Submitted on: 08/03/2025
Approved on: 10/22/2025

ORIGINAL ARTICLE

# Temporal Distribution and Burden of Respiratory Syncytial Virus Infections in Critically Ill Children (2021-2024)

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**Keywords:**
Critical Care.
Severe Acute Respiratory Syndrome.
Seasons.
Brazil.
Respiratory Syncytial Virus Infections

## Abstract

Objective: We aimed to characterize the temporal pattern and burden of RSV-positive cases admitted to the pediatric intensive care unit (PICU) at two pediatric hospitals in Rio de Janeiro and compare these findings with data obtained from Influenza Epidemiological Surveillance Information System (SIVEP-Influenza). Methods: We retrospectively evaluated 5,207 RSV tests in children and adolescents admitted to PICUs from March 2021 to December 2024. We analyzed the distribution of cases over the epidemiological weeks (EW) and, to verify and compare data from both sources regarding the time trend of RSV burden, we used count regression models for the statistical analysis. Results: We observed a shift from the previously acknowledged seasonal pattern of RSV in 2021, with increased activity in spring and early summer. There was a tendency to return to the typical seasonality in 2022-23 and a more usual circulation in 2024. In our PICUs, the percentage of total RSV positive cases, between EW 10 and 36, were 52.9%, 69.7%, 90.5% and 93.6% in 2021, 2022, 2023 and 2024, respectively. We found a significantly higher RSV positive test rate in 2023-24 compared to 2021-22 (IRR = 1.73; 95% CI: 1.42-2.10; $p < 0.001$). Conclusions: According to the temporal analysis of severe RSV infections, the disruption of the usual seasonality in 2021 was not sustained in the following years. In contrast to reports from other countries, the burden of severe disease did not rise in the years following the relaxation of COVID-19 mitigation measures, specifically from 2021 to 2022.

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DOI: https://doi.org/10.25060/residpediatr-2026-1526

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## INTRODUCTION

Respiratory syncytial virus (RSV) is a significant respiratory pathogen that primarily affects infants and young children, and the impact of RSV infections is substantial, leading to a high disease burden in pediatric populations worldwide [1].

The respiratory virus epidemiology is impacted by the virus's evolving virulence as well as environmental and social factors. Measures implemented to reduce the spread of SARS-CoV-2 beginning in 2020, including facemasks, hand hygiene, stay-at-home orders, and closure of schools and local/national borders, likely had a significant impact in the spread on other respiratory pathogens [2,3]. The World Health Organization (WHO) declared the end of the most critical phase of the global emergency on May 5, 2023.

In many countries, it was observed a sharp decline in the number of RSV cases in 2020 followed by a surge in cases in 2021, particularly affecting children under 5 [4, 5]. Several studies reported disrupted seasonality of RSV infection during 2020–2021 [6, 7], with an unprecedented summer surge of RSV activity in 2021 [8] or, in the southern hemisphere, beginning in spring and extending into summer in late 2020 [9].

The Influenza Epidemiological Surveillance Information System (SIVEP-Influenza) was implemented in Brazil in 2000 to track the influenza virus across the nation. Later, to follow the simultaneous spread of the novel coronavirus (SARS-CoV-2) and other respiratory viruses, the Brazilian Ministry of Health's Secretariat (SVS/MS) modified the Acute Respiratory Syndromes Health Surveillance System. With this system, it is possible to track the temporal trend of hospitalized cases of many respiratory virus' severe acute respiratory syndromes in both adults and children.

According to a retrospective review of data from Brazil's SIVEP database, in 2021, the peak of RSV positivity occurred during the epidemiological week (EW) 11, period corresponding to summer, followed by a second peak at EW 46. In 2022, it was observed a peak in EW 16 and another growing trend from EW 37 [10]. The occurrence of a second peak of cases in the spring of 2021 indicates a change in RSV seasonality[10].

To address the hypothesis that the COVID-19 pandemic altered the circulation and burden of RSV in Rio de Janeiro, we examined the temporal distribution and positivity rates of RSV infections from 2021 to 2024. We conducted this analysis using two distinct data sources: (1) records of children and adolescents admitted to the PICUs of two pediatric referral hospitals, and (2) surveillance data from the SIVEP-Influenza system. Furthermore, we carried out a comparative analysis to assess the congruence between these two databases.

