JAMA | Original Investigation

Nirsevimab vs RSVpreF Vaccine for Respiratory Syncytial Virus–Related Hospitalization in Newborns

Marie-Joelle Jabagi, PharmD, PhD; Marion Bertrand, MSc; Amélie Gabet, PhD; Epiphane Kolla, MD, PhD; Valérie Olié, PhD; Mahmoud Zureik, MD, PhD

IMPORTANCE Respiratory syncytial virus (RSV) is a leading cause of hospitalization in infants. The comparative effectiveness of 2 recently introduced preventive strategies (infant immunization through placental antibody transfer after maternal vaccination with the RSV prefusion F protein [RSVpreF] vaccine and passive infant immunization with nirsevimab) remains unknown.

OBJECTIVE To compare the associations of maternal vaccination with the RSVpreF vaccine vs passive infant immunization with nirsevimab for the prevention of RSV-related hospitalization.

DESIGN, SETTING, AND PARTICIPANTS This population-based cohort study used data from the French National Health Data System. Maternal vaccination with the RSVpreF vaccine occurred during 32 to 36 weeks' gestation among infants born in mainland France between September 1 and December 31, 2024. Passive infant immunization with nirsevimab occurred prior to hospital discharge. Infants were matched 1:1 by maternity ward discharge date, sex, gestational age, and region. Follow-up ended at the time of RSV hospitalization or death or on February 28, 2025.

EXPOSURES Maternal immunization with the RSVpreF vaccine and passive infant immunization with nirsevimab.

MAIN OUTCOMES AND MEASURES The primary outcome was hospitalization for RSV-associated lower respiratory tract infection. The secondary outcomes included admission to the pediatric intensive care unit (PICU), admission to high-dependency unit, ventilator support, and oxygen therapy. The hazard ratios (HRs) were estimated using conditional Cox proportional hazards models with inverse probability of treatment weighting.

RESULTS A total of 42 560 infants (mean age, 3.7 [SD, 1.4] days; 51.7% male) were included in the study (21 280 per group) with a median follow-up of 84 days (IQR, 70-99 days). Of the 481 hospitalizations for RSV-associated lower respiratory tract infection, 212 (44.1%) occurred in the nirsevimab group vs 269 (55.9%) in the RSVpreF vaccine group (between-group difference, −11.8% [95% CI, −18.1% to −5.5%]). Compared with the RSVpreF vaccine, passive infant immunization with nirsevimab was associated with a lower risk of hospitalization for RSV-associated lower respiratory tract infection (adjusted HR, 0.74 [95% CI, 0.61 to 0.88]). Compared with the RSVpreF vaccine, passive infant immunization with nirsevimab was associated with a lower risk of severe outcomes, including PICU admission (adjusted HR, 0.58 [95% CI, 0.42 to 0.80]), requiring ventilator support (adjusted HR, 0.57 [95% CI, 0.40 to 0.81]), or requiring oxygen therapy (adjusted HR, 0.56 [95% CI, 0.38 to 0.81]). The results were consistent across subgroups and in the sensitivity analyses.

CONCLUSIONS AND RELEVANCE Compared with maternal vaccination with the RSVpreF vaccine, passive infant immunization with nirsevimab was associated with lower risks of RSV-related hospitalization and severe outcomes. These findings reflect the first RSV season with use of these immunization strategies in mainland France; their use should be reevaluated in future studies.

JAMA. doi:10.1001/jama.2025.24082
Published online December 22, 2025.

Supplemental content

Related articles at jamapediatrics.com

Author Affiliations: French National Agency for Medicines and Health Products Safety and French National Health Insurance (EPI-PHARE), Saint-Denis, France (Jabagi, Bertrand, Gabet, Kolla, Olié, Zureik); Anti-Infective Evasion and Pharmacoepidemiology, INSERM, Center for Research in Epidemiology and Population Health, University of Paris-Saclay, Montigny le Bretonneux, France (Zureik).

Corresponding Author: Marie-Joelle Jabagi, PharmD, PhD, French National Agency for Medicines and Health Products Safety, 143-147 Boulevard Anatole France, Saint-Denis CEDEX F-93285, France (marie-joelle.jabagi@ansm.sante.fr).

Respiratory syncytial virus (RSV) is a major cause of infant hospitalization for acute lower respiratory tract infections (LRTIs) worldwide,[1,2] but has lacked effective preventive options. Recently, 2 immunoprophylactic interventions have become available. In 2022, the European Medicines Agency[3] and the US Food and Drug Administration[4] approved nirsevimab, a long-acting monoclonal antibody directed to the fusion protein of RSV that provides season-long protection after a single intramuscular dose. In 2023, a maternal vaccine targeting the RSV prefusion F protein (RSVpreF) was approved to induce transplacental transfer of RSV-neutralizing antibodies; vaccination was authorized at 24 to 36 weeks' gestation.[5,6]

Nirsevimab reduced medically attended RSV-associated LRTIs by approximately 70% to 75% in a phase 2b trial[7] and in a phase 3 trial.[8] A pooled analysis showed a reduction by 76% in RSV-associated hospitalizations.[9] Real-world effectiveness studies,[10] including our French population-based study,[11] confirmed reductions by 65% in RSV-associated LRTI hospitalizations and reductions by 75% in admissions to the pediatric intensive care unit (PICU). These findings were consistent with those from Spain[12] and the US.[13]

The RSVpreF vaccine demonstrated an efficacy rate of 82% against severe RSV-associated LRTIs through 90 days of life and an efficacy rate of 69% through 180 days in the phase 3 MATISSE trial.[14] These results were consistent with real-world effectiveness data from Argentina showing reductions by 79% in RSV-associated hospitalizations among infants younger than 3 months and by 77% in those younger than 6 months.[15]

Although both agents effectively reduce RSV-associated LRTI hospitalizations in infants, they differ in immunologic mechanisms and timing of administration, underscoring the necessity of comparative evaluations to assess their potential interchangeability in immunization campaigns. To date, a direct comparison of maternal RSV immunization vs infant nirsevimab immunization in preventing severe RSV outcomes in early infancy has not been performed. This French national population-based cohort study compared infant nirsevimab immunization vs maternal RSVpreF vaccination to assess associations with RSV-related hospitalization in infants (**Figure 1**).

Key Points

Question How does maternal vaccination with the respiratory syncytial virus prefusion F protein (RSVpreF) vaccine compare with passive infant immunization with nirsevimab for the prevention of RSV-related hospitalization?

Findings In this French nationwide study, infant immunization with nirsevimab was associated with a lower risk of RSV-related hospitalization compared with maternal vaccination with the RSVpreF vaccine (hazard ratio, 0.74). The risk of severe outcomes, including admission to the pediatric intensive care unit and requiring ventilator support or oxygen therapy, was also lower.

