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► **To cite this version:**

Victorine Boccard, Blandine Prevost, Sophie Denamur, Elora Peulier-Maitre, Nadia Nathan, et al..
Bronchiolitis: Increased severity in the post-COVID-19 era. *Pediatric Pulmonology*, 2024, Online
ahead of print. 10.1002/ppul.27172 . hal-04683648

HAL Id: hal-04683648

<https://hal.science/hal-04683648v1>

Submitted on 8 Oct 2024

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Bronchiolitis: Increased severity in the post-COVID-19 era

Victorine Boccard MD^{1,2} | Blandine Prevost MD^{1,2} | Sophie Denamur MD^{1,2} |
Elora Peulier-Maitre MD^{1,2} | Nadia Nathan MD^{1,3}  | Harriet Corvol MD^{1,2} 

¹Sorbonne Université, Assistance Publique-Hôpitaux de Paris (AP-HP), Hôpital Trousseau, Service de Pneumologie Pédiatrique, Centre de Référence des Maladies Respiratoires Rares RespiRare, Paris, France

²Sorbonne Université, Centre de Recherche Saint-Antoine (CRSA), Inserm UMR_S938, Paris, France

³Sorbonne Université, Laboratory of Childhood Genetic Diseases, Inserm UMR_S933, Paris, France

Correspondence

Harriet Corvol, MD, Pediatric Pulmonology Department, Trousseau Hospital, 26 Ave du Dr Netter, 75012 Paris, France.
Email: harriet.corvol@aphp.fr

Funding information

None

Abstract

Introduction: Acute bronchiolitis is a pressing public health concern, leading to numerous infant hospitalizations worldwide annually. The notable decrease in bronchiolitis hospitalizations during the COVID-19 pandemic sparked concerns about a potential resurgence post-pandemic. Questions also arose about the severity of post-pandemic cases compared to prepandemic ones. This study aimed to compare bronchiolitis severity before and after the COVID-19 pandemic, alongside changes in the epidemiology of bronchiolitis viral agents.

Material and Methods: We conducted a retrospective analysis of medical records concerning infants under 12 months hospitalized for acute bronchiolitis in our pediatric pulmonology department over a period of 5 years: 2 pre-COVID years (2018–2020), the COVID year (2020), and 2 post-COVID years (2021–2023). Clinical and laboratory data were collected using standardized forms.

Results: Hospital admissions exhibited comparable rates pre- and post-COVID but witnessed a decline during the COVID period. Post-COVID, bronchiolitis severity increased, with longer hospitalization durations ($p < 0.001$) and increased oxygen therapy ($p = 0.04$), coinciding with a surge in the prevalence of RSV infections ($p = 0.01$). Patients testing positive for RSV were significantly younger ($p = 0.005$) and exhibited more severe symptoms.

Discussion and Conclusion: This study reveals a significant increase in bronchiolitis severity and a rise in RSV cases following the COVID pandemic. The implementation of preventive measures such as nirsevimab is crucial to alleviate the burden of respiratory illnesses in vulnerable populations. Continued vigilance and research are needed to address the evolving challenges of bronchiolitis in the post-COVID era.

KEYWORDS

acute bronchiolitis, acute lower respiratory infection, COVID-19, infant, RSV

Victorine Boccard and Blandine Prevost contributed equally to the study.

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1 | INTRODUCTION

Bronchiolitis is an acute lower respiratory infection predominantly affecting infants. Respiratory syncytial virus (RSV) is the most frequent cause of bronchiolitis, accounting for approximately 60%–80% of cases, particularly during peak epidemic periods.^{1,2} Additionally, various other viruses can trigger this condition, including rhinovirus, (para)influenza virus, human metapneumovirus, and coronaviruses.³ Notably, bronchiolitis stands as the most common cause of hospital admissions among infants within their first year of life.²

In Europe, the seasonal surge typically begins in late October, reaching its peak in mid-December, creating a substantial increase in consultations with GPs and a notable influx of patients into emergency rooms.¹ In France alone, it is estimated to affect nearly 30% of infants under the age of two annually, totaling around 480,000 cases each year.⁴ Approximately 2–3% of infants below 12 months require hospitalization due to severe bronchiolitis yearly.