## METHODOLOGY

We retrospectively analyzed RSV infections using two data sources: (1) records from pediatric intensive care units (PICUs) at our hospitals for patients aged 0–17 years (March 2021–December 2024), and (2) data from the SIVEP-Influenza System for patients aged 0–15 years with severe acute respiratory syndrome in Rio de Janeiro State (January 2021–December 2024). RSV circulation over the epidemiological weeks was analyzed from both sources and compared with the usual pattern described in the literature. We compared the positivity rates, as a measure of disease burden, during COVID-19 pandemic (2021-22) and post-pandemic (2023-24) years.

We included all children and adolescents, from birth to 17 years and 11 months of age, admitted to the PICUs with respiratory symptoms who have been tested for RSV during the study period. Symptoms included nasal discharge or obstruction, cough, shortness of breath (dyspnea) or rapid breathing (tachypnea).

The families of the patients were informed about how to collect nasopharyngeal swab, and informed consent was obtained. We employed an immunochromatographic technique for the qualitative identification of RSV antigen in samples from the upper airways, called the RSV ECO test (TR.0015CA-diagnostic ECO).

We checked notifications obtained from SIVEP/Influenza, State Department of Health, Sub secretariat of Health Surveillance, updated until 10/01/2025. Data from SIVEP are accessible to the public at the electronic address https://sistemas.saude.rj.gov.br/tabnetbd/dhx.exe?sivep_gripe/sivep_gripe.def [11].

In order to verify and compare data from both sources regarding the time trend of RSV burden, first, we performed a basic analysis, examining counts and positivity rates during the study period. For the statistical modeling, we used count regression models. We started with a Poisson regression model, which accounted for the different number of tests performed. Data were then analyzed for overdispersion (meaning it had more variation than the Poisson model expects). If it was, we used a Negative Binomial regression model instead. We created separate models for each data source. A combined model was made to see if the trends over time were different between the Hospital and SIVEP sources. We compared the trends between pandemic (2021-2022) and post-pandemic (2023-2024) periods. The results are shown as Incidence Rate Ratios (IRR) with their 95% confidence intervals and *p*-values. A *p*-value less than 0.05 was considered statistically significant. All analyses were done using R software, version 4.4.1.

This study was approved by the Instituto D'Or de Pesquisa e Ensino (IDOR) Ethics Committee (Plataforma Brasil CAAE: 90844825.0.0000.5249).

## RESULTS

Between March 2021 and December 2024, 5,207 samples were collected for respiratory virus testing in our PICUs. In 2021, we collected 806 samples, comprising 656 negative results, 54 RSV-positive samples, 2 samples with COVID-19 co-infections, and 1 with Adenovirus co-infection.

Among the 1,494 samples in 2022, 1,347 were negative, 93 were positive for RSV, 3 had co-infections with COVID-19, and 1 had co-infections with Flu A. In 2023, 1,362 samples were obtained, among which, 1,173 were negative, 159 were positive for RSV, and 3 were co-infections with Flu A. A total of 1,545 samples were obtained in 2024, being that 1,317 negative, 162 positive for RSV, 1 co-infected with COVID-19, 1 with Flu A, 1 with Adenovirus and 1 with Rhinovirus.

The positivity rates for RSV obtained were 6.7% in 2021, 6.2% in 2022, 11.7% in 2023 and 10.5% in 2024, in PICUs patients and 5.3% in 2021, 9.2% in 2022, 7.1% in 2023 and 15.6% in 2024 in SIVEP data. (Figure 1). In both sources, the average positivity rate for RSV was similar (≈9%).

In 2021, the reference year, the RSV positive case rates observed in hospitals and in SIVEP were similar, with no statistical difference between the two sources (IRR = 0.88; $p$ = 0.595). In our hospitals, a significant upward trend in positivity rates was identified over the years, with an estimated average increase of 22% per year (IRR = 1.22; $p$ = 0.035). In SIVEP, an increase in rates was also observed, and this growth did not differ statistically from that observed in the hospital (IRR = 1.11; $p$ = 0.408) (table1).