Meaning Compared with maternal vaccination with the RSVpreF vaccine during the first RSV season in France, infant immunization with nirsevimab was associated with a lower risk of RSV-related hospitalization.

Methods

Data Source

This study used the French National Health Data System, a nationwide database containing longitudinal, individual-level data for nearly the entire French population. The system integrates pseudonymized data from the National Health Insurance Claims Database for outpatient care, the National Hospital Discharge Database for inpatient care, and mortality records from the national registry linked through a unique pseudonymized identifier with national quality controls (with a coding error rate of <2%).[16] The French National Health Data System captures detailed data on diagnoses, procedures, prescriptions, and health care use that have been used in large-scale pharmacoepidemiological studies.[17,18]

French RSV Immunization Campaign for 2024-2025

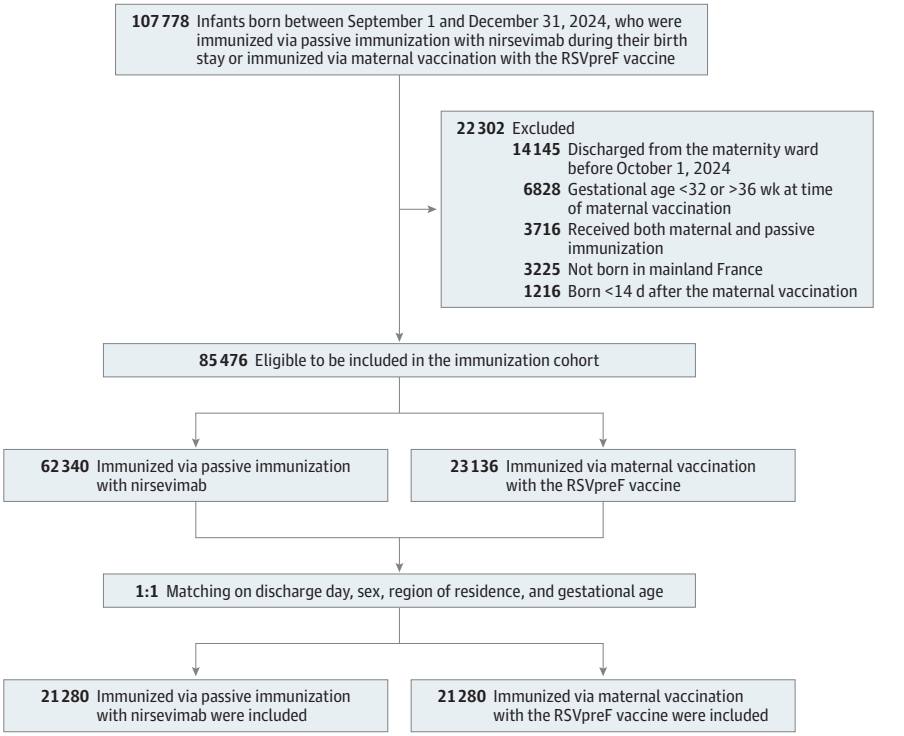
During the 2024-2025 RSV immunization campaign, 3 preventive options were available for infants in France: the 2 monoclonal antibodies of palivizumab (Synagis) and nirsevimab (Beyfortus) and 1 maternal RSVpreF vaccine (Abrysvo). Nirsevimab was recommended during their first RSV season for all infants born on or after January 1, 2024, it was available in outpatient settings starting from September 1, 2024, and it was offered to all newborns in maternity hospitals before maternity discharge starting on September 15, 2024. Maternal vaccination with the RSVpreF vaccine was recommended at 32 to 36 weeks' gestation from September 1, 2024, to January 31, 2025 (eFigure 1 in Supplement 1). Use of palivizumab has been very limited (approximately 150 infants) since the arrival of nirsevimab.

The choice between nirsevimab and the RSVpreF vaccine was made by health care professionals and parents. The national campaign concluded on January 31, 2025. For the 2024-2025 RSV season, daily RSV-associated LRTI hospitalizations occurred from October 2024 to February 2025 and peaked mid-November 2024 to early January 2025 among births in 2024 (eFigure 2 in Supplement 1).

Study Population

Infants were eligible if (1) born between September 1 and December 31, 2024, (2) discharged from maternity wards on or after October 1, 2024, and (3) immunized either through maternal vaccination or passive immunization with nirsevimab. The October 1, 2024, date corresponded to the first maternity discharges of infants born to vaccinated mothers. Infants were excluded if (1) they received both preventive strategies, (2) their mothers were vaccinated before 32 or after 36 weeks' gestation (because the vaccine is recommended during the eighth month of pregnancy), or (3) their birth occurred within 14 days of maternal vaccination, for whom catch-up monoclonal antibody immunization is advised. Due to differences in nirsevimab availability and delayed RSV circulation in overseas territories, the study was limited to mainland France.

Figure 1. Flow of Infant Cohort by Passive Immunization With Nirsevimab vs Maternal Vaccination With the Respiratory Syncytial Virus Prefusion Protein F (RSVpreF) Vaccine



Study Design

For each day between October 1 and December 31, 2024, every infant born to a mother vaccinated with the RSVpreF vaccine was matched to an infant who received nirsevimab on the same maternity discharge day, using random sampling without replacement. To ensure comparability between the 2 groups, we further matched infants based on sex, gestational age (preterm birth: <37 weeks; term birth: ≥37 weeks), and region of residence (mainland France includes 13 regions). This process achieved a match rate of 92% (eTable 1 in Supplement 1). Follow-up started at the infant's discharge from the birth hospitalization (time zero) and continued until the outcome event, unrelated death, or February 28, 2025, whichever occurred first. According to French regulations (Public Health Code Articles L 1461-3 and R 1461-11), research using pseudonymized data from the French National Health Data System does not require ethics committee review or individual informed consent. This report followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline. Key methods are summarized in eTable 2 in Supplement 1. The prespecified statistical analysis plan appears in the eMethods in Supplement 1.

Exposures

Immunization status was classified as passive immunization for infants who received nirsevimab during their maternity stay and as maternal immunization for those whose mothers received the RSVpreF vaccine between 32 and 36 weeks' gestation. Nirsevimab was identified in the inpatient setting using the Anatomical Therapeutic Chemical classification code J06BD08; the injection date was defined as the maternity discharge date. Maternal vaccination with the RSVpreF vaccine was identified through community pharmacy dispensations (Anatomical Therapeutic Chemical classification code J07BX05).