Global surveillance data indicates that meteorological factors play a significant role in the transmission of bronchiolitis, particularly with indoor environments fostering its spread.⁵ The onset of the COVID-19 pandemic markedly influenced the epidemiology of viral infections. In France, the sanitary measures implemented in 2020 to mitigate the spread of COVID-19, such as rigorous hand hygiene, mask-wearing, social distancing, and lockdown measures, resulted in a delayed onset of the bronchiolitis epidemic that year, leading to a substantial decrease in cases.^{6–8} Similar trends were observed across various European countries.^{9,10} Conversely, in Australia, the advent of the COVID-19 pandemic coincided with the usual RSV bronchiolitis season, initially resulting in the absence of an RSV epidemic. However, a resurgence of RSV occurred 6 months later, surpassing the typical number of cases seen in previous years.¹¹

This scenario has prompted pediatricians to ponder the possibility of an upsurge in the bronchiolitis epidemic following the abbreviated winter season in 2020–2021 due to COVID-19. Additionally, there is speculation about the severity of postpandemic cases compared to those occurring before the COVID-19 era. Therefore, this study endeavors to compare the severity of bronchiolitis cases before and after the COVID-19 pandemic, elucidating the altered epidemiology of bronchiolitis viral agents.

2 | MATERIALS AND METHODS

2.1 | Study design and patients

This retrospective, observational, and monocentric study was conducted in the pulmonary pediatric department of the University Hospital Armand Trousseau, Assistance Publique Hôpitaux de Paris, located in Paris, France. The study included infants aged less than 12 months admitted to the department for a first episode of acute bronchiolitis during the autumn/winter seasons across a 5-year period from 2018 to 2023. These seasons comprised 2018–2019; 2019–2020; 2020–2021; 2021–2022; and 2022–2023, spanning

from October 1 to March 31. Exclusion criteria encompassed patients aged over 12 months, those with a history of a second or subsequent episode of bronchiolitis, and/or those experiencing an asthma attack, aligning with the French National Guidelines for bronchiolitis.¹²

Patient selection relied on the use of ICD10 code diagnoses for bronchiolitis. Three physicians reviewed the medical records to collect demographic and clinical data as well as laboratory tests results using a standardized specific form. Collected data included patient age and weight at the time of hospitalization, gender, presence of underlying conditions (such as prematurity, bronchopulmonary dysplasia, congenital heart disease, esophageal atresia, sickle cell disease, intrauterine growth restriction, diaphragmatic hernia, or genetic diseases), and results of PCR testing on nasopharyngeal swabs or aspirates for virus identification. Additionally, medical evolution data were gathered, including the duration of hospitalization, admission to the intensive care unit (ICU), respiratory support (such as oxygen therapy, noninvasive ventilation, invasive ventilation, and extracorporeal membrane oxygenation), and nutritional support modalities.

The study was approved by the institutional review board of the French Society for Respiratory Medicine (Société de Pneumologie de Langue Française, #CEPRO_2020-080). In accordance with French laws for observational studies, the requirement for written informed consent was waived (study BronChioVID N°20201119185601).

2.2 | Statistical analysis

Patients' characteristics are presented as means with 95% confidence intervals [CI 95%] for continuous variables and as numbers and percentages for categorical variables. We conducted a comparison of patients' characteristics across three distinct periods: pre-COVID (spanning 2 years from October 1 to March 31 in the years 2018–2019 and 2019–2020), COVID (from October 1, 2020, to March 31, 2021), and post-COVID (spanning 2 years from October 1 to March 31 in the years 2021–2022 and 2022–2023). Proportions for categorical variables were compared using the Chi-squared (χ^2) test, while the Kruskal–Wallis test was employed for continuous variables (the normality of distribution for continuous variables was assessed using the Shapiro–Wilk test and found to be rejected for each variable). Additionally, we analyzed patients' characteristics based on their RSV status, utilizing the Mann–Whitney test for continuous variables and the chi-squared test, along with Fisher's exact tests for proportions. Statistical analyses were performed using R project version 4.2.2, with a *p* Value of ≤ 0.05 deemed significant.

3 | RESULTS

3.1 | Clinical characteristics of the infants

During the post-COVID period (2021–2023), our department admitted 292 patients for acute bronchiolitis over the course

of 2 years, averaging 146 infants per winter. This contrasts with 95 infants admitted during the COVID period (2020–2021), but aligns closely with the 315 infants admitted during the 2 years pre-COVID (2018–2020), averaging 157 infants per winter.

