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ORIGINAL RESEARCH

Impact of Nirsevimab on Pediatric RSV-Related Lower Respiratory Tract Infections: A Retrospective Pre–Post Observational Study in Tuscany, Italy

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ABSTRACT

Introduction: Respiratory syncytial virus (RSV) is the leading cause of respiratory infections and hospitalization among infants and a major burden on pediatric emergency department (EDs). Nirsevimab has recently been introduced for universal use in all infants entering their first RSV season. However, real-world data on its public health impact are still limited, particularly regarding attendances at pediatric ED.

Methods: We conducted a retrospective, observational, pre–post intervention study at the Meyer Children's Hospital (Tuscany, Italy). The 2024–25 RSV season, when nirsevimab was firstly implemented, was compared with the three preceding seasons. ED attendances, hospitalization, and pediatric intensive care unit (PICU) admissions for lower respiratory tract infections (LRTIs) of any etiology were analyzed.

Results: During the 2024–25 season, overall ED attendances for LRTIs, regardless of etiology, decreased by 67.3%. Hospital admissions for LRTIs dropped by 64.7%, and PICU admissions by 86.2%. RSV-confirmed LRTIs declined by 96.5%.

Conclusions: Universal nirsevimab prophylaxis markedly reduced the burden of respiratory infections in eligible infants, leading to a significant reduction in the use of healthcare resources, including ED visits, hospitalization, and PICU admissions.

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PLAIN LANGUAGE SUMMARY

Respiratory syncytial virus is a common virus that infects the lungs and airways. It is the main cause of serious breathing problems and hospital admissions in babies. These infections also create a heavy workload for pediatric emergency departments. Respiratory syncytial

virus infection season may commonly run from October to April. Nirsevimab is a long-acting preventive antibody that helps protect babies from severe respiratory syncytial virus disease. In Italy, healthcare services started giving nirsevimab to babies entering their first respiratory syncytial virus season during the 2024–25 season. We studied the real-world impact of this prevention strategy at Meyer Children's Hospital in Tuscany, Italy. We compared the 2024–25 respiratory syncytial virus season with the three previous seasons. We analyzed visits to the pediatric emergency department, hospital admissions, and intensive care admissions for lower respiratory tract infections, both when respiratory syncytial virus was confirmed and when the cause of infection was not confirmed. After the introduction of nirsevimab, visits to the emergency department for lower respiratory tract infections dropped by more than two-thirds. Hospital admissions for these infections fell sharply, and intensive care admissions decreased by more than 80%. Confirmed respiratory syncytial virus lower respiratory tract infections almost disappeared. These findings show that protecting eligible babies with nirsevimab greatly reduced serious respiratory infections and eased pressure on hospitals and emergency departments.

Keywords: Lower respiratory tract infections; Nirsevimab; Pediatric respiratory infections; Public health impact; Respiratory syncytial virus

Key Summary Points

Why carry out this study?

Respiratory syncytial virus causes a high burden of pediatric emergency department use and hospitalizations, and real-world data on the public health impact of nirsevimab, especially from emergency department settings, remain limited.

This study assessed whether universal nirsevimab immunization reduced emergency department visits due to lower respiratory tract infections in infants.

What was learned from the study?

After implementation of nirsevimab, emergency department visits for lower respiratory tract infections decreased by 67.3%, and laboratory-confirmed respiratory syncytial virus lower respiratory tract infections decreased by 96.5%.

Universal nirsevimab prophylaxis markedly reduced the burden of respiratory infections in eligible infants and led to a substantial reduction in healthcare resource use, including emergency department visits, hospitalizations, and pediatric intensive care unit admissions.

INTRODUCTION

Respiratory tract infections—including lower respiratory tract infections (LRTIs)—remain a leading cause of emergency department (ED) visits and hospitalization among infants and young children worldwide. The burden is greatest during the first year of life [1, 2].

Nirsevimab (Beyfortus), an extended half-life human monoclonal antibody, approved by several regulatory agencies, is designed to provide passive protection against respiratory syncytial virus (RSV) in all infants entering their first RSV season [3]. In a recent meta-analysis [4] nirsevimab demonstrated high effectiveness and public health impact, reducing RSV-related hospitalization by 83% [4].

Nirsevimab has the potential to reduce pediatric emergency department visits and the associated healthcare costs. However, while modeling studies are available [5, 6] real-world data from ED settings remain limited [7, 8], highlighting the need to assess the public health impact of nirsevimab across multiple clinical outcomes.