Nirsevimab administration increased rapidly in early October 2024 and declined thereafter, whereas RSVpreF vaccine uptake increased steadily, reaching similar numbers by late December (eFigure 2 in Supplement).

Outcomes

The primary outcome was hospitalization for RSV-associated LRTI. The primary outcome was identified using *International Statistical Classification of Diseases and Related Health Problems, Tenth Revision (ICD-10)* RSV codes for acute bronchiolitis (J210), pneumonia (J121), and acute bronchitis (J205). The RSV-specific *ICD-10* codes in French hospital data are assigned for laboratory-confirmed infections and are thereby considered specific indicators of RSV-related hospitalization. The secondary outcomes included RSV-associated LRTI cases requiring admission to a PICU or high dependency unit, ventilator support, or supplemental oxygen. Additional secondary outcomes included length of inpatient hospitalization, extracorporeal membrane oxygenation use, nitric oxide use, and in-hospital death. All outcomes were prespecified in the study protocol.

Covariates

For each infant, the characteristics collected were age at study entry, month of birth, gestational age, sex, birth weight, type of birth hospital, complimentary solidarity health insurance status, consultations in maternal and child welfare centers, region, and social security affiliation type. Clinical variables encompassed serious infections during the birth stay and risk factors for LRTIs[19-22] (such as bronchopulmonary dysplasia; cystic fibrosis; neonatal respiratory distress syndrome; meconium aspiration syndrome; pneumothorax; pulmonary hypertension; congenital heart defects; and major chromosomal, respiratory, esophageal, or neuromuscular anomalies). Residential determinants included the French Deprivation Index,[23] the General Practitioners' Localized Potential Accessibility, and the French version of the European Deprivation Index.[24] Maternal data comprised age at childbirth, parity, comorbidities, lifestyle habits, and other vaccinations received during pregnancy (tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis [Tdap]; influenza; or COVID-19). For maternal recipients of the RSVpreF vaccine, the gestational age at vaccination and the interval to maternity discharge were calculated. The *ICD-10* codes were adapted from definitions used in prior national studies using the French National Health Data System database[25,26] (eTable 3 in Supplement 1).

Statistical Analysis

To address the nonrandomized assignment of immunization type, a propensity score was estimated using binomial logistic regression that included all baseline characteristics for the infants and mothers (parameter estimates appear in eTable 4 in Supplement 1). Inverse probability of treatment weighting based on the propensity score was applied to reduce confounding and improve between-group covariate comparability.[27,28] Stabilized weights were calculated by multiplying the inverse probability of treatment weighting by the marginal probability of receiving the assigned immunization. Covariate balance before and after weighting was evaluated using standardized differences (eFigure 3 in Supplement 1).[29] Weighted conditional Cox proportional hazards models were fitted to account for the matched design and estimate hazard ratios (HRs) with 95% CIs.[30]

The subgroup analyses were conducted by sex (male vs female), gestational age (preterm birth [<37 weeks] vs term birth [≥37 weeks]), French Deprivation Index (least [quintiles 1 and 2] vs most deprived [quintiles 3, 4, and 5]), time since cohort entry (0-7 days, 8-30 days, 31-60 days, >60 days), interval between maternal RSVpreF vaccination and inclusion (<5 weeks vs ≥5 weeks), and the intensity of RSV circulation (2 lower periods: October 1-November 14, 2024, and January 6-February 28, 2025 vs 1 higher period: November 15, 2024-January 5, 2025). The sensitivity analyses included: (1) applying a 7-day and a 14-day lag between the maternity discharge day and the beginning of follow-up to account for incubation and symptom onset of RSV; (2) multivariate regression models including variables from the propensity score; (3) trimming the propensity score distribution by excluding observations below the 1st percentile and above the 99th percentile; (4) restricting the analysis to infants whose mothers were vaccinated at least 30 days before delivery; and (5) including pregnancies with maternal RSVpreF vaccination before 32 weeks of gestation with matched controls.

The analyses were conducted using SAS Enterprise Guide version 9.4 (SAS Institute Inc) and R software version 4.0.2 (R Foundation for Statistical Computing). The statistical tests were 2-sided. A P value <.05 was considered statistically significant.

Results

Of the 107 778 infants born in mainland France between September 1 and December 31, 2024, who received RSV immunization, 85 476 met the study eligibility criteria. Among these 85 476 infants, 62 340 (72.9%) received passive immunization with nirsevimab and 23 136 (27.1%) received immunization via maternal vaccination with the RSVpreF vaccine. From the maternal vaccination group, 21 280 infants (92%) were matched 1:1 to infants in the nirsevimab group based on maternity discharge date, sex, gestational age, and region of residence (Figure 1).

The 42 560 infants in the matched analysis had a median follow-up of 84 days (IQR, 70-99 days). The population was predominantly male (51.7%) and born at term (98.7%), mostly in November and December 2024 (91%). The mean age at maternity ward discharge (inclusion) was similar at 3.8 days (SD, 1.5 days) in the nirsevimab group vs 3.7 days (SD, 1.3 days) in the RSVpreF vaccine group (**Table 1**). Serious infections during the birth stay were more frequent in the nirsevimab group (377; 1.8%) compared with the RSVpreF vaccine group (176; 0.8%), whereas the frequency of congenital anomalies was similar in both groups (183 [0.9%] vs 207 [1.0%], respectively). Infants in the nirsevimab group were more often socioeconomically disadvantaged and had higher complementary solidarity health insurance compared with the RSVpreF vaccine group (4262 [20.0%] vs 1854 [8.7%], respectively), had greater use of maternal and child welfare services (1314 [6.2%] vs 992 [4.7%]), and resided in the most deprived municipalities (quintile 5 using the French Deprivation Index; 4588 [21.7%] vs 2913 [13.8%]).

Mothers in the nirsevimab group were slightly younger (31 [IQR, 27-34] years vs 32 [IQR, 29-35] years in the RSVpreF vaccine group), less often primiparous (10 434 [49.0%] vs 11 306 [53.1%]), and less likely to have received the Tdap, influenza, or COVID-19 vaccine during pregnancy (**Table 2** and eTable 5 in Supplement 1). After applying inverse probability of treatment weighting, the maternal and infant characteristics were perfectly balanced between the 2 groups (eFigure 3 in Supplement 1).

A total of 481 infants met the primary outcome of hospitalization for RSV-associated LRTI; there were 212 (44.1%) in the nirsevimab group vs 269 (55.9%) in the RSVpreF vaccine group (between-group difference, −11.8% [95% CI, −18.1% to −5.5%]; **Table 3**). Infant immunization with nirsevimab was associated with a lower risk of hospitalization for RSV-associated LRTI compared with maternal RSVpreF vaccination (adjusted HR, 0.74 [95% CI, 0.61 to 0.88]) (**Figure 2** and eFigure 4 in Supplement 1). The mean age at hospitalization was 38.9 days (SD, 22.2 days).

