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Nirsevimab and a Community Recall-Based Immunization Strategy for Child Bronchiolitis Prevention

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Introduction

Respiratory syncytial virus (RSV) is a leading cause of infant bronchiolitis and seasonal health care burden.[1,2] Although nirsevimab effectively prevents RSV-confirmed disease, its community impact in primary care is less defined.[3,4] We examined the association of a nirsevimab recall-based immunization strategy with the incidence of clinically diagnosed all-cause bronchiolitis in an Italian community pediatric practice during the 2024-2025 RSV season.

Methods

This retrospective, 1:1, nested matched cohort study used data from Italian family pediatricians practicing in the Pedianet Network (eAppendix 1 in Supplement 1). The study and database access were approved by the Internal Scientific Committee of Società Servizi Telematici Srl. Written informed consent was obtained from participants' legal guardians or next of kin. The study followed the STROBE reporting guideline for cohort studies.

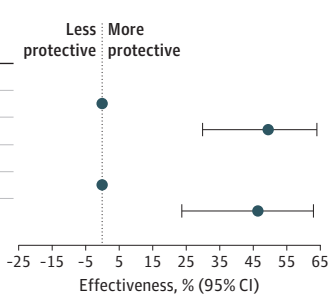
We included children born between January 1 and August 31, 2024, in the Veneto or Emilia-Romagna regions. In October 2024, Veneto implemented a recall-based nirsevimab campaign for infants born since January 1, 2024 (coverage >80%), whereas Emilia-Romagna limited immunization to infants born from September 1, 2024, onward (eAppendix 2 in the Supplement 1). Follow-up was from mid-October 2024 to April 30, 2025, or until loss to follow-up.

Nirsevimab exposure was identified using Anatomical Therapeutic Chemical code J06BD08 and free text in the vaccination registry. Clinical bronchiolitis was identified using a validated Pedianet text classification algorithm based on diagnostic records and *International Classification of Diseases, Ninth Revision, Clinical Modification* codes (eAppendix 3 in Supplement 1).

Infants were matched 1:1 using age-stratified propensity scores (within a caliper width of 0.02), pairing immunized with nonimmunized infants within the week after the matching date. Propensity scores were estimated using logistic regression among children in Veneto, adjusting for sex, prior

Figure 1. Forest Plot of Nirsevimab Protection Associated With Bronchiolitis by As-Treated and Per-Protocol Analyses in Infants

Comparison group	Infants, No. (%)	Bronchiolitis episodes, infants, No. (%)	Effectiveness, % (95% CI)
As-treated			
No immunization	3132 (50)	115 (3.7)	0 [Reference]
Nirsevimab	3132 (50)	67 (2.1)	48 (29-62)
Per-protocol			
No immunization	1565 (50)	103 (6.6)	0 [Reference]
Nirsevimab	1565 (50)	70 (4.5)	45 (23-61)



The as-treated analysis included censored matched pairs when the control group received nirsevimab. The per-protocol analysis excluded pairs in which the control group received nirsevimab. Models were adjusted for propensity score, age (in months) at matching, and bronchiolitis episodes before matching.

+ Supplemental content

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bronchiolitis diagnoses, antibiotic use, and family pediatrician visits before follow-up as proxies for morbidity and then applied to children in Emilia-Romagna. Overlap between groups was assessed by examining propensity score distributions before matching (eFigure in Supplement 1). Cox proportional hazards models stratified by matched pairs estimated hazard ratios with time 0 as the matching date; results are expressed as 1 minus the hazard ratio, then multiplied by 100. Analyses were conducted under both as-treated and per-protocol frameworks, with stratification by age at matching (0-3, 4-6, and >6 months). Analyses were performed using SAS, version 9.4 (SAS Institute Inc) and Python, version 3.10.8 (Python Software Foundation).

