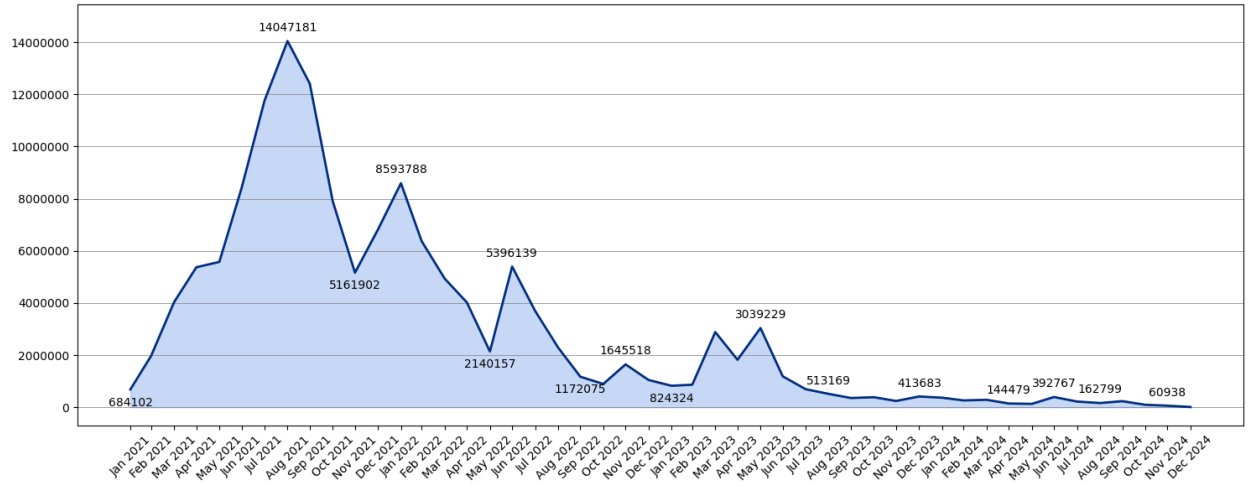

Fig. 4. Time series depicting the monthly number of vaccine doses administered in the state of São Paulo from January 2021 to December 2024.

Infectious disease-related deaths

Compared to major infectious diseases, COVID-19 was the second leading cause of such deaths in the state of São Paulo (Figure 5). Viral pneumonia accounted for 27,695 deaths, making it the top cause in this category. Notably, COVID-19 surpassed dengue, despite the 2024 outbreak being the largest ever recorded in Brazil [21], and exceeded mortality from HIV/AIDS, tuberculosis, viral hepatitis, and influenza.

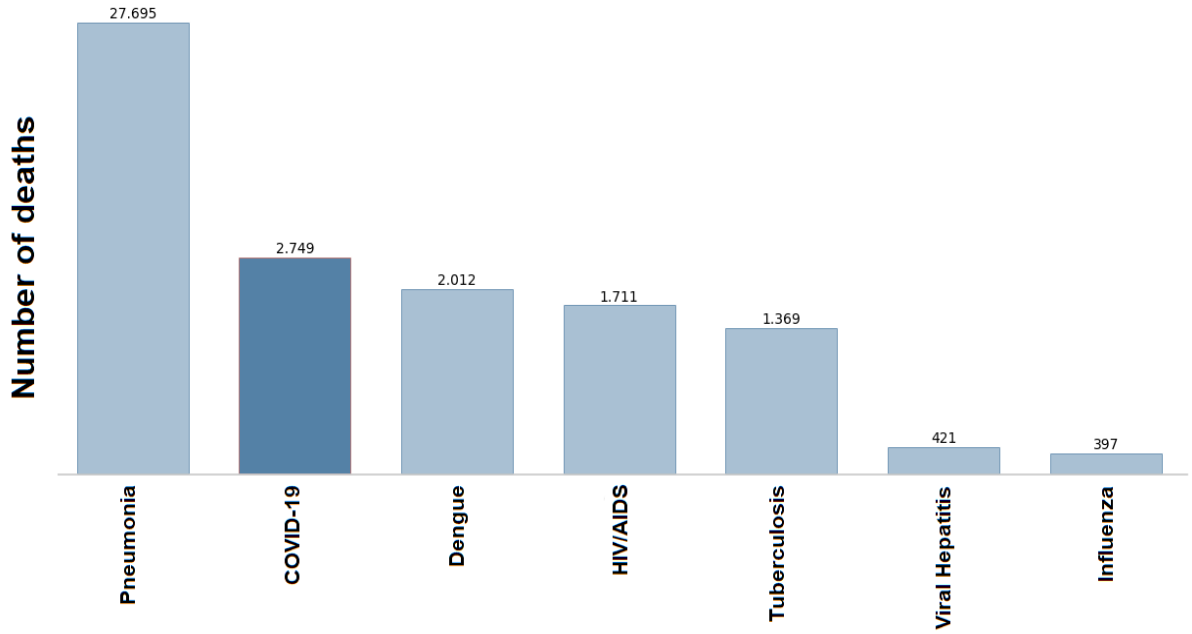

Fig. 5. Comparative analysis of the number of deaths caused by major infectious diseases in the state of São Paulo between August 2023 and August 2024.