Table 1. Infant Characteristics

	Unmatched cohort			Matched cohort		
	Nirsevimab (n = 62 340)	RSVpreF vaccine (n = 23 136)	SMD[a]	Nirsevimab (n = 21 280)	RSVpreF vaccine (n = 21 280)	SMD[a]
Sex, No. (%)[b]						
Male	32 079 (51.5)	11 861 (51.3)	0.004	10 998 (51.7)	10 998 (51.7)	0
Female	30 261 (48.5)	11 275 (48.7)	−0.004	10 282 (48.3)	10 282 (48.3)	0
Preterm birth (gestational age <37 wk), No. (%)[b]	2142 (3.4)	342 (1.5)	0.13	278 (1.3)	278 (1.3)	0
Term birth (gestational age ≥37 wk), No. (%)[b]	60 198 (96.6)	22 794 (98.5)	−0.13	21 002 (98.7)	21 002 (98.7)	0
Age at maternity ward discharge, d						
Mean (SD)	3.8 (1.6)	3.7 (1.3)	0.07	3.8 (1.5)	3.7 (1.3)	0.04
Median (IQR)	3 (3-4)	4 (3-4)		3 (3-4)	4 (3-4)	
Month of birth, No. (%)			1.09			0.02
September	3512 (5.6)	7 (<0.1)		16 (0.1)	7 (<0.1)	
October	27 015 (43.3)	1843 (8.0)		1889 (8.9)	1841 (8.7)	
November	18 830 (30.2)	8658 (37.4)		8491 (39.9)	8473 (39.8)	
December	12 983 (20.8)	12 628 (54.6)		10 884 (51.1)	10 959 (51.5)	
Description of birth weight size, No. (%)[c]			0.23			0.23
Small for gestational age (<10th percentile)	7167 (11.5)	2343 (10.4)		2456 (11.5)	2157 (10.4)	
Appropriate for gestational age (10th-90th)	48 391 (77.7)	17 679 (78.5)		16 485 (77.5)	16 254 (78.5)	
Large for gestational age (>90th)	6749 (10.8)	2494 (11.1)		2331 (11.0)	2293 (11.1)	
Date range of discharge for birth hospitalization, No. (%)			1.15			0
Oct 1-15	13 866 (22.2)	160 (0.7)		151 (0.7)	151 (0.7)	
Oct 16-31	13 572 (21.8)	1129 (4.9)		1122 (5.3)	1122 (5.3)	
Nov 1-15	10 835 (17.4)	2840 (12.3)		2791 (13.1)	2791 (13.1)	
Nov 16-30	9062 (14.5)	4893 (21.1)		4781 (22.5)	4781 (22.5)	
Dec 1-15	7710 (12.4)	6222 (26.9)		5709 (26.8)	5709 (26.8)	
Dec 16-31	7295 (11.7)	7892 (34.1)		6726 (31.6)	6726 (31.6)	
Region of residence, No. (%)[b]			0.28			0
Auvergne-Rhône-Alpes	7742 (12.4)	3193 (13.8)		2939 (13.8)	2939 (13.8)	
Bourgogne-Franche-Comté	2535 (4.1)	600 (2.6)		600 (2.8)	600 (2.8)	
Bretagne	2429 (3.9)	1872 (8.1)		1214 (5.7)	1214 (5.7)	
Centre-Val de Loire	2604 (4.2)	850 (3.7)		833 (3.9)	833 (3.9)	
Corse	338 (0.5)	40 (0.2)		40 (0.2)	40 (0.2)	
Grand Est	4999 (8.0)	1583 (6.8)		1566 (7.4)	1566 (7.4)	
Hauts-de-France	6795 (10.9)	2184 (9.4)		2153 (10.1)	2153 (10.1)	
Ile-de-France	13 751 (22.1)	4427 (19.1)		4427 (20.8)	4427 (20.8)	
Normandie	3805 (6.1)	1166 (5.0)		1138 (5.3)	1138 (5.3)	
Nouvelle-Aquitaine	4522 (7.3)	2160 (9.3)		1837 (8.6)	1837 (8.6)	
Occitanie	4662 (7.5)	2014 (8.7)		1828 (8.6)	1828 (8.6)	
Pays de la Loire	3334 (5.3)	1785 (7.7)		1443 (6.8)	1443 (6.8)	
Provence-Alpes-Côte d'Azur	4824 (7.7)	1262 (5.5)		1262 (5.9)	1262 (5.9)	
French Deprivation Index, No. (%)[d]			0.29			0.34
Quintile 1 (least deprived)	11 402 (18.4)	6259 (27.2)		3558 (16.8)	5926 (28.0)	
Quintile 2 (slightly deprived)	12 142 (19.6)	5403 (23.5)		4110 (19.4)	4893 (23.1)	
Quintile 3 (moderately deprived)	12 354 (19.9)	4331 (18.8)		4200 (19.9)	3899 (18.4)	
Quintile 4 (highly deprived)	12 914 (20.8)	3916 (17.0)		4689 (22.2)	3535 (16.7)	
Quintile 5 (most deprived)	13 168 (21.2)	3104 (13.5)		4588 (21.7)	2913 (13.8)	
European Deprivation Index, No. (%)[e]			0.19			0.16
Quintile 1 (least deprived)	10 186 (16.4)	5114 (22.2)		3406 (16.1)	4520 (21.4)	
Quintile 2 (slightly deprived)	11 188 (18.1)	4455 (19.4)		3884 (18.4)	4001 (18.9)	
Quintile 3 (moderately deprived)	12 267 (19.8)	4131 (18.0)		4211 (19.9)	3821 (18.1)	
Quintile 4 (highly deprived)	13 158 (21.2)	5059 (22.0)		4612 (21.8)	4658 (22.0)	
Quintile 5 (most deprived)	15 182 (24.5)	4253 (18.5)		5034 (23.8)	4165 (19.7)	

(continued)

Table 1. Infant Characteristics (continued)