Table 1 presents the clinical characteristics of these infants. The age distribution and sex ratio did not show significant differences across the three periods ($p=0.07$ and 0.11 , respectively). The proportion of patients with comorbidities also remained stable at 14.6%, 11.6%, and 16.4% during the pre-COVID, COVID, and post-COVID periods, respectively ($p=0.51$).

In the post-COVID period, the duration of hospitalization significantly increased, with a mean of 5.6 days [95% CI: 5.2–6.0], compared to 4.1 days [95% CI: 3.4–4.8] during the COVID period and 3.9 days [95% CI: 3.5–4.3] during the pre-COVID period ($p < 0.001$), indicating increased severity of the patients. Additionally, there was a significant increase in the proportion of patients who received oxygen therapy in the post-COVID period (70.9% vs. 56.8% and 65.4% in the COVID and pre-COVID periods respectively, $p=0.04$). There were however no significant differences in the proportions of patients admitted to the ICU or who needed noninvasive ventilation across the three periods ($p=0.47$ and $p=0.55$ respectively).

TABLE 1 Comparison of clinical characteristics of the infants hospitalized for acute bronchiolitis across pre-, during-, and post-COVID periods over 5 years.

	Pre-COVID period (2018–2020)			COVID period (2020–2021)	Post-COVID period (2021–2023)			<i>p</i> Value ^a
	2018–2019	2019–2020	2018–2020 aggregated data		2021–2022	2022–2023	2021–2023 aggregated data	
Number of infants, <i>n</i>	160	155	315	95	151	141	292	
Age (months): Mean [CI 95%]	3.0 [2.6–3.4]	2.8 [2.4–3.1]	2.9 [2.7–3.2]	3.2 [2.7–3.7]	2.9 [2.6–3.3]	2.7 [2.3–3.1]	2.8 [2.5–3.1]	0.07
Gender: Boys, <i>n</i> (%)	87 (54.4)	87 (56.1)	174 (55.2)	52 (54.7)	84 (55.6)	76 (53.9)	160 (54.8)	0.11
Comorbidities, <i>n</i> (%)	29 (18.1)	18 (11.6)	47 (14.9)	11 (11.6)	28 (18.5)	20 (14.2)	48 (16.4)	0.51
Weight (kg): Mean [CI 95%]	5.5 [5.3–5.7]	5.4 [5.1–5.7]	5.5 [5.3–5.7]	5.6 [5.3–5.9]	5.4 [5.1–5.7]	5.3 [5–5.6]	5.3 [5.1–5.5]	0.19
Evolution								
Duration of hospitalization (days): Mean [CI 95%]	3.5 [3.1–3.9]	4.4 [3.8–5]	3.9 [3.5–4.3]	4.1 [3.4–4.8]	5.4 [4.7–6.1]	5.9 [5.3–6.5]	5.6 [5.2–6.0]	<0.001
Oxygen therapy, <i>n</i> (%)	102 (63.7)	104 (67.1)	206 (65.4)	54 (56.8)	103 (68.2)	104 (73.8)	207 (70.9)	0.04
Intensive care unit, <i>n</i> (%)	10 (6.2)	25 (16.1)	35 (11.1)	10 (10.5)	24 (15.9)	17 (12.1)	41 (14.0)	0.47
Noninvasive ventilation, <i>n</i> (%)	10 (6.2)	25 (16.1)	35 (11.1)	10 (10.5)	24 (15.9)	16 (11.3)	40 (13.7)	0.55
Invasive ventilation, <i>n</i> (%)	3 (1.9)	2 (1.3)	5 (1.6)	2 (2.1)	5 (3.3)	6 (4.3)	11 (3.8)	^b
Extracorporeal circulation, <i>n</i> (%)	0 (0.0)	1 (0.6)	1 (0.3)	0 (0)	0 (0.0)	0 (0.0)	0 (0)	^b

^a*p* Value for the comparison between pre-COVID aggregated data, COVID data and post-COVID aggregated data using χ^2 test for categorical variables and Kruskal–Wallis test for continuous variables.

^bCondition of χ^2 test not met.