The aim of the study was to evaluate the public health impact of nirsevimab utilization on ED visits due to LRTIs ending in hospital admissions

(either in pediatric wards or pediatric intensive care unit, PICU) or in home discharges to generate data to inform policymakers and clinicians and to support future decisions on nirsevimab prophylaxis.

METHODS

Definitions

For the purposes of this study, an LRTI were defined as any diagnosis included in the lists reported in Table 1.

A case of bronchiolitis or pneumonia was defined as RSV-related if a laboratory report confirming RSV positivity was available before the patient's discharge from the ED. In such cases, the discharge diagnosis was coded respectively as ICD-9 466.11 ("Acute bronchiolitis due to RSV") or as ICD9 480.1 ("Pneumonia due to RSV").

A bronchiolitis or pneumonia case was classified as having an unspecified etiology if no laboratory test was performed or if the laboratory report became available only after the child's discharge from the ED. In these cases, the discharge code was respectively ICD-9 466.19 or 486. These cases without laboratory confirmation may include both RSV-related LRTI and LRTI caused by other respiratory pathogens.

Analytic subgroups were defined a priori based on clinical presentation, RSV laboratory testing, and availability of test results at the time of ED discharge. A schematic overview of subgroup definitions is provided in Table 2

In the event of repeated visits to the ED for the same child within a period of 10 days, only the first visit was considered.

Following evaluation in the ED, LRTI-related visits were classified according to patient disposition into two mutually exclusive outcome categories: "hospital admission", defined as transfer from the ED to a pediatric ward or to the PICU, and "ED discharge home", defined as discharge directly from the ED without subsequent inpatient hospitalization. These outcomes were analyzed separately to distinguish changes in disease burden requiring inpatient care from those managed exclusively at the ED level.

On the basis of our previous reports of RSV seasonality in Tuscany [5, 9] and on the admissions data from our hospital shown in Fig. 1, the RSV season was defined as lasting from October 1 to April 30, encompassing 7 months each year. In fact, these reports showed how RSV cases may occur also in October and April, due to early start and/or later end of RSV circulation.

Table 1 ICD-9-CM codes applied for the classification of LRTIs in children

ICD-9-CM	Diagnosis description
466	Acute bronchitis
466.11	Acute bronchiolitis due to RSV*
466.19	Acute bronchiolitis of unspecified etiology
480.1	Pneumonia due to RSV*
485	Bronchopneumonia, organism unspecified
486	Pneumonia, organism unspecified

ICD-9-CM International Classification of Diseases, Ninth Revision, Clinical Modification, *LRTI* lower respiratory tract infection, *RSV* respiratory syncytial virus

*Laboratory-confirmed RSV

Nirsevimab Immunization

Nirsevimab was first introduced in Italy at the end of October 2024. The immunization program was organized on a regional basis. In Tuscany, an extended strategy was implemented, and nirsevimab was offered free of charge to all infants during their first RSV season, specifically those born between April 1, 2024 and March 31, 2025 (target cohort).

As nirsevimab became available only at the end of October 2024, infants born between November 1, 2024 and March 31, 2025 were immunized in maternity wards before discharge, preferably on the second day of life. In contrast, infants born between April 1 and October 31, 2024 were immunized by their primary care pediatricians as soon as possible after October 28. During the first RSV immunization

Table 2 Definition of analytic subgroups included in the study

Analytic group	Clinical definition	RSV laboratory testing	Operational definition in the study
LRTI—RSV-confirmed	Lower respiratory tract infection (bronchiolitis or pneumonia)	Positive RSV molecular test	ED visits or hospitalizations for LRTI with laboratory-confirmed RSV infection
LRTI—not microbiologically attributable at discharge	Lower respiratory tract infection (bronchiolitis or pneumonia)	RSV test performed, but result not yet available at the time of ED discharge	LRTI episodes coded using ICD-9-CM diagnosis codes without RSV attribution at discharge; these cases may include RSV-related infections and LRTI caused by other pathogens
Bronchiolitis—RSV-confirmed	Bronchiolitis	Positive RSV molecular test	ED visits or hospitalizations for bronchiolitis with laboratory-confirmed RSV infection
Bronchiolitis—not microbiologically attributable at discharge	Bronchiolitis	RSV test performed, but result not yet available at the time of ED discharge	Bronchiolitis episodes coded without RSV attribution at discharge
Control group	Children not eligible for nirsevimab prophylaxis	Not applicable	Children who had already experienced at least one RSV season prior to the study season and were evaluated during their subsequent RSV season, matched by age range but not eligible for nirsevimab

ED emergency department, *LRTI* lower respiratory tract infection, *RSV* respiratory syncytial virus

campaign, nirsevimab coverage reached 87.8% of the target population [10].