	Unmatched cohort			Matched cohort		
	Nirsevimab (n = 62 340)	RSVpreF vaccine (n = 23 136)	SMD[a]	Nirsevimab (n = 21 280)	RSVpreF vaccine (n = 21 280)	SMD[a]
General Practitioners' Localized Potential, No. (%)[f]			0.20			0.20
Quartile 1 (<3.0)	17 251 (27.8)	4793 (20.8)		5879 (27.8)	4423 (20.9)	
Quartile 2 (3.0-3.8)	15 654 (25.3)	5376 (23.4)		5424 (25.7)	4989 (23.6)	
Quartile 3 (3.9-4.7)	15 660 (25.3)	6343 (27.6)		5340 (25.3)	5855 (27.7)	
Quartile 4 (>4.7)	13 416 (21.6)	6502 (28.3)		4503 (21.3)	5900 (27.9)	
Complementary solidarity health insurance status, No. (%)[g]	11 459 (18.4)	1977 (8.5)	0.29	4262 (20.0)	1854 (8.7)	0.33
Maternal and child protection centers, No. (%)[h]	4151 (6.7)	1044 (4.5)	0.094	1314 (6.2)	992 (4.7)	0.067
Facility of birth, No. (%)			0.70			0.71
General	56 195 (90.1)	15 121 (65.4)		19 274 (90.6)	13 924 (65.4)	
Private nonprofit	4706 (7.5)	2605 (11.3)		1533 (7.2)	2408 (11.3)	
Private for-profit	1406 (2.3)	4791 (20.7)		465 (2.2)	4373 (20.5)	
Other	33 (0.1)	619 (2.7)		8 (<0.1)	575 (2.7)	
Type of social security, No. (%)[i]			0.028			0.030
General health	60 081 (96.4)	22 206 (96.0)		20 513 (96.4)	20 451 (96.1)	
Agricultural	1632 (2.6)	629 (2.7)		562 (2.6)	558 (2.6)	
Other special	627 (1.0)	301 (1.3)		205 (1.0)	271 (1.3)	
Serious infections during the birth stay, No. (%)[j]	995 (1.6)	220 (1.0)	0.058	377 (1.8)	176 (0.8)	0.083
Bacterial	919 (1.5)	200 (0.9)	0.057	354 (1.7)	160 (0.8)	0.076
Viral	73 (0.1)	21 (0.1)	0.008	20 (0.1)	15 (0.1)	0.005
Fungal	17 (<0.1)	4 (<0.1)	0.007	6 (<0.1)	3 (<0.1)	0.006
Congenital anomalies, No. (%)[k]	635 (1.0)	233 (1.0)	0.001	183 (0.9)	207 (1.0)	−0.012
Chronic comorbidities, No. (%)						
Congenital heart disease	61 (0.1)	35 (0.2)	−0.015	13 (0.1)	25 (0.1)	−0.019
Bronchopulmonary dysplasia	1 (<0.1)	1 (<0.1)	−0.005	0	1 (<0.1)	−0.01

Abbreviations: RSVpreF, respiratory syncytial virus prefusion F protein; SMD, standardized mean difference.

[a] The SMDs are presented as unitless measures of imbalance. An SMD of approximately 0.2 is conventionally considered a small effect; 0.5, a moderate effect; and 0.8, a large effect. A positive SMD indicates the nirsevimab group tends to have higher mean scores, taking into account data variability. A negative SMD indicates the RSVpreF vaccine group tends to have higher mean scores, taking into account data variability. For continuous variables, the SMDs were computed as the difference in means divided by the pooled SD. For binary variables, the SMDs were calculated as the difference in proportions divided by the pooled SD of the proportions. For categorical variables with more than 2 levels, the SMDs were calculated using the multivariate Mahalanobis distance approach, which compares the full between-group distribution for the category probabilities.

[b] This variable was used in the matching process.

[c] Defined according to national reference growth charts for gestational age.

[d] An ecological, area-based measure of social disadvantage in France, constructed at the commune level using 4 standardized variables (median household income per consumption unit, percentage of employed population in manual occupations, unemployment rate, and percentage of adults without a baccalaureate degree). Higher quintiles indicate greater deprivation.

[e] An ecological, small-area indicator of relative socioeconomic deprivation developed using harmonized methods across European countries. Higher quintiles indicate greater deprivation.

[f] Indicator of access to primary care physicians. Calculated from the density of general practitioners relative to population needs in each area. Higher quartiles indicate greater access.

[g] National public insurance program providing full coverage of health care costs for low-income individuals and families.

[h] Public community health services providing preventive medical care and social support to mothers and infants.

[i] Categorized according to the French national insurance schemes.

[j] Documented with *International Statistical Classification of Diseases and Related Health Problems, Tenth Revision* (*ICD-10*) codes during the initial hospitalization after delivery. The full list of *ICD-10* codes used for classification appears in eTable 3 in Supplement 1.

[k] Includes major structural or chromosomal anomalies. The frequency and description of individual anomalies appear in eTable 5 in Supplement 1. The major categories include congenital heart defects and diseases, nervous system and chromosomal abnormalities, respiratory and esophageal abnormalities, digestive system and abdominal wall defects, kidney urinary and genital malformations, limb and musculoskeletal anomalies, craniofacial anomalies, and other teratogenic anomalies. The *ICD-10* codes appear in eTable 3 in Supplement 1.

Most cases of RSV-associated LRTI were bronchiolitis (464; 96.5%); there were few cases of bronchitis or pneumonitis. Hospitalizations requiring PICU admission were less frequent in the nirsevimab group compared with the RSVpreF vaccine group (adjusted HR, 0.58 [95% CI, 0.42-0.80]) as were those requiring admission to a high-dependency unit (adjusted HR, 0.87 [95% CI, 0.60-1.25]). Hospitalizations involving oxygen therapy were also significantly lower in the nirsevimab group compared with the RSVpreF vaccine group (adjusted HR, 0.56 [95% CI, 0.38-0.81]) as were those requiring ventilator support (adjusted HR, 0.57 [95% CI, 0.40-0.81]) (Figure 2). The median length of hospital stay was 5 days (IQR, 4-7 days).

In the unadjusted analyses, hospital stays exceeding 1 week were less frequent in the nirsevimab group compared with the