3.2 | Viral epidemiology

The frequency of PCR tests conducted on nasopharyngeal swabs or aspirates for virus detection notably increased since the COVID pandemic, with a rise from 51% in the pre-COVID era to 96% during COVID, and 95% post-COVID ($p < 0.001$), as illustrated in Table 2 and Figure 1. RSV has consistently been the predominant virus detected, with rates of 72% in the pre-COVID period and 74.7% during COVID. However, its prevalence surged significantly in the post-COVID period to 83.5% ($p=0.01$, Table 2). The progressive trend in the proportions of positive RSV PCR tests over the span of five winters is depicted in Figure 1.

The rhinovirus emerged as the second most frequently detected virus, yet no significant differences were observed between the three periods ($p=0.73$). Additionally, SARS-CoV-2 was detected in 12 patients during both the COVID and post-COVID periods, consistently in coinfection with at least one other virus.

3.3 | Comparison of patients characteristics based on RSV infection status

Patient characteristics based on their RSV status (positive vs. negative) were compared across the entire study cohort, including

TABLE 2 Temporal trends in PCR results for virus identification in infants hospitalized for acute bronchiolitis: A 5-year comparative analysis pre-, during-, and post-COVID eras.

	Pre-COVID period (2018–2020)			COVID period (2020–2021)	Post-COVID period (2021–2023)			p Value ^a
	2018–2019	2019–2020	2018–2020 aggregated data		2021–2022	2022–2023	2021–2023 aggregated data	
Number of infants, <i>n</i>	160	155	315	95	151	141	292	
Nasal PCR, <i>n</i> (%)	73 (45.6)	88 (56.8)	161 (51)	91 (96)	143 (94.7)	135 (95.7)	278 (95)	<0.001
Negative, <i>n</i> (%)	11 (15.1)	5 (5.7)	16 (9.9)	3 (3.3)	2 (1.4)	0 (0.0)	2 (0.7)	-
Respiratory Syncytial Virus, <i>n</i> (%)	49 (67.1)	67 (76.1)	116 (72.0)	68 (74.7)	117 (81.8)	115 (85.2)	232 (83.5)	0.01
Rhinovirus, <i>n</i> (%)	12 (16.4)	25 (28.4)	37 (23)	21 (23.1)	41 (28.7)	30 (22.2)	71 (25.5)	0.73
Adenovirus, <i>n</i> (%)	2 (2.7)	3 (3.4)	5 (3.1)	5 (5.5)	7 (4.9)	2 (1.5)	9 (3.2)	- ^b
Metapneumovirus, <i>n</i> (%)	4 (5.5)	4 (4.5)	8 (5)	8 (8.8)	6 (4.2)	7 (5.2)	13 (4.7)	- ^b
Influenzae A, <i>n</i> (%)	1 (1.4)	0 (0)	1 (0.6)	0 (0.0)	2 (1.4)	6 (4.4)	8 (2.9)	- ^b
Influenzae B, <i>n</i> (%)	2 (2.7)	0 (0)	2 (1.2)	0 (0.0)	0 (0)	2 (1.5)	2 (0.7)	- ^b
Parainfluenzae, <i>n</i> (%)	2 (2.7)	1 (1.1)	3 (1.9)	9 (9.9)	10 (7.0)	10 (7.4)	20 (7.2)	- ^b
Enterovirus, <i>n</i> (%)	1 (1.4)	4 (4.5)	5 (3.1)	1 (1.1)	11 (7.7)	7 (5.2)	18 (6.5)	- ^b
Bocavirus, <i>n</i> (%)	1 (1.4)	2 (2.3)	3 (1.9)	6 (6.6)	6 (4.2)	1 (0.7)	7 (2.5)	- ^b
Coronavirus 229E, <i>n</i> (%)	0 (0)	0 (0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.4)	- ^b
SARS-CoV-2, <i>n</i> (%)	0 (0)	0 (0)	0 (0.0)	3 (3.3)	3 (2.1)	6 (4.4)	9 (3.2)	- ^b

^ap Value for the comparison between pre-COVID aggregated data, COVID data and post-COVID aggregated data using χ^2 test for categorical variables.

^bCondition of χ^2 test not met.