Study Design

We conducted this retrospective, observational, pre–post intervention study at the ED of the Meyer Children's Hospital, the only tertiary pediatric hospital in Tuscany. This pediatric referral center records an average of 21,061 live births per year (2022–2024). It admits the most severe and complex pediatric cases and is the only pediatric hospital in the region equipped with a PICU. In addition to its regional referral role, Meyer Children's Hospital IRCCS also contributes to pediatric healthcare delivery for the City of Florence (average 2259 live births per year, 2022–2024) and for the surrounding municipalities of the Province of Florence (average 5580 live births per year, 2022–2024), together with three other secondary-level hospitals providing pediatric inpatient care. During the four RSV seasons included in the analysis (2021/22–2024/25), the ED recorded a mean of 24,271 visits per season (range 22,834–26,431).

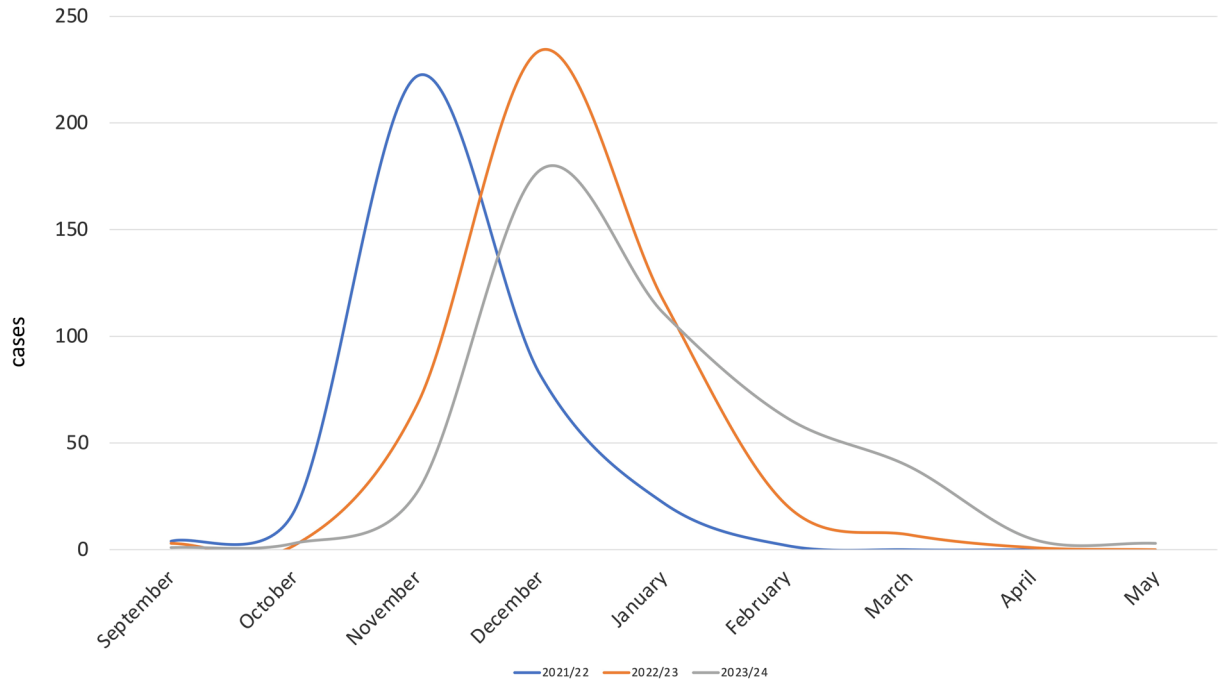

Fig. 1 Monthly distribution of RSV-related hospitalizations over three consecutive pre-intervention RSV seasons among pediatric patients of all ages (0–16 years). *RSV* respiratory syncytial virus

The study aimed to assess the public health impact of nirsevimab prophylaxis in terms of the reduction of ED visits, hospital admissions, and home discharges for LRTIs (particularly bronchiolitis), regardless of etiology, as well as for laboratory-confirmed RSV-related LRTIs. A secondary aim was to evaluate PICU admissions. Four RSV seasons (2021/22–2024/25) were evaluated. For the 2024/25 RSV season, outcomes were evaluated in children born between April 1, 2024 and March 31, 2025, who were hospitalized between October 1, 2024 and April 30, 2025, corresponding to their first RSV season. The same approach was applied to the three preceding RSV seasons, with each season's birth cohort defined as children born between April 1 and March 31 of the following year, and outcomes assessed during the corresponding RSV epidemic period (October 1–April 30).