Results

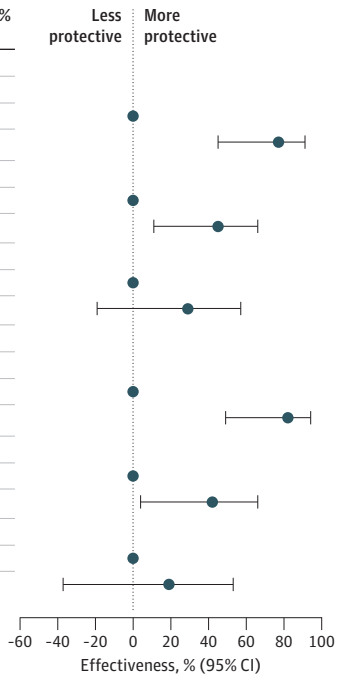
A total of 4900 infants were included. Before matching, immunized vs nonimmunized infants were younger (aged 2-3 months, 891 [28.4%] vs 362 [20.5%]), had higher health care use (number of visits ≥5 before the start of follow-up, 1944 [62.0%] vs 974 [55.2%]), and had a greater history of bronchiolitis (≥1 bronchiolitis diagnosis before start of follow-up, 270 [8.6%] vs 106 [6.0%]). Overall, 3132 immunized infants (median [IQR] age, 6.3 [4.1-8.5] months; 1536 female [49.0%] and 1596 male [51.0%]) were matched 1:1 with nonimmunized infants (median [IQR] age, 6.3 [4.2-8.5] years; 1577 female [50.4%] and 1555 male [49.7%]), with good balance (all standardized mean differences <0.05).

In the as-treated analysis, median (IQR) follow-up was 61 (12-164) days in immunized and 42 (11-161) days in nonimmunized infants. Bronchiolitis occurred in 67 (2.1%) immunized and 115 (3.7%) nonimmunized infants, corresponding to a nirsevimab effectiveness of 48% (95% CI, 29%-62%) (**Figure 1**). Results were similar in the per-protocol analysis (nirsevimab effectiveness, 45% [95% CI, 23%-61%]).

Stratified analyses showed decreasing nirsevimab effectiveness with age (immunized at age 2-3 months, 77% [95% CI, 45%-91%]; age 4-6 months, 45% [95% CI, 11%-66%]; age >6 months, 29% [95% CI, −19% to 57%]). Similar per-protocol results were found but with overlapping confidence intervals (**Figure 2**).

Figure 2. Forest Plot of Nirsevimab Protection Associated With Bronchiolitis by Infant Age at Propensity Score Matching in the As-Treated and Per-Protocol Analyses

Comparison group	Infants, No. (%)	Bronchiolitis episodes, infants, No. (%)	Effectiveness, % (95% CI)
As-treated analysis			
Age 2-3 mo			
No immunization	488 (50)	29 (5.9)	0 [Reference]
Nirsevimab	488 (50)	10 (2.1)	77 (45 to 91)
Age 4-6 mo			
No immunization	1150 (50)	49 (4.3)	0 [Reference]
Nirsevimab	1150 (50)	27 (2.4)	45 (11 to 66)
Age >6 mo			
No immunization	1494 (50)	37 (2.5)	0 [Reference]
Nirsevimab	1494 (50)	30 (2.0)	29 (-19 to 57)
Per-protocol analysis			
Age 2-3 mo			
No immunization	168 (50)	25 (14.9)	0 [Reference]
Nirsevimab	168 (50)	10 (6.0)	82 (49 to 94)
Age 4-6 mo			
No immunization	576 (50)	44 (7.6)	0 [Reference]
Nirsevimab	576 (50)	30 (5.2)	42 (4 to 66)
Age >6 mo			
No immunization	821 (50)	34 (4.1)	0 [Reference]
Nirsevimab	821 (50)	30 (3.7)	19 (-37 to 53)



The as-treated analysis included censored matched pairs when the control group received nirsevimab. The per-protocol analysis excluded pairs in which the control group received nirsevimab. Models were adjusted for propensity score, age (in months) at matching, and bronchiolitis episodes before matching.

Discussion

In this cohort study of pediatric primary care, nirsevimab was associated with a 45% to 48% lower risk of clinically diagnosed all-cause bronchiolitis among infants born before the RSV season and immunized later. Infants aged 2 to 3 months experienced the most benefit, consistent with higher RSV attribution early in life and prior studies.[5]

Although lower than estimates for RSV-confirmed outcomes, these findings align with expectations for an all-cause bronchiolitis end point.[3] Potential limitations included a small sample size and the possibility of residual regional confounding. Our findings support the value of recall-based nirsevimab immunization strategies in community pediatric practice, particularly for older, previously unexposed infants.

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Author Contributions: Dr Boracchini and Dr Cantarutti had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Prof Baraldi and Dr Cantarutti contributed equally as co-senior authors.

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SUPPLEMENT 1.

eAppendix 1. The Pedianet Database
eAppendix 2. Immunization Strategies Adopted in Italy
eAppendix 3. Outcome Definition
eFigure. Flowchart Depicting the Cohort Selection Process, Matching Procedure, and Statistical Modeling Strategies
eReferences.

SUPPLEMENT 2.

Data Sharing Statement