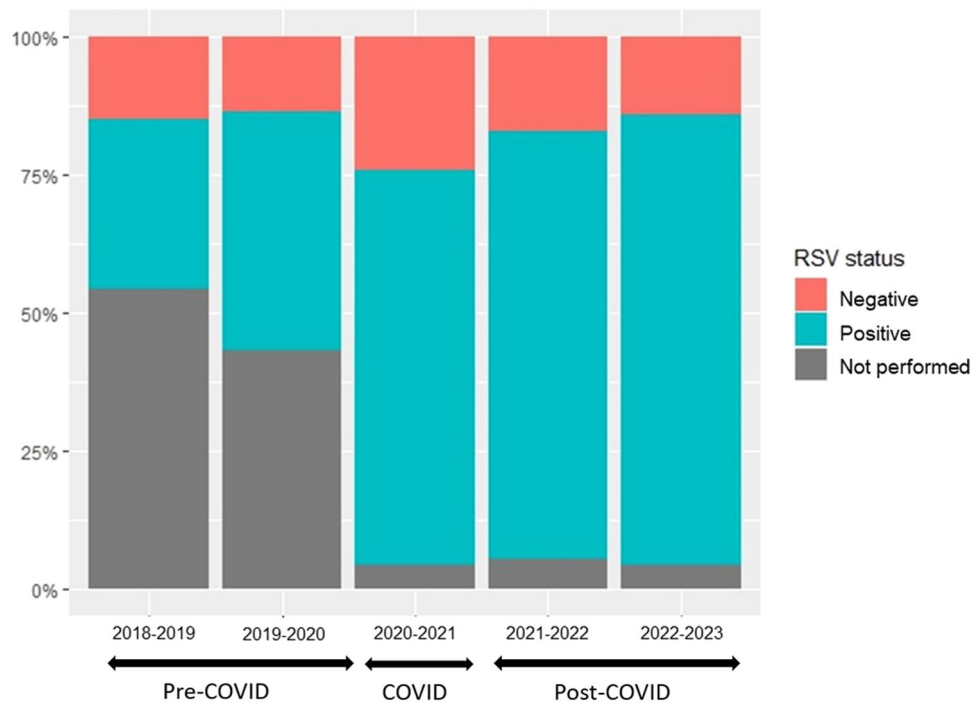
**FIGURE 1** Percent stacked bar chart illustrating the progressive trend in PCR test frequency and RSV positivity over time. PCR, polymerase chain reaction; RSV, respiratory syncytial virus. [Color figure can be viewed at [wileyonlinelibrary.com](https://onlinelibrary.wiley.com)]

TABLE 3 Comparative clinical characteristics of hospitalized infants with acute bronchiolitis stratified by RSV infection status over 5 years (2018–2023).

RSV infection status	RSV-positive group	RSV-negative group	p Value ^a
Number of infants, <i>n</i>	416	114	
Age (months): Mean [CI 95%]	2.6 [2.4–2.8]	3.1 [2.7–3.5]	0.005
Gender: Boys, <i>n</i> (%)	221 (53.1)	72 (63.2)	0.007
Comorbidities, <i>n</i> (%)	58 (10.9)	22 (4.1)	0.2
Weight (kg): Mean [CI 95%]	5.2 [5.0–5.4]	5.5 [5.2–5.8]	0.06
Evolution			
Length of hospitalization (days): Mean [CI 95%]	5.7 [5.3–6.1]	3.7 [3.1–4.3]	<0.001
Oxygen therapy, <i>n</i> (%)	322 (77.4)	54 (47.4)	<0.001
Intensive care unit, <i>n</i> (%)	77 (18.5)	7 (6.1)	0.002
Age [0–3] months, <i>n</i> (%)	69 (23.4)	6 (9.0)	0.02
Age [3, 6] months, <i>n</i> (%)	5 (6.3)	1 (2.7)	1
Age [6, 12] months, <i>n</i> (%)	3 (7.0)	0 (0.0)	1
Noninvasive ventilation, <i>n</i> (%)	76 (18.3)	7 (6.1)	0.003
Invasive ventilation, <i>n</i> (%)	15 (3.6)	3 (2.6)	0.77

Abbreviation: CI, confidence interval; RSV, respiratory syncytial virus.
^a*p* Value for the comparison between RSV-positive and RSV-negative groups using χ^2 and Fisher's exact tests for categorical variables, and Mann–Whitney test for continuous variables.

those who underwent nasal PCR testing on nasopharyngeal swabs or aspirates, as outlined in Table 3. Patients hospitalized with identified RSV exhibited a significantly longer duration of hospitalization of 5.7 days [95% CI: 5.3–6.1], compared to those with negative RSV results, who had a duration of 3.7 days [95% CI: 3.1–4.3] ($p < 0.001$) (Figure 2). Additionally, there was a notable increase in the proportion of patients who required oxygen therapy (77.4% vs. 47.4%, $p < 0.001$), were admitted to the ICU (18.5% vs. 6.1%, $p = 0.002$), and needed noninvasive ventilation (18.3% vs. 6.1%, $p = 0.003$) within the RSV-positive group compared to the RSV-negative group. Interestingly, RSV-positive patients appeared significantly younger than RSV-negative ones ($p = 0.005$).