The study population is an open cohort, predominantly composed of infants residing in the Tuscany region and presenting to the Meyer Children's Hospital during the study period. Infants entering their first RSV season were included each year, regardless of prior attendance, reflecting real-world healthcare utilization rather than a fixed closed cohort.

To avoid potential bias associated with milder RSV seasons, we evaluated the same outcomes (ED visits, hospitalization, and intensive care unit admissions) among children who were not eligible according to age.

Statistical Analysis

For pre-intervention seasons, mean annual counts of ED visits, hospital admissions either in pediatric wards or in PICU, and home discharges were calculated. Rate ratios (RR) and 95% confidence intervals (CI) were estimated using log-linear Poisson regression models for count data. In cases where no events occurred during the intervention season, a continuity correction of 0.5 was applied before calculating adjusted RR, CI, and *p* values. Percentage reductions were computed as $(1 - RR) \times 100$. Statistical significance was assessed using the exact conditional Poisson test, with two-sided tests applied throughout.

RSV Testing Policy and Laboratory Methods

At the Meyer Children's Hospital, infants presenting to the ED with a clinical diagnosis of LRTI are routinely tested for respiratory viruses including RSV. Respiratory specimens are collected at presentation and processed in the hospital's laboratory.

RSV detection was performed using the Allplex™ Respiratory Panel 1 (Seegene Inc., CE-IVD marked), a multiplex real-time reverse transcription polymerase chain reaction (RT-PCR) assay capable of detecting influenza A, influenza B, RSV A and RSV B targets within a single reaction. The assay is run on a CFX96™ Real-Time PCR System (Bio-Rad) according to the manufacturer's instructions and includes an internal control (bacteriophage MS2) to monitor the efficiency of nucleic acid extraction and amplification. Amplification was interpreted using Seegene Viewer software v2.0, and a sample was defined as positive for RSV if amplification occurred with a cycle threshold (Ct) value < 42 within 45 PCR cycles.

The Allplex™ Respiratory Panel 1 assay has been evaluated in clinical studies demonstrating high sensitivity for RSV detection (~ 95.2%) and specificity (~ 100%), making it suitable for routine clinical and surveillance testing [11].

Ethical Approval

This study was conducted in accordance with the principles of the Declaration of Helsinki. This retrospective observational study was approved by the Tuscany Region Ethics Committee (approval no. 285-2021). This retrospective, non-interventional observational study was conducted at AOU Meyer IRCCS under the provisions of Article 110-bis of Legislative Decree 101/2018 and Article 9(2)(j) of the EU General Data Protection Regulation (Regulation EU 2016/679).

RESULTS

In the three pre-intervention RSV seasons (2021/22, 2022/23, and 2023/24) and in the post-intervention season (2024/25, with nirsevimab administration), a total of 2333 ED visits for respiratory diseases listed in Table 1 were recorded in children born between April and March of the following year and experiencing their first RSV season (617, 740, 659, and 317 cases, respectively). Of these, 521 (22.3%) were born between November and March, while 1812 (77.7%) were born before the RSV season (April–October).

Visits to the Pediatric ED

In the three pre-intervention RSV seasons, an average of 395 LRTIs were observed each season (349, 456, and 380 cases) compared with 129 cases in 2024/25. This corresponded to a 67.3% reduction (95% CI 60.8–72.8%; RR 0.33; $p < 0.0001$) (Fig. 2).

In the 2024/25 season, the LRTI rate declined to 5.65 per 1000 ED visits (129 LRTI over 22,834 visits). This corresponded to a 65% reduction in LRTI rates compared with the pre-intervention period (RR 0.35; 95% CI 0.29–0.42; $p < 0.0001$), confirming a statistically significant decrease consistent with the reduction observed in absolute LRTI counts.

When stratified by month of birth (April–July, August–October, November–March), the reduction in LRTI cases remained significant across all subgroups (Table 3).

Infants born between April and October accounted for 76.1% of all hospitalization due to LRTI in the pre-intervention seasons, and this proportion remained unchanged in 2024/25 (74.4%). For RSV-confirmed LRTI, 119 ED visits were reported in the three pre-intervention years (respectively 45, 32, and 42; mean 39.7 per year) compared with 1 visit in 2024/25, corresponding to a 97.5% reduction (95% CI 83.2–99.7%; RR 0.025; $p < 0.0001$) (Fig. 2).