Table 2. Maternal Characteristics

	Unmatched cohort			Matched cohort		
	Nirsevimab (n = 62 340)	RSVpreF vaccine (n = 23 136)	SMD[a]	Nirsevimab (n = 21 280)	RSVpreF vaccine (n = 21 280)	SMD[a]
Age at childbirth, y						
Median (IQR)	31 (27-34)	32 (29-35)		31 (27-34)	32 (29-35)	
Distribution, No. (%)			0.25			0.29
15-24	8593 (13.8)	1709 (7.4)		3187 (15.0)	1548 (7.3)	
25-29	17 498 (28.1)	5629 (24.3)		5984 (28.1)	5132 (24.1)	
30-34	20 855 (33.5)	8816 (38.1)		6947 (32.6)	8125 (38.2)	
35-49	15 394 (24.7)	6982 (30.2)		5162 (24.3)	6475 (30.4)	
Parity, No. (%)			0.16			0.19
1	31 010 (49.7)	12 289 (53.1)		10 434 (49.0)	11 306 (53.1)	
2	20 635 (33.1)	8057 (34.8)		6964 (32.7)	7399 (34.8)	
3	7426 (11.9)	2143 (9.3)		2665 (12.5)	1975 (9.3)	
≥4	3269 (5.2)	647 (2.8)		1217 (5.7)	600 (2.8)	
Mode of delivery, No. (%)						
Vaginal	48 879 (78.8)	18 094 (78.6)	0.005	16 716 (78.9)	16 650 (78.6)	0.007
Cesarean	13 152 (21.2)	4926 (21.4)	−0.005	4459 (21.1)	4522 (21.4)	−0.007
Time between vaccination and delivery, median (IQR), d		5.1 (4.0-6.1)			5.0 (4.0-6.1)	
Other vaccinations received during pregnancy, No. (%)						
Tdap	48 735 (78.2)	22 413 (96.9)	−0.59	16 079 (75.6)	20 609 (96.8)	−0.65
Influenza	2522 (4.0)	7144 (30.9)	−0.76	1569 (7.4)	6389 (30.0)	−0.61
COVID-19	952 (1.5)	2312 (10.0)	−0.37	428 (2.0)	2087 (9.8)	−0.34
Comorbidities, No. (%)						
Gestational diabetes	9788 (15.7)	3356 (14.5)	0.033	3230 (15.2)	3106 (14.6)	0.016
Obesity	5902 (9.5)	1770 (7.7)	0.065	1989 (9.3)	1639 (7.7)	0.059
Preeclampsia	2520 (4.0)	888 (3.8)	0.010	819 (3.8)	804 (3.8)	0.004
Chronic hypertension	909 (1.5)	348 (1.5)	−0.004	277 (1.3)	320 (1.5)	−0.017
Preexisting diabetes	523 (0.8)	183 (0.8)	0.005	176 (0.8)	166 (0.8)	0.005
Lifestyle habits, No. (%)						
Tobacco use	7745 (12.4)	2439 (10.5)	0.059	2689 (12.6)	2200 (10.3)	0.072
Alcohol consumption	423 (0.7)	103 (0.4)	0.031	138 (0.6)	93 (0.4)	0.029

Abbreviations: RSVpreF, respiratory syncytial virus prefusion F protein; SMD, standardized mean difference; Tdap, tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis.

[a] The SMDs are presented as unitless measures of imbalance. An SMD of approximately 0.2 is conventionally considered a small effect; 0.5, a moderate effect; and 0.8, a large effect. A positive SMD indicates the nirsevimab group tends to have higher mean scores, taking into account data variability. A negative SMD indicates the RSVpreF vaccine group tends to have higher mean scores, taking into account data variability. For the continuous variables, SMDs were computed as the difference in means divided by the pooled SD. For the binary variables, SMDs were calculated as the difference in proportions divided by the pooled SD of the proportions. For the categorical variables with more than 2 levels, SMDs were calculated using the multivariate Mahalanobis distance approach, which compares the full distribution of category probabilities between groups.

RSVpreF vaccine group (45 [21.2%] vs 75 [27.9%]). Infants in the nirsevimab group also had a lower rate of PICU admission compared with the RSVpreF vaccine group (55 [25.9%] vs 101 [37.5%]), required noninvasive ventilation less frequently (51 [24.1%] vs 86 [32.0%]), and required oxygen therapy less frequently (39 [18.4%] vs 76 [28.3%]) (Table 3). No in-hospital deaths occurred.

In the subgroup analyses, the risk of RSV-associated LRTI hospitalization remained consistently lower among infants in the nirsevimab group compared with the RSVpreF vaccine group for males (adjusted HR, 0.68 [95% CI, 0.53-0.87]), for females (adjusted HR, 0.81 [95% CI, 0.61-1.09]), those with term birth (adjusted HR, 0.75 [95% CI, 0.62-0.90]), those with preterm birth (adjusted HR, 0.28 [95% CI, 0.06-1.37]), those who resided in the most deprived municipalities (quintile 3, 4, or 5 on the French Deprivation Index [moderately, highly, or most deprived, respectively]; adjusted HR, 0.66 [95% CI, 0.47-0.92]), and those who resided in the least deprived municipalities (quintile 1 or 2 on the French Deprivation Index [least or slightly deprived, respectively]; adjusted HR, 0.81 [95% CI, 0.53-1.25]). The risk pattern for RSV-associated LRTI hospitalization varied with time since study inclusion; the nirsevimab group had higher risk during the first 7 days compared with the RSVpreF vaccine group (adjusted HR, 2.94 [95% CI, 1.19-7.69]), but lower risk from day 31 to day 60 (adjusted HR, 0.62 [95% CI, 0.45-0.84]) and an even lower risk after 60 days (adjusted HR, 0.51 [95% CI, 0.30-0.86]).

Table 3. Primary Outcome and Secondary and Severe Outcomes

	No. (%)[a]		Between-group difference (95% CI), %	*P* value
	Nirsevimab	RSVpreF vaccine		
Primary outcome, No./total (%)				
Hospitalization for RSV-associated lower respiratory tract infection	212/481 (44.1)	269/481 (55.9)	−11.8 (−18.1 to −5.5)	<.001
By matched cohort	212/21 280 (1.0)	269/21 280 (1.3)	−0.3 (−0.5 to −0.1)	.009
Secondary and severe outcomes				
Type of RSV-associated lower respiratory tract infection	(n = 212)	(n = 269)		
Bronchiolitis	206 (97.2)	258 (95.9)	1.3 (−2.0 to 4.6)	.60
Bronchitis	4 (1.9)	9 (3.3)	−1.5 (−4.3 to 1.4)	
Pneumonitis	2 (0.9)	2 (0.7)	0.2 (−1.5 to 1.9)	
Length of inpatient hospitalization				
Median (IQR), d	5 (3-7)	5 (4-8)		
Distribution	(n = 212)	(n = 269)		
1 d	3 (1.4)	2 (0.7)	0.7 (−1.2 to 2.6)	.08
2-3 d	56 (26.4)	57 (21.2)	5.2 (−2.5 to 12.9)	
4 d-1 wk	108 (50.9)	135 (50.2)	0.8 (−8.2 to 9.7)	
>1 wk	45 (21.2)	75 (27.9)	−6.7 (−14.3 to 1.0)	
Admission to special unit	(n = 212)	(n = 269)		
HDU, PICU, or both	99 (46.7)	149 (55.4)	−8.7 (−17.7 to 0.3)	.06
HDU[b]	58 (27.4)	67 (24.9)	2.5 (−5.2 to 10.1)	.54
PICU	55 (25.9)	101 (37.5)	−11.6 (−19.8 to −3.3)	.007
Type of treatment	(n = 212)	(n = 269)		
Oxygen therapy	39 (18.4)	76 (28.3)	−9.9 (−17.4 to −2.4)	.01
Ventilator support	51 (24.1)	89 (33.1)	−9.0 (−17.0 to −1.0)	.03
Noninvasive ventilation	51 (24.1)	86 (32.0)	−7.9 (−15.9 to 0.1)	.06
Invasive ventilation	2 (0.9)	4 (1.5)	−0.5 (−2.5 to 1.4)	.59
Extracorporeal membrane oxygenation	0	0		
Nitric oxide	0	0		
In-hospital death	0	0		

Abbreviations: HDU, high-dependency unit; PICU, pediatric intensive care unit; RSV, respiratory syncytial virus; RSVpreF, RSV prefusion F protein.