4 | DISCUSSION

During the COVID-19 pandemic, there was a noticeable decrease in the number of infants requiring hospitalization for acute bronchiolitis, a trend previously noted by our team and others.^{6–10} However, in the post-COVID-19 period, the admission rate for acute bronchiolitis in our department rebounded to levels similar to those seen pre-

COVID-19. Notably, during this post-COVID-19 phase, both the duration of hospitalization and the frequency of oxygen therapy saw significant increases, indicating a heightened severity among hospitalized patients. Additionally, we observed a substantial surge in the prevalence of RSV during the post-COVID era, which was also associated with an increased severity.

The increase in severity observed in bronchiolitis cases post-COVID-19 aligns with findings from other studies worldwide.^{13–17} For example, Guitart et al. in Spain described a more severe bronchiolitis season in 2021 compared to the previous 10 years in terms of duration of hospitalization and necessity for pediatric ICU.¹⁵ Similarly, an Italian team compared patients hospitalized for acute bronchiolitis in the year after COVID-19 (2021–2022) to patients before and during the COVID-19 period.¹³ They also observed increased severity with more ICU admissions in the post-COVID period. Additionally, similar to our findings, this study indicated that patients with RSV bronchiolitis required more oxygen support, intensive care, and had a longer hospital stay compared to those with RSV-negative bronchiolitis throughout the entire study period. While many studies support the observation of increased bronchiolitis severity between the pre- and post-COVID periods, some indicate no significant difference.^{18–20} This suggests that, although a general trend of increased severity is noted, the impact may vary based on regional differences, healthcare systems, and study methodologies.

Potential explanations for the rebound in post-COVID-19 bronchiolitis include the cessation of preventive measures such as wearing masks and hand washing, along with an increase prevalence of RSV-naïve children.^{7,13,21,22} Children with bronchiolitis during 2021–2022 were born during the COVID-19 pandemic and, therefore, were potentially more protected against viruses. However, our study reveals that a year later, the peak of bronchiolitis remains high, despite these children being born after the SARS-CoV-2 pandemic period and thus being more exposed to pathogens. Further studies will be necessary to determine if the elevated peak of bronchiolitis persists in the years following the COVID-19 pandemic.

The higher incidence of RSV-bronchiolitis could potentially be attributed to viral genetic causes. During SARS-CoV-2 pandemic, Thielen et al. described a genetic lineage shift in RSV associated with an outbreak of severe RSV disease in Minnesota.²³ Another plausible explanation during the COVID-19 pandemic is the significant drop in air pollution associated with lockdown measures. This suggests that air pollution and climate factors may influence the transmission of RSV, as described in several studies.^{24–26} Further investigation is required to clarify these associations.

The escalating incidence of RSV bronchiolitis highlights the crucial need for prevention measures. Although preventive treatments are already available, they were until recently typically reserved for infants at the highest risk of severe RSV disease.^{27,28} However, new therapies, such as nirsevimab—a long-acting monoclonal antibody neutralizing RSV—are currently being developed for broader application. This innovative treatment has received approval