Actually, a total of 1078 ED visits for bronchiolitis of any etiology (discharge code ICD9: 466.19 or 466.11) were registered in the three pre-intervention years (respectively 325, 416, and 337; mean 359 per year), compared with 106 in 2024/25. Therefore, the overall reduction in bronchiolitis cases of any etiology was 70.5% (95% CI 64.0–75.8%; RR 0.29; $p < 0.0001$).

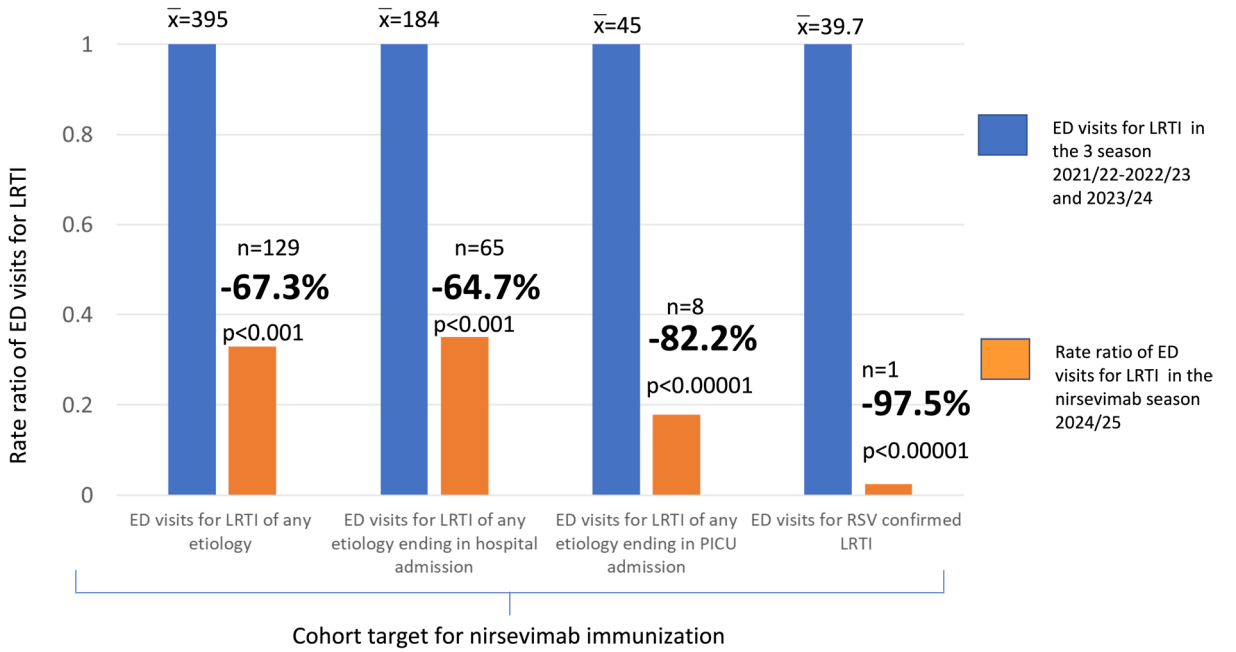

Fig. 2 Impact of nirsevimab on different outcomes associated with LRTI in the intervention season (2024/25) and in the 3 previous seasons. When LRTI rates were calculated using the total number of ED visits as the denominator, the three pre-intervention RSV seasons showed a combined rate of 16.0 LRTI per 1000 ED visits (1185 LRTI over 74,251 visits). *ED* emergency department, *LRTI* lower respiratory tract infection, *PICU* pediatric intensive care unit, $\bar{x}$ mean (average), *RSV* respiratory syncytial virus

Table 3 Emergency department visits for LRTI by month of birth and RSV season

Month of birth	2021/22	2022/23	2023/24	Mean annual cases (pre-intervention)	2024/25	Reduction (%)	RR	95% CI	*p* value
April–July	111	169	104	128.0	49	61.7%	0.38	0.29–0.52	< 0.0001
August–October	194	182	142	172.7	47	72.8%	0.27	0.20–0.37	< 0.0001
November–March	44	105	135	94.3	33	65.0%	0.35	0.24–0.50	< 0.0001

Reduction calculated as (1 – RR) × 100. Rate ratios were estimated using Poisson regression models comparing the 2024/25 season with the mean of the three pre-intervention seasons

CI confidence interval, *LRTI* lower respiratory tract infection, *RR* rate ratio, *RSV* respiratory syncytial virus

For RSV-confirmed bronchiolitis, 118 ED visits were reported in the three pre-intervention seasons (mean 39.3 per year) versus 1 in 2024/25, corresponding to a 97.5% reduction (95% CI 96.7–98.1%; RR 0.03; $p < 0.00001$.