In 2021, we observed the peak of RSV positivity in EW 47 and 48, corresponding to October (spring). There were three peaks reported in the first semester, in epidemiological weeks 3, 4, and 8 (summer), and, similarly, in epidemiological weeks 47 and 48, based on data from SIVEP related to that year. In 2021, we began gathering samples from EW 10.

The peaks of RSV positivity in our hospitals were subsequently verified during EW 19, fall, which was also the week with the greatest number of cases reported in SIVEP in 2022, and, with a smaller number of cases, in EW 25, early winter. There was a considerable number of cases in the first weeks of the year, during the summer season and RSV-positive admissions were seen during all the first semester in our PICUs. In SIVEP data, the RSV-positive cases grew in numbers from the end of summer (EW 10) and nearly vanished after EW 29-32.

In 2023, nearly all the RSV positive samples from SIVEP and our data were found in EW 2-35 and 6-33, respectively, over the summer, fall, and winter. We found two peaks, one in EW 13 and the other in EW 15, and two peaks in SIVEP (EW 15 and 19). There was a steady decline in the number of positive samples until week 25 (early winter); beyond that, there were much fewer records.

The RSV cases, in 2024, started in week 10 (the end of summer), progressively decreased after the end of fall, but, unlike the previous year, continued at substantial levels during winter. The peak of PICU positivity was detected in EW 15, while the peak of SIVEP was found in EW 20, both in fall season. In contrast to previous years, there was no significant

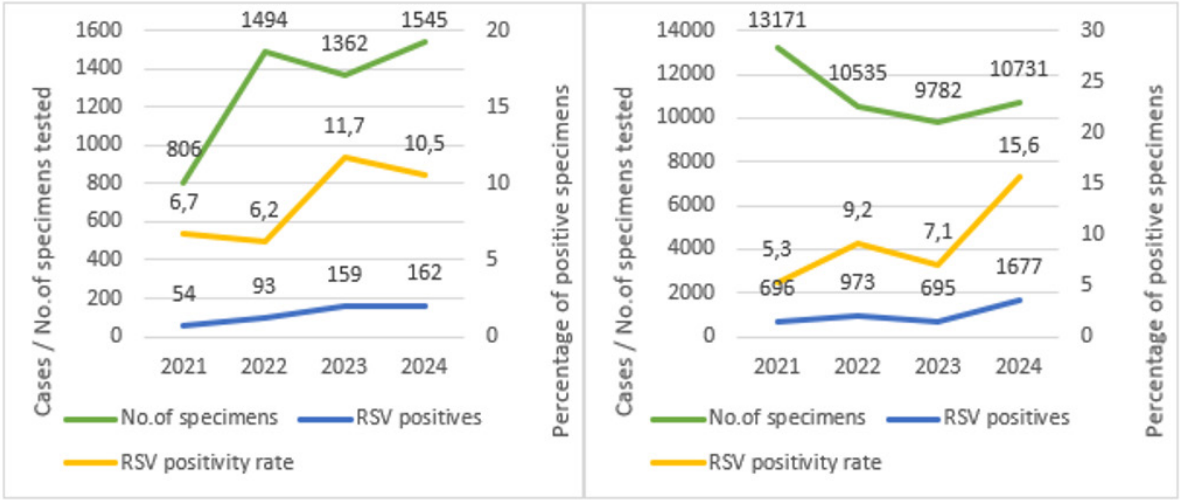



**Figure 1**: Left- Temporal trend of tests performed (samples), positive cases and positive rate for RSV in children and adolescents (0-17 years) admitted to PICUs, from 2021 to 2024. Right- Temporal trend of tests performed (samples), positive cases and positive rate for RSV in children and adolescents (0-15 years) from SIVEP-Influenza, the Influenza Epidemiological Surveillance Information System, Rio de Janeiro, from 2021 to 2024.