A z-proportion test comparing the number of deaths from COVID-19 to other infectious diseases revealed statistically significant differences in all cases (Bonferroni-corrected, $P < 0.001$). COVID-19 mortality was significantly higher than that of dengue, AIDS, tuberculosis, hepatitis, and influenza. The only exception was pneumonia, which exhibited a significantly greater number of deaths than COVID-19. These findings demonstrated the impact of COVID-19 among infectious diseases in the analyzed period.

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DISCUSSION

The analysis of COVID-19 data in the state of São Paulo illustrated the rapid spread of SARS-CoV-2, with sharp increases in hospitalizations and deaths, consistent with global patterns [2]. It also revealed a temporal association between the implementation of vaccination campaigns and the subsequent reduction in hospitalizations and fatalities, though confounders such as natural immunity may contribute.

The initial phase of the pandemic, characterized by an exponential rise in hospitalizations and deaths, highlighted the the vulnerability of the healthcare system when faced with an unprecedented surge from a novel disease. During this critical period, containment measures—such as lockdowns, social isolation and distancing, school and business closures, travel restrictions, and mask mandates—were implemented. These measures were unpopular among the population of the state of São Paulo due to their direct economic impact on workers and small business owners, as well as the population's exhaustion from prolonged restrictions. Additionally, the spread of misinformation, the unequal perception of the disease's risk (*e.g.*, by education level), and the lack of structured social support contributed to society's resistance to containment measures, even in the face of the severity of the health crisis [9].

Despite these efforts, hospitals faced considerable strain. Concurrently, widespread resistance to protective behaviors emerged among the population—a condition referred to as pandemic fatigue, regarded as a natural and anticipated reaction to the protracted duration of the crisis and its accompanying challenges [22, 23]. By the end of 2021, Brazil accounted for more than 10% of the world's total COVID-19 deaths [24]. From February 2020 to April 2024, Brazil registered a total of 38,795,966 cases and 712,038 deaths from COVID-19 [25]. This severe scenario fueled high expectations that vaccination would curb the spread of the virus and lead to a decline in both hospitalizations and COVID-19-related deaths.

The Period 2 demonstrated that vaccination had a substantial impact on protecting the population against COVID-19 and stabilizing the healthcare system. The decline in the number of infections, hospitalizations, and deaths underscored the effectiveness of the available vaccines. In this context, studies evaluating the impact of mass vaccination in Europe [26] and assessing vaccine efficacy in older adults in Australia [27] found that vaccination was associated with substantial reductions in mortality. In the state of São Paulo, by the end of the Period 1, 121,960 deaths had been recorded. During the Period 2, an additional 58,031 deaths occurred, bringing the cumulative total to 179,991. While the absolute number continued to grow, the rate of increase slowed considerably, indicating a substantial reduction in mortality growth following mass vaccination.

Even after the widespread distribution of SARS-CoV-2 vaccines and the decline in case numbers, new surges in infections, hospitalizations, and deaths were observed, particularly during the Omicron waves in late 2021 and early 2022. Low adherence to protective measures—such as mask use, social distancing, and avoiding large gatherings—played a significant role in the resurgence of cases, hospitalizations, and fatalities during the pandemic, even after the initiation of vaccination [26, 27]. Despite the progress of immunization and the initial reduction in severe cases, combining vaccination with protective measures remained one of the most effective strategies for controlling the pandemic [28]. The relaxation of these measures, coupled with the high transmissibility of new viral variants, facilitated the spread of COVID-19 [28], particularly in settings with insufficient vaccine coverage or where booster doses had not been widely administered [29].

The emergence of new SARS-CoV-2 variants was a major factor behind resurgences in infection cases, even after widespread vaccine administration [30]. This was partly due to the fact that some vaccines, originally developed for the ancestral strain, were less effective at preventing infection with newer strains [31,32]. However, vaccination continued to provide strong protection against severe outcomes. Individuals vaccinated against pre-Omicron lineages who later became infected with Omicron variants experienced substantially less severe symptoms and lower hospitalization rates [33]. These findings underscore that immunization, while not always preventing infection, plays a crucial role in reducing disease severity and limiting viral spread, contributing to broader public health protection.