[a] Unless otherwise indicated.

[b] Defined as a unit providing continuous monitoring and specialized care for infants requiring a higher level of observation and treatment than standard pediatric wards but was not an intensive care unit.

For the analyses stratified by the interval between maternal vaccination and inclusion, the adjusted HR was 0.72 (95% CI, 0.53-0.99) for less than 5 weeks and the adjusted HR was 0.74 (95% CI, 0.58-0.93) for 5 weeks or longer (**Figure 3**). The sensitivity analyses with weighted HRs showed similar results as the main analysis (eTable 6 in Supplement 1).

Discussion

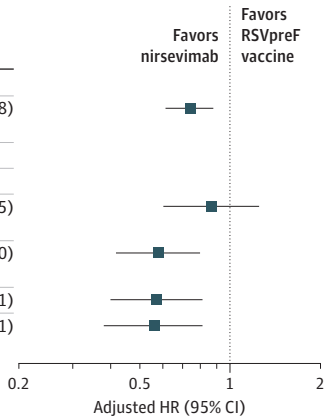
This French national population-based study found that passive immunization with nirsevimab was associated with lower risk of RSV-associated hospitalization during early infancy than maternal RSVpreF vaccination. Findings were similar for severe outcomes, including the need for PICU admission, ventilator support, and oxygen therapy. Even though both interventions have shown high efficacy in clinical trials, the current study was the first, to our knowledge, to compare the interventions in a real-world setting in a national population.

These results expand current evidence by comparing outcomes after the 2 preventive strategies during their initial season of implementation. Both nirsevimab and the RSVpreF vaccine have demonstrated efficacy in randomized clinical trials, with nirsevimab reducing RSV-related illness and hospitalizations by approximately 70% to 75%[7-9] and maternal RSVpreF vaccination reducing severe infant RSV disease by 70% to 80%.[14] These trial data have since been supported by emerging real-world evidence from France, the US, and multiple other countries.[11,15,31-35] The current study found that in real-world conditions, and when evaluated within the same population and during the same epidemic period, passive immunization with nirsevimab was associated with lower observed rates of RSV-related hospitalization and severe outcomes compared with maternal RSVpreF vaccination. Infants who received nirsevimab also had lower observed risks of PICU admission and requirement for respiratory support, suggesting a reduced disease progression once hospitalized.

Nirsevimab confers passive immunity via a single intramuscular dose at birth, offering direct antibody transfer to the infant regardless of maternal vaccination status or gestational age. Nirsevimab appears to maintain consistent effectiveness

Figure 2. Comparative Analysis for Primary Outcome of Hospitalization for Respiratory Syncytial Virus (RSV)–Associated Lower Respiratory Tract Infection and Secondary Outcomes Among Matched Infants

	No. (%)				
	Nirsevimab (n = 21 280)	RSVpreF vaccine (n = 21 280)	Between-group difference (95% CI), %	HR[a] (95% CI)	Adjusted HR[b] (95% CI)
Primary outcome					
Hospitalization for RSV-associated lower respiratory tract infection	212 (1.0)	269 (1.3)	-0.3 (-0.5 to -0.1)	0.79 (0.65 to 0.94)	0.74 (0.61 to 0.88)
Secondary outcomes					
RSV-associated lower respiratory tract infection					
With high-dependency unit admission[c]	58 (0.3)	67 (0.3)	0 (-0.1 to 0.1)	0.86 (0.61 to 1.23)	0.87 (0.60 to 1.25)
With pediatric intensive care unit admission	55 (0.3)	101 (0.5)	-0.2 (-0.3 to -0.1)	0.54 (0.39 to 0.76)	0.58 (0.42 to 0.80)
With ventilatory support	51 (0.2)	89 (0.4)	-0.2 (-0.3 to -0.1)	0.56 (0.40 to 0.79)	0.57 (0.40 to 0.81)
With oxygen therapy[d]	39 (0.2)	76 (0.4)	-0.2 (-0.3 to -0.1)	0.51 (0.34 to 0.76)	0.56 (0.38 to 0.81)



HR indicates hazard ratio; RSVpreF, RSV prefusion protein F. The median follow-up was 84 days (IQR, 70-99 days) for both infants with passive immunization with nirsevimab and those with immunization from maternal vaccination with the RSVpreF vaccine. Time zero and the censoring definitions used were identical in both groups.

[a]Unweighted data. Infants were matched by the variables of sex, gestational age, day of discharge from the maternity ward, and region of residence.

[b]Derived using an inverse probability of treatment weighting method that was applied to the matched dataset to further balance the residual covariates.

[c]Defined as a unit providing continuous monitoring and specialized care for infants requiring a higher level of observation and treatment than standard pediatric wards but not an intensive care unit.

[d]Includes the administration of supplemental oxygen but does not include ventilator or respiratory support.

over a median follow-up of nearly 4 months (IQR, 76-125 days), aligning with the duration of an RSV season.[11] In contrast, maternal RSVpreF vaccination depends on administration within a limited gestational window and on adequate placental antibody transfer. Real-world data on the durability of RSVpreF vaccine–derived infant protection remain limited. In this study, the lower observed risks with nirsevimab beyond 30 and 60 days of follow-up may reflect potential waning of maternally derived antibodies or insufficient initial antibody levels among some infants in the RSVpreF vaccine group. Past studies have shown that maternal antibody transfer depends more on the time between vaccination and delivery than on gestational age at vaccination.[36,37] In the current study, the results did not differ by vaccination-to-delivery interval, and inclusion of vaccinations before 32 weeks during pregnancy yielded similar results.