**Table 1.** Negative binomial regression with offset (log of number of tests): comparison between sources and trend over time.

| Variable | IRR | CI95% (Inferior) | CI95% (Superior) | *p*-value |
|---|---|---|---|---|
| Intercept (Hospitals; Year=2021) | 0,063 | 0,044 | 0,092 | <0,001 |
| Baseline difference (SIVEP vs Hospitals, year 2021) | 0,879 | 0,546 | 1,418 | 0,595 |
| Annual trend (Hospitals) | 1,222 | 1,013 | 1,478 | 0,035 |
| Annual trend difference (SIVEP vs Hospitals) | 1,110 | 0,866 | 1,422 | 0,408 |

number of cases before EW 10 in 2024, during the summer season. (Figures 2 and 3).

The percentage of total RSV-positive cases during the habitual RSV season in Rio de Janeiro, between EW 10 and 36, were 52.9%, 69.7%, 90.5% and 93.6% in 2021, 2022, 2023 and 2024, respectively in our data and 29.1%, 94.4%, 90.2%, 94.0% in SIVEP data (Table 2).

In the pooled analysis, considering the years 2021–2022 as the pandemic period and 2023–2024 as the post-pandemic period, in our PICUs, we found a significantly higher RSV positive test rate in the post-pandemic period compared to the pandemic period, with an increase of approximately 73% (IRR = 1.73; 95% CI: 1.42–2.10; $p < 0.001$). In the analysis of data obtained from SIVEP, we observed that the positive rate was 1.57 times higher in the post-pandemic period. However, unlike what was observed in the data from our hospitals, this difference did not reach statistical significance (IRR = 1.57; 95% CI: 0.82–3.00; $p = 0.180$) (Table 3).

## DISCUSSION

Our results confirm that the disruption of the usual RSV circulation pattern, previously described in other regions, also occurred in Rio de Janeiro in 2021. However, we did not find a higher burden of severe disease in the last two years of the COVID-19 pandemic (2021-22), after easing of non-pharmacological mitigation measures.

Ongoing monitoring of local temporal patterns is essential for guiding the timing of RSV immunoprophylaxis. Countries with continental dimensions such as Brazil, Australia, China, and the USA may present heterogeneity in the circulation of respiratory viruses, with differences in burden and seasonality between regions [9, 12-14]. In Brazil, the period indicated for starting prevention with monoclonal antibodies against RSV varies according to the region, starting in January in the North, February in the Northeast, Midwest and Southeastern, and March in the South.

**Table 2.** Percentage of positive RSV cases between epidemiological weeks 10 and 36 according to PICUs and SIVEP data from 2021 to 2024.

| SOURCE | 2021 | 2022 | 2023 | 2024 |
|---|---|---|---|---|
| PICUs | 52.9% | 69.7% | 90.5% | 93.6% |
| SIVEP | 29.1% | 94.4% | 90.2% | 94.0% |

**SIVEP** = Sistema de Vigilância Epidemiológica da Gripe.

**Table 3.** Negative binomial regression with offset (log of the number of tests): positivity rate ratio in the post-pandemic period compared to the pandemic period.

| SOURCE | IRR | Inferior CI95% | Superior CI95% | *p*-value |
|---|---|---|---|---|
| PICUs | 1,73 | 1,42 | 2,10 | **<0,001** |
| SIVEP | 1,57 | 0,82 | 3,00 | 0,180 |

**IRR** = Incidence Rate Ratio, obtained from negative binomial regression with a log link. **95% CI** calculated using the Wald method. **Offset** = log of the number of tests performed. **Pandemic period:** years 2021-2022; **post-pandemic period:** years 2023-2024.