The Period 3 marked a new reality—a significant decline in COVID-19 cases, hospitalizations, and deaths. The reduction in disease indicators created a sense of reduced urgency among populations worldwide, leading to the discontinuation of protective measures aimed at preventing viral spread. Although vaccines have proven effective at reducing severe disease and mortality, COVID-19 remains a relevant public health concern. The emergence of new variants and the potential waning of immunity over time necessitate ongoing surveillance. Notably, despite lower case numbers, COVID-19 continued to have a significant impact, with a higher number of deaths than most infectious diseases, as highlighted in the findings of this study.

The persistence of COVID-19 cases and deaths underscores the need for greater efforts in vaccination campaigns and booster dose administration, emphasizing that the fight against COVID-19 is not a one-time event but an ongoing and sustained effort. Our findings showed that, from 2023 onward, vaccine coverage remained significantly below initial levels. At the peak of the mass vaccination campaign, 14 million COVID-19 vaccine doses were administered in June 2021 alone. In the following months, millions of doses continued to be

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administered monthly. However, from July 2023 onward—after the WHO declared the end of COVID-19 as a PHEIC —the monthly number of administered doses no longer approached one million. This scenario underscores the importance of enhancing health communication, strengthening public education, and implementing more effective campaigns to encourage booster dose uptake. Such measures are essential to sustaining progress in pandemic control and preventing future outbreaks.

The present study demonstrated that the COVID-19 pandemic, initially characterized as a health crisis, has transitioned into a more controlled epidemiological scenario. However, when comparing mortality data from infectious diseases in the state of São Paulo, COVID-19 remains one of the leading causes of death. In 2024, even during the worst dengue epidemic ever recorded in the state and in the country, COVID-19 caused more deaths than dengue, as well as more than HIV/AIDS, tuberculosis, viral hepatitis, and influenza. These findings highlight the continued public health relevance of COVID-19, even after the end of its classification as a PHEIC. Previous studies supported this observation, showing that in many settings, COVID-19 still has a higher mortality rate than other respiratory illnesses [34,35]. We recommend broader studies to compare mortality indicators across regions and contexts. Nevertheless, the data from São Paulo clearly show that COVID-19 remains a significant concern for public health policy.

Moreover, the persistence of the COVID-19 pandemic must be addressed due to the emergence of long-term complications, such as long COVID. Estimates of long COVID prevalence vary widely depending on case definitions, study populations, and timing of assessment. Some studies indicated that even among vaccinated individuals, 10% to 20% of those infected with SARS-CoV-2 developed long COVID [36–38], while estimates made by the CDC showed that long COVID developed in less than 5% of those infected [39]. Among unvaccinated individuals who were hospitalized with severe COVID-19, between 50% and 85% developed long COVID, whereas among unvaccinated individuals who were not hospitalized, the prevalence ranged from 10% to 35% [36]. As a result, millions of people worldwide have developed long COVID, and a significant number will continue to be affected, experiencing chronic fatigue, respiratory difficulties, and neurological or cardiovascular problems. These complications impair quality of life and work capacity, often requiring long-term medical care, rehabilitation, and psychological support [36,40]. The persistence of these symptoms reinforces the critical importance of transmission control, vaccination, and ongoing research to improve treatment options and understanding of this condition.

During the COVID-19 pandemic, the rapid emergence of SARS-CoV-2 variants—driven by sustained high levels of viral transmission —posed significant challenges to public health policies and had severe consequences for the population [41]. The lesson from variant emergence must be consistently considered to effectively combat the persistence of COVID-19.