Hospital and PICU Admission

Hospital admissions following ED visits for LRTI decreased from an average of 184 per year in the pre-intervention seasons to 65 in 2024/25,

representing a 64.7% reduction. Similarly, ED visits for LRTI ending in discharge home decreased from an average of 211 per year to 61, representing a 71.1% reduction. For RSV-confirmed LRTI, hospital admissions declined from a mean of 28.3 per season to a single case in 2024/25, corresponding to a 96.5% reduction. Likewise, home discharges for RSV-confirmed LRTI decreased from a mean of 11.3 per season to zero, representing a 95.6% reduction. Detailed results are presented in Table 4.

A focused analysis of bronchiolitis cases revealed that hospital admissions for bronchiolitis of any etiology decreased from 489 over 3 years (mean 163 per season) to 57 in 2024/25, representing a 65.0% reduction (95% CI 54.0–73.4%; RR 0.35; $p<0.0001$). Similarly, home discharges declined from 572 cases (mean 190.7) to 49 in 2024/25, representing a 74.3% reduction (95% CI 65.6–80.8%; RR 0.26; $p<0.0001$).

As expected, RSV-confirmed bronchiolitis showed more marked decreases: hospital admissions dropped from 84 over 3 years (mean 28) to 1 in 2024/25, representing a 96.4% reduction (95% CI 74.3–99.5%; RR 0.04; $p<0.001$); similarly, 34 children were discharged home in the pre-intervention seasons (mean 11.3 per season), whereas none were discharged in 2024–25, representing a 95.6% reduction (95% CI 28.8%–99.7%; RR 0.04; $p=0.028$).

To ensure that differences in the number of admitted patients across seasons were not due to nonclinical factors, such as changes in hospital admission policies from the ED, we assessed the proportion of children admitted out of the total number presenting to the ED for LRTIs. The proportion of children presenting with LRTIs who were subsequently admitted to hospital was similar in the pre- and post-intervention seasons, averaging 47.0% across the three pre-intervention seasons and 50.0% in the 2024–2025 season.

Patients admitted to the PICU because of LRTI either directly from the ED or after hospitalization in a pediatric ward of any etiology decreased by 86.2% (95% CI 65.1–94.6%; $p<0.001$), from an average of 36.3 per year in the pre-intervention seasons to 5 in 2024–2025. PICU admissions per 1000 ED visits decreased from 1.47 in pre-intervention seasons (mean of 2021–22, 2022–23, 2023–24) to 0.22 in 2024–25 (~85% reduction; $p<0.001$), confirming a significant decline even accounting for the decrease in overall ED visits.

Controls

To account for potential confounding factors, i.e., differences in RSV season severity, we analyzed outcomes in a control cohort composed of children not eligible for nirsevimab

Table 4 LRTI-related and RSV-confirmed LRTI-related outcomes by RSV season

Outcome	2021/22	2022/23	2023/24	2024/25	Point estimate (RR)	Reduction (%)	*p* value
LRTI—hospital admissions	188	194	170	65	0.35	64.7%	< 0.001
LRTI—ED discharge home	161	262	210	61	0.29	71.1%	< 0.001
RSV-confirmed LRTI—hospital admissions	33	21	31	1	0.04	96.5%	< 0.001
RSV-confirmed LRTI—ED discharge home	12	11	11	0	0.04	95.6%	< 0.05

CI confidence interval, *ED* emergency department, *LRTI* lower respiratory tract infection, *RR* rate ratio, *RSV* respiratory syncytial virus

immunization. This group included children who had already experienced one RSV season (or part of it) earlier in life and who therefore presented to the ED for LRTI or bronchiolitis during their second RSV season.

Specifically, for the 2024/25 RSV season, the control cohort comprised children born between April 1, 2023 and March 31, 2024. At the time of ED presentation for LRTI during the 2024/25 season, their age ranged from 184 days (children born on March 31, 2024 and presenting to the ED for LRTI on October 1, 2024) to 730 days (children born on April 1, 2023 and presenting on March 31, 2025).