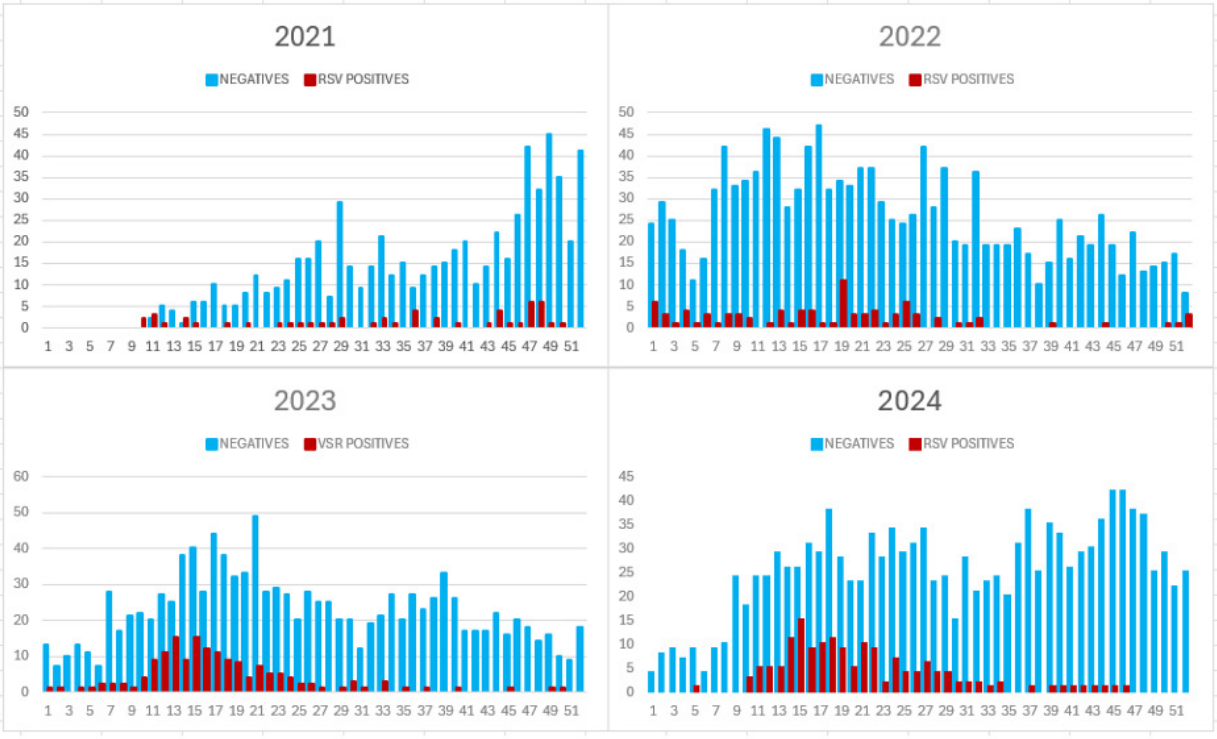



**Figure 2.** No. of negative specimens and RSV positivity, PICUs (2021-24).

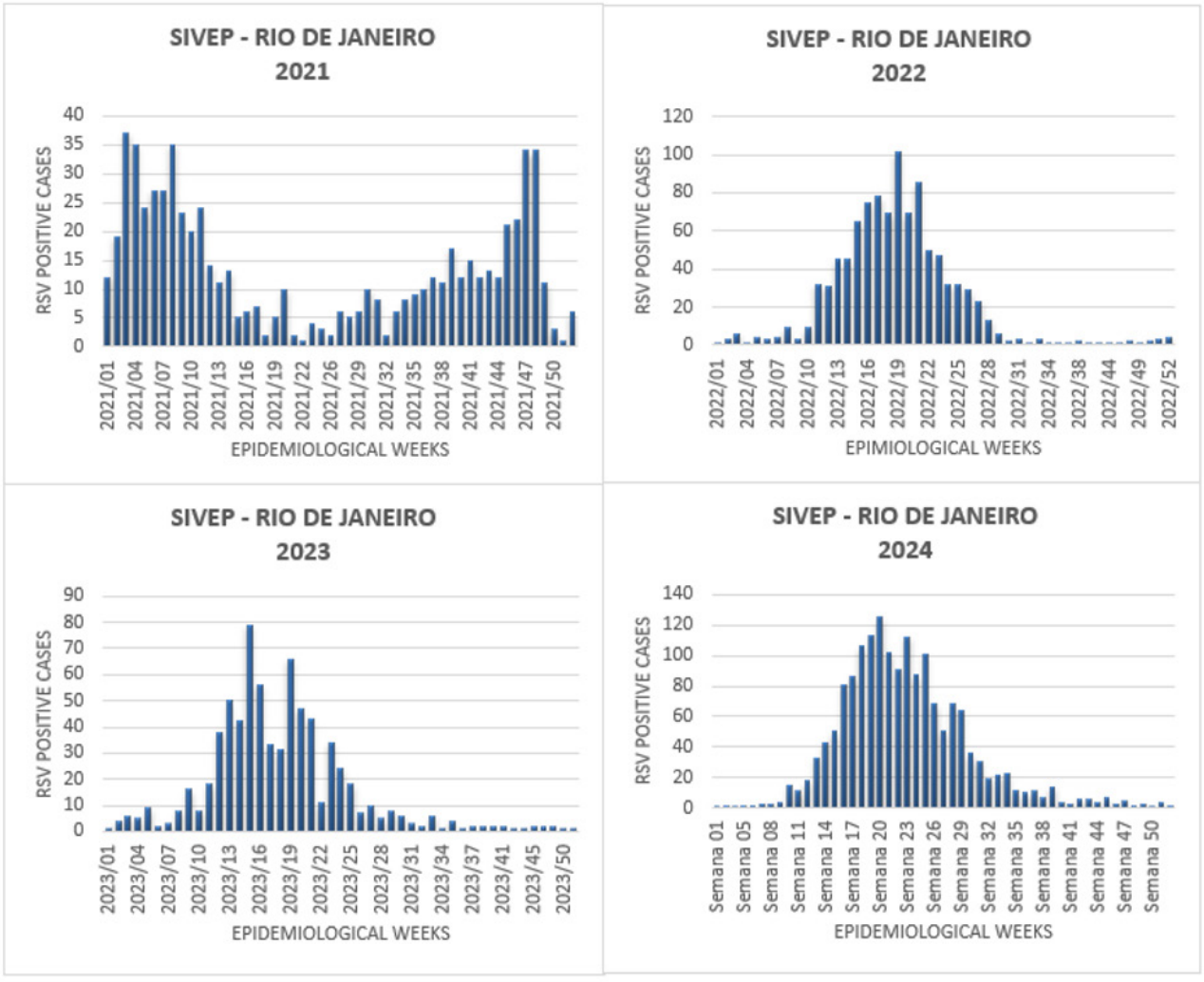



**Figure 3.** No. of RT-PCR positive RSV in State of Rio de Janeiro (2021-24)

In temperate countries, RSV peak activity generally starts in the fall and peaks in the winter [15]. In contrast, in tropical countries, there is a wide variability in the timing and duration of epidemics and the correlation between climatic factors and viral activity is controversial [13].

While the RSV wave typically begins in March and ends in October in the Southern Hemisphere, there is a significant difference in seasonality between Brazil's five geographic areas[13,16,17]. Research conducted in Rio de Janeiro demonstrated that the pre-pandemic seasonality of RSV showed consistent trends, with specimen positivity concentrated between EW 10 (early March / late summer) and 36 (early September / winter)[16].

In the USA, although RSV outbreaks usually peak in December or January, the usual winter epidemic did not materialize in the 2020–21 season during the pandemic timeframe. The 2021–22 season deviated significantly from the typical RSV seasonality, starting later in May, peaking in July, and ending in January. The 2022–2023 season began and peaked later than the previous season but earlier than pre-pandemic years, indicating a gradual restoration to more regular seasonal patterns. The disruption caused by the COVID-19 pandemic prompted a shift in the timing of RSV outbreaks [14].

This reduced RSV-associated activity during the usual season in 2020 was described in another continents [8,9] and between 2020 and 2022, the COVID-19 pandemic upset seasonal rhythms of RSV outbreaks in other countries [9, 18]. Similarly, data from SIVEP-Influenza found a reduction in the circulation of RSV in 2020[11].

In 2021, according to SIVEP-Influenza data, RSV peak activity took place during the summer and spring, which deviates from the typical seasonality. This early summer peak could not be captured in our data because routine respiratory virus testing was only implemented after EW 10. However, the peak of activity recorded in spring clearly demonstrates a deviation from the regular seasonal pattern.

The proportion of severe RSV-positive cases at our hospitals, spanning between EW 10 and 36, indicates a return to consistent seasonal patterns in the last two years (2023-24) in

our data. **This trend aligns with the broader pattern observed in the SIVEP data beginning in 2022**.