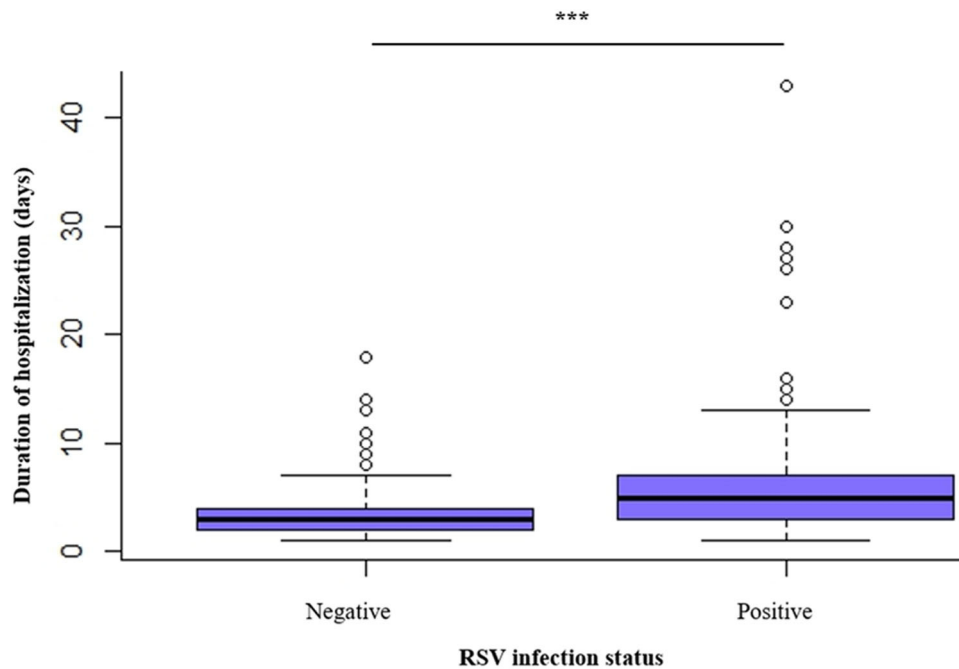


FIGURE 2 Boxplot comparison of hospitalization duration by RSV infection status. The central line is the median, the edges of the boxes are Q1 (25th percentile) and Q3 (75th percentile). The ends of the whiskers are the upper and lower adjacent values, which are the most extreme values within $Q3 + 1.5(Q3 - Q1)$ and $Q1 - 1.5(Q3 - Q1)$, respectively. All circles outside these whiskers represent outliers. $***p < 0.001$ for difference between the groups. RSV, respiratory syncytial virus. [Color figure can be viewed at wileyonlinelibrary.com]

and was initiated in France, as well as in the European Union, the United Kingdom, and the United States during the 2023–2024 winter.²⁹ Early real-world estimates from Spanish teams, following multicenter active surveillance in nine hospitals across three regions of Spain, have been published.³⁰ These estimates confirmed the effectiveness of nirsevimab (>70%) in preventing hospitalizations in infants with RSV-positive bronchiolitis.

Acknowledging study limitations, including its retrospective nature and single-center design, is crucial. Additionally, the increased frequency of PCR tests conducted on nasopharyngeal swabs or aspirates for virus detection since the COVID pandemic could introduce bias regarding the percentage of RSV detection. Despite these limitations, the study sheds light on the lingering effects of the COVID pandemic on respiratory health.

In conclusion, this study highlights a significant surge in the incidence of bronchiolitis 2 years after the COVID-19 pandemic. This increase is coupled with a prolonged duration of hospitalization and a heightened requirement for oxygen therapy compared to the pre-COVID-19 period. Importantly, there is a significant rise in the proportion of cases attributed to RSV during the post-COVID-19 period. These findings underscore the lingering impact of the pandemic on respiratory health, necessitating ongoing attention and further investigation into the evolving dynamics of bronchiolitis in the post-COVID era. The implementation of preventive measures such as nirsevimab is greatly welcomed to mitigate the burden of respiratory illnesses in vulnerable populations.

AUTHOR CONTRIBUTIONS

Victorine Boccard, Blandine Prevost, and Harriet Corvol conceptualized and designed the study, collected the data, drafted the initial manuscript, and reviewed and revised the manuscript. Blandine Prevost carried out the statistical analyses. Sophie Denamur, Elora Peulier-Maitre, and Nadia Nathan participated in the study conceptualization, the data collection; and critically revised the manuscript. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ETHICS STATEMENT

The study was approved by the institutional review board of the French Society for Respiratory Medicine (Société de Pneumologie de Langue Française, #CEPRO_2020-080). In accordance with French laws for observational studies, the requirement for written informed consent was waived (study BronChioVID N°20201119185601).

ORCID

Nadia Nathan  <http://orcid.org/0000-0001-5149-7975>

Harriet Corvol  <http://orcid.org/0000-0002-7026-7523>

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How to cite this article: Boccard V, Prevost B, Denamur S, Peulier-Maitre E, Nathan N, Corvol H. Bronchiolitis: increased severity in the post-COVID-19 era. *Pediatr Pulmonol*. 2024; 1-7. doi:10.1002/ppul.27172