An analogous approach was applied to the three preceding RSV seasons, using the same birth cohort definition, age range, and outcome definitions. This strategy ensured that the control population was as close in age as possible to the nirsevimab-eligible cohort, while remaining clearly non-eligible for immunization, thereby reducing potential age-related confounding and strengthening causal inference regarding the impact of nirsevimab on LRTI-related healthcare utilization.

In the control cohort, ED visits for LRTI (286 events) and bronchiolitis (97 events) during the season 2024/25 were comparable to the mean of the three preceding years (288.7 and 103.3 events, respectively). The RR was 0.99 for LRTI (95% CI − 13.2% to + 13.2%; p = ns) and 0.94 for bronchiolitis (6.1% reduction; 95% CI − 23.9% to + 38.8%; p = ns).

DISCUSSION

This is the first study conducted in Italy to assess the public health impact of RSV prevention with nirsevimab on pediatric ED visits for LRTI of any etiology, as well as on subsequent hospitalization. The analyses, which did not depend on virological tests, confirm the relevant public health impact of nirsevimab with a marked reduction of these outcomes among children within the target age group for RSV prevention.

The public health impact observed in our study (− 65% for hospitalization for LRTI of any etiology and − 85% for admissions to PICU) appears greater than that reported in previous studies [12, 13], where the reduction in hospitalization was approximately 50%.

As expected, given the age of the patients included in this study, bronchiolitis accounted for the majority of LRTI cases and the decrease in attendances was primarily driven by a decline in bronchiolitis cases.

The higher public health impact found in our setting does not seem to be explained by differences in the proportion of children hospitalized among those attending the ED, that is 46.5% in our study vs. 54% in the French study [13]. Rather, it is more likely attributable to the higher immunization coverage achieved in Tuscany, where an overall uptake rate of 87.8% was achieved.

There is still ongoing debate in countries that have introduced or are about to introduce nirsevimab immunization regarding the optimal target population to be included in the program. Some have chosen to immunize only infants born during the RSV season, while others have opted to extend prophylaxis to all infants experiencing their first RSV season.

In the 2024/25 season, the first in which nirsevimab became available in Italy, the 20 Italian regions adopted heterogeneous implementation strategies. Although all regions offered immunization to infants born up to March 31, 2025, the starting point of the target birth cohort varied widely: four regions offered immunization to all infants born since January 2024, four from April, three from July, two from August, one from September, and six only to those born between November and March (Fig. 3) [14].

In our study, when outcomes were analyzed according to birth period (infants born between November and March versus those born between April and October), higher numbers were consistently observed among children born before the RSV season across all outcomes. This finding was not unexpected, as infants born before the season are exposed to the entire RSV circulation period, whereas those born during the season—although younger and therefore more vulnerable—are exposed to only part of it. Consistent with our results, studies conducted in other countries

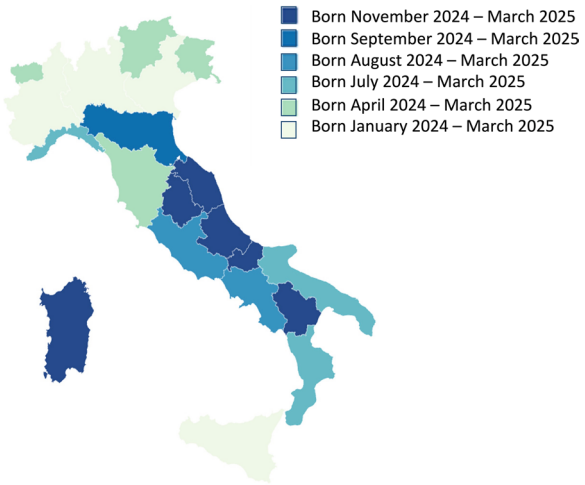

Fig. 3 Cohorts of infants included in nirsevimab immunization across different Italian regions during the 2024–2025 RSV season, the first in which the antibody was available in Italy. *RSV* respiratory syncytial virus

[15–17] have also shown, albeit with varying proportions, that most hospitalization and PICU admissions occur among infants born before the RSV season. These findings suggest that a strategy offering immunization only to a subset of infants facing their first RSV season, rather than to all of them, would markedly reduce the overall impact of the immunization program.

In our study, we deliberately examined a 7-month RSV season, from 1 October to 30 April, to avoid missing early or late RSV cases, in contrast with other studies adopting shorter surveillance periods. By extending the observation window to include April, we intentionally tested the effectiveness of nirsevimab beyond its expected 6-month duration of protection. Moreover, the 2024–25 season was analyzed starting from 1 October, although in Tuscany the administration of nirsevimab commenced between late October and early November. Compared with studies adopting shorter observation periods, these factors may have contributed to a lower estimated impact of nirsevimab.