Furthermore, given the probable zoonotic origin of SARS-CoV-2 —meaning it jumped from wild animals to humans—it is crucial to significantly reduce viral circulation to minimize the risk of spillback from humans to susceptible animal populations [42]. In the early phases of the pandemic, for example, SARS-CoV-2 variants were detected in mink populations, which later transmitted the virus back to humans [43,44]. Previous studies have shown that SARS-CoV-2 variants can not only jump from humans to white-tailed deer (*Odocoileus virginianus*), but also spill back from these animals to humans [45]. Deer species of the genus *Mazama* are among the closest evolutionary relatives of the genus *Odocoileus*, sharing conserved genetic sequences that may increase their susceptibility to SARS-CoV-2 infection [46]. Given that SARS-CoV-2 has been shown to infect and circulate widely in *Odocoileus* species, such as the white-tailed deer, it is plausible that *Mazama* species could also serve as potential hosts. Notably, two *Mazama* species—the small red brocket (*Mazama bororo*) and the pygmy brocket (*Mazama nana*)—have been recorded in the state of São Paulo [47]. In addition, the SARS-CoV-2 receptor molecule (angiotensin-converting enzyme 2, ACE2) is highly conserved among cervids, which may further support the likelihood of cross-species transmission [48]. Given that SARS-CoV-2 spillback to humans has been documented, there is a substantial risk that certain viral variants may adapt to different hosts in ways that could trigger new outbreaks in humans. This highlights the ongoing need for vigilant surveillance, vaccination efforts, and research to prevent future pandemic threats.

In summary, although the state of São Paulo had made significant progress toward stabilizing the situation, the pandemic still requires constant monitoring, rapid responses to new variants, and a strong focus on ongoing vaccination campaigns. The control of COVID-19 in Brazil is a dynamic process that demands continuous preparedness and adaptation to prevent or address future public health challenges.

As a limitation, this study did not perform imputation or exclusion of missing data. Epidemiological indicators—cases, deaths, and hospitalizations—were analyzed as reported in the official databases (SEADE and SIM), reflecting real-world reporting practices and the availability of information at different points during the pandemic. While this approach preserves the authenticity of the data, it also introduces limitations related to the quality, consistency, and completeness of the source data. Underreporting, delayed reporting, and the cessation of mandatory hospitalization notifications may have impacted data accuracy, potentially influencing observed

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trends, and consequently may have harmed decision-making in public health policies.

Additionally, variations in COVID-19 testing rates over time may have affected case detection. Changes in testing availability, policies, and population behavior throughout the pandemic could contribute to periods of underestimation or overestimation of cases. These factors should be considered when interpreting epidemiological trends and making comparisons across different time frames.

In conclusion, through a quantitative and descriptive approach, this study highlighted that the state of São Paulo transitioned from a crisis phase—characterized by the beginning of the pandemic, rapid increases in infections and deaths, and the absence of vaccines—to a subsequent phase of monitoring and control of COVID-19 following the implementation of mass immunization strategies. This shift was evidenced by a consistent decline in cases, hospitalizations, and deaths, as well as the strengthening of public health responses. As a result, the burden on the healthcare system was alleviated, contributing to the stabilization of key health indicators.

Although Brazil has made significant progress toward stabilizing the pandemic, COVID-19 has continued to cause a considerable number of hospitalizations and deaths. Given that vaccination remains a central pillar in controlling the disease, the population's declining interest in receiving booster doses may have contributed to the persistence of viral transmission and its consequences. One possible factor influencing this reduced engagement could be the World Health Organization's declaration ending COVID-19 as a PHEIC, which may have been perceived by some members of the public as signaling the end of the pandemic. This misperception likely weakened the sense of urgency regarding vaccination and other preventive measures [49]. Concerns have been raised that the reduction in public surveillance could lead to diminished interest in protective measures against COVID-19 and increased vaccine hesitancy, thereby facilitating greater viral circulation and spread [50].

These findings underscore the importance of maintaining high vaccination coverage and investing in effective public health communication strategies to address emerging variants. Sustained efforts will be essential not only to prevent new surges but also to consolidate the advances already achieved in pandemic control.

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CONFLICTS OF INTEREST

The authors declared that there are no conflicts of interest associated with this manuscript.

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AI DISCLOSURE

Artificial intelligence was applied to review the text in the final version of the manuscript.

DATA AVAILABILITY

The data obtained for the analysis of this study can be accessed on the SEADE portal (https://www.seade.gov.br/coronavirus/), through the SEADE repository and on GitHub (https://github.com/seade-R/dados-covid-sp).

AUTHORS' CONTRIBUTIONS

APA: Conceptualization; Data curation; Formal analysis; Investigation; Methodology; Writing – original draft; writing – review & editing. AMS: Data curation; Formal analysis; Methodology; Writing – review & editing. PBP: Data curation; Formal analysis; Supervision; Writing – review & editing. LRL: Conceptualization; Data curation; Formal analysis; Investigation; Supervision; Methodology; Writing – original draft; Writing – review & editing.

ETHICS STATEMENT

According to Resolution No. 674 (2022) of the National Health Council, in Chapter IX, Article 26 and item V, there was no need for ethical evaluation since this research was carried out exclusively with publicly available information or data already made available in an aggregated form, without the possibility of individual identification.

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