It is important to note that there have been previous reports of early onset of RSV activity in southeastern of Brazil. In 1997/98 and 2018, there were early onset of RSV circulation in Espírito Santo State. The occurrence began in January/February, amid the summer, and ended in the late fall rather than during winter [13,19].

In 2021, we detected RSV cases year-round, with a seasonal distribution that was not sharply defined. This pattern was characterized by a higher number of cases in the spring, a finding consistent with the national SIVEP-Influenza data. However, in state of Rio Grande do Sul, southern region, RSV infections were detected year-round, but with the highest number of cases occurring in June-July, during the winter season[4].

The sharp reduction in infections during the initial COVID-19 waves likely contributed to the surge of RSV hospitalizations in the summer/early autumn of 2021. This phenomenon, reported globally, resulted in rates that exceeded the pre-pandemic average across all age groups [20-23]. The following hypotheses have supporting and conflicting evidence: a decrease in population immunity due to the interruption of RSV circulation (immunity debt) and/or reduced viral genetic diversity, with local emergence of distinct, more virulent clades (genetic bottleneck), and/or immune dysregulation from a previous SARS-CoV-2 infection, which may increase susceptibility to subsequent RSV infections and/or higher rates of a first RSV infection [24]. In 2021, contrary to the pattern seen in many high-income countries, we did not observe a rebound increase in RSV-related hospitalizations. This absence of a rebound, with a low incidence of RSV-associated lower respiratory tract illness (RSV-LRTI), has been previously described in some low and middle-income countries [25].

A retrospective analysis of the number of positive cases and diagnostic tests in 32 US hospitals indicated that the higher case counts seen in 2021–2023 are probably due to an increase in RSV testing rather than viral circulation. These findings call for a critical evaluation of the immunity debt theory [26].

In Rio de Janeiro, the first COVID-19 cases were reported in March 2020. Low adherence and delayed adoption of non-pharmacological mitigation measures lead to a more critical phase with collapse of the healthcare system. Spikes in the illness were still being observed even after attempts to step up these interventions[27]. There was a scenario of medium-level mitigation measures that differed from that seen in European countries, which adopted stricter measures with the imposition of a total lockdown. Therefore, we would not expect the same level of "immunity debt" in any case. The distinct timeline of restriction easing and the variable public adherence to mitigation measures in Brazil likely explain the differences in the observed RSV epidemiological patterns compared to other countries.

Case counts and positivity rates were lower in the 2021-22 "resurgence" period compared to the 2023-24 period, although a comparison with the pre-pandemic era was not possible due to a lack of data. Similarly, in SIVEP-Influenza data, the merged number of cases in 2021-22 was lower than those observed in 2023-24. Although the fluctuation patterns between years were not identical in the two datasets, both indicate a post-pandemic resumption and intensification of RSV circulation.

We recognize as limitations of this study the relatively small number of positive RSV cases and the lack of information about the local circulation of RSV in the pre-pandemic period. The RSV Eco Test has good sensitivity (92.4%) but a small percentage of false-negative results still occurs.

Continued surveillance in the coming years will be essential to confirm the definitive return of RSV seasonality to its pre-pandemic pattern.

## CONCLUSION

Although SIVEP-Influenza data show an increase in RSV incidence and positivity rates in 2022 compared to 2021, they do not indicate an epidemic "rebound" phenomenon in Rio de Janeiro. A higher disease burden among critically ill children was observed in the 2023-24 period compared to the 2021-22 biennium in our and in SIVEP-Influenza data.

Temporal analysis of severe RSV infections in Rio de Janeiro in both sources indicated an initial disruption of the usual seasonality in 2021, which was not sustained in subsequent years. While low-level summer circulation occurred from 2021 to 2023, this pattern was absent in 2024. Instead, the 2024 season was more typical, beginning in late summer, peaking in autumn, and declining sharply by early winter.

These findings suggest that RSV circulation in Rio de Janeiro is showing signs of returning to its pre-pandemic seasonal pattern.

## ADDITIONAL INFORMATION

Funding: The authors declare that they received no specific funding for this study.

Conflict of interest: The authors declare no conflicts of interest.

CAAE approval number from the Research Ethics Committee: 90844825.0.0000.5249

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