The main limitation of this study is that it is based on a single-center cohort. On the other hand, this aspect may also be considered an advantage, as the hospital represents the only tertiary care center in the entire Tuscany region and the only one with a PICU. This ensures sample homogeneity and reduces potential biases commonly associated with multicenter studies, such as selection biases, differences in hospitalization practices, variations in coding of respiratory conditions as described by Payne et al. [18], disparities in diagnostic technologies, and unequal access to these technologies over the years.

However, the use of aggregated administrative data based on ICD-9-CM discharge codes precluded stratification by individual clinical risk factors such as prematurity, congenital heart disease, or other comorbidities, as well as the assessment of prior palivizumab prophylaxis. However, long-term pre-nirsevimab epidemiological data from the same institution show that prematurity accounted for approximately 16% of RSV-related hospitalizations, congenital heart disease for 5.5%, and that among infants younger than 1 year of age the overall prevalence of comorbidities (including prematurity) was slightly above 25% [19].

In addition, the Meyer Children's Hospital has been a long-standing institution (founded in 1884), and no new hospitals were opened in the Tuscany region during the study period (2021–2025). Furthermore, there were no legislative or regulatory changes affecting the social security system that could have influenced hospital attendance patterns during this time.

Another limitation is that all analyses relied on discharge diagnoses from the ED, which may be subject to misclassification. Moreover, the analyses did not account for potential comorbidities that could have influenced clinical decisions regarding hospitalization of children presenting to the ED.

An important consideration in communicating with families is that nirsevimab does not confer complete protection against all LRTI or bronchiolitis cases. In our study, while the reduction in emergency visits for LRTI of any etiology was approximately 65%, the reduction in RSV-confirmed cases exceeded 95%. This clearly indicates that a small proportion of infections continues to occur as a result of other viral pathogens.

Clear and accurate communication with both healthcare providers and parents is therefore

essential to contextualize these residual cases, preventing them from being misconstrued as failures of the prophylaxis. Such an approach helps maintain confidence in immunization programs overall and supports informed decision-making regarding preventive interventions.

CONCLUSIONS

Universal nirsevimab prophylaxis markedly reduced the burden of LRTI in eligible infants, leading to a significant reduction in the use of healthcare resources, including ED visits, hospitalization, and PICU admissions.

Author Contributions. Francesco Nieddu and Chiara Azzari drafted the manuscript. Marta Verzieri, Marina Vignoli, Valeria Astorino, Silvia Boscia, Francesca Di Berardino, Francesca Figlioli and Laura Pisano collected and curated the data. Francesco Nieddu, Marta Verzieri, Silvia Ricci, Lorenzo Lodi, Valentina Guarnieri, Stefano Masi, Giuseppe Indolfi, Chiara Azzari, and Maria Moriondo contributed to the conception and design of the study. Marta Verzieri, Silvia Boscia, and Chiara Azzari performed the statistical analyses. Francesco Nieddu, Marta Verzieri, Silvia Boscia, Maria Moriondo and Chiara Azzari coordinated the study and oversaw data quality. All authors contributed to the interpretation of the results, critically revised the manuscript for intellectual content, and approved the final version.

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Data Availability. The datasets analyzed during the current study are available from the corresponding author on request.

Declarations

Conflict of Interest. Chiara Azzari has received research grants and/or scientific consulting fees for having participated at advisory board and/or sponsored symposia from AstraZeneca, GSK, Merck, Moderna, Sanofi and Pfizer. Francesco Nieddu, Marta Verzieri, Marina Vignoli, Valeria Astorino, Silvia Boscia, Laura Pisano, Silvia Ricci, Lorenzo Lodi, Valentina Guarnieri, Francesca Di Berardino, Francesca Figlioli, Stefano Masi, Giuseppe Indolfi, Maria Moriondo declare no conflicts of interest.

Ethical Approval. This study was conducted in accordance with the principles of the Declaration of Helsinki. This retrospective observational study was approved by the Tuscany Region Ethics Committee (approval no. 285-2021). This retrospective, non-interventional observational study was conducted at AOU Meyer IRCCS under the provisions of Article 110-bis of Legislative Decree 101/2018 and Article 9(2)(j) of the EU General Data Protection Regulation (Regulation EU 2016/679).

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