This study compared outcomes after passive immunization with nirsevimab vs RSVpreF vaccination, and its findings should not be interpreted as evidence against the efficacy of the RSVpreF vaccine. Although nirsevimab offers direct infant protection and is less dependent on gestational timing, its affordability in low- and middle-income countries remains uncertain. In high-income settings, however, its feasibility and acceptance are more evident. In a French maternity ward, 91.6% of parents accepted nirsevimab for their newborns (without excess adverse events).[38] Data from the US indicated higher uptake at hospital discharge than for maternal vaccination during pregnancy.[39] Conversely, maternal RSVpreF vaccination may be more practical in settings with strong prenatal programs but limited postnatal follow-up. Although nirsevimab is associated with lower RSV-related hospitalization risk, its broad use could theoretically create selective pressure on the virus, but no major resistance mutations have been detected yet.[40,41] In contrast, RSVpreF vaccines generate active immunity against multiple neutralizing epitopes, making immune evasion less likely. The Global Pediatric Pulmonology Alliance and international expert reviews highlight that both products should be viewed as complementary tools.[42]

This study did not assess the safety of the 2 agents. Prior evidence indicates that nirsevimab has demonstrated a favorable safety profile in both trials and real-world settings. In contrast, early trials of the RSVpreF vaccine raised concern about a potential association with preterm birth,[43,44] but a more recent trial found no difference in overall prematurity rate.[14] Furthermore, data from real-world settings found no increased risk of preterm birth when RSVpreF vaccination occurred within the recommended 32- to 36-week window.[45,46]

This study has several strengths. The French National Health Data System provides comprehensive, longitudinal health care information for the entire French population with detailed data on maternal and infant characteristics, allowing extensive adjustment for potential confounders. Missing data and the misclassification of exposure or outcomes are possible but rare owing to the routinely validated coding of the diagnoses and procedures. The study design accounted for calendar-time bias, variable exposure uptake, and baseline differences. Immortal time bias was minimized via the use of matching, inverse probability weighting, and initiating follow-up at maternity discharge. Last, this study aligned the timing of eligibility assessment, treatment assignment, and start of follow-up within the same RSV epidemic period and population and provides an opportunity to compare associations between maternal RSVpreF vaccination and infant

Figure 3. Subgroup Analyses for Primary Outcome of Hospitalization for Respiratory Syncytial Virus (RSV)–Associated Lower Respiratory Tract Infection Among Matched Infants

Subgroup analysis	No./total (%)		Follow-up, median (IQR)	Between-group difference (95% CI), %	HR[a] (95% CI)	Adjusted HR[b] (95% CI)
	Nirsevimab	RSVpreF vaccine				
Sex						
Male	122/10 998 (1.1)	165/10 998 (1.5)	84 (70 to 99)	-0.4 (-0.7 to -0.1)	0.74 (0.58 to 0.93)	0.68 (0.53 to 0.87)
Female	90/10 282 (0.9)	104/10 282 (1.0)	84 (70 to 100)	-0.1 (-0.4 to 0.1)	0.86 (0.65 to 1.15)	0.81 (0.61 to 1.09)
Gestational age, wk						
Preterm birth (<37)	3/278 (1.1)	6/278 (2.2)	87 (70 to 102)	-1.1 (-2.8 to 0.6)	0.50 (0.13 to 2.00)	0.28 (0.06 to 1.37)
Term birth (≥37)	209/21 002 (1.0)	263/21 002 (1.3)	84 (70 to 99)	-0.3 (-0.5 to -0.1)	0.79 (0.66 to 0.95)	0.75 (0.62 to 0.90)
French Deprivation Index[c]						
Least deprived (Q1 and Q2)	44/4493 (1.0)	50/4493 (1.1)	87 (71 to 101)	-0.1 (-0.6 to 0.3)	0.88 (0.59 to 1.32)	0.81 (0.53 to 1.25)
Most deprived (Q3, Q4, and Q5)	67/7132 (0.9)	95/7132 (1.3)	85 (70 to 98)	-0.4 (-0.7 to 0)	0.70 (0.52 to 0.96)	0.66 (0.47 to 0.92)
Time since cohort entry, d						
0-7	15/21 279 (0.1)	5/21 279 (<0.1)	7 (7 to 7)	0 (0 to 0.1)	3.03 (1.09 to 8.33)	2.94 (1.19 to 7.69)
8-30	97/21 252 (0.4)	116/21 252 (0.5)	22 (22 to 22)	-0.1 (-0.2 to 0)	0.83 (0.64 to 1.10)	0.79 (0.60 to 1.05)
31-60	73/21 035 (0.3)	109/21 035 (0.5)	29 (29 to 29)	-0.2 (-0.3 to -0.1)	0.67 (0.50 to 0.90)	0.62 (0.45 to 0.84)
>60 (maximum of 148)	26/19 849 (0.1)	39/19 849 (0.2)	25 (12 to 40)	-0.1 (-0.2 to 0)	0.67 (0.41 to 1.10)	0.51 (0.30 to 0.86)
Time between RSVpreF vaccine and inclusion, wk						
<5	83/7311 (1.1)	102/7311 (1.4)	88 (72 to 105)	-0.3 (-0.6 to 0)	0.81 (0.61 to 1.09)	0.72 (0.53 to 0.99)
≥5	129/13 969 (0.9)	167/13 969 (1.2)	81 (69 to 95)	-0.3 (-0.5 to 0)	0.77 (0.61 to 0.96)	0.74 (0.58 to 0.93)
Description of period of RSV circulation intensity						
Lower (Oct 1–Nov 14)	1/3827 (<0.1)	2/3827 (0.1)	9 (4 to 17)	0 (-0.1 to 0.1)	0.50 (0.05 to 5.56)	0.40 (0.03 to 5.26)
Higher (Nov 15–Jan 5)	132/21 274 (0.6)	174/21 274 (0.8)	26 (15 to 37)	-0.2 (-0.4 to 0)	0.76 (0.61 to 0.95)	0.76 (0.60 to 0.95)
Lower (Jan 6–Feb 28)	78/20 960 (0.4)	93/20 960 (0.5)	53 (53 to 53)	-0.1 (-0.2 to 0.1)	0.84 (0.62 to 1.14)	0.69 (0.51 to 0.95)

HR indicates hazard ratio; RSVpreF, RSV prefusion protein F.

[a]Unweighted data. Infants were matched by the variables of sex, gestational age, day of discharge from the maternity ward, and region of residence.

[b]Derived using an inverse probability of treatment weighting method that was applied to the matched dataset to further balance the residual covariates.

[c]An ecological, area-based measure of social disadvantage in France, constructed at the commune level using 4 standardized variables (median household income per consumption unit, percentage of employed population in manual occupations, unemployment rate, and percentage of adults without a baccalaureate degree). Higher quintiles indicate greater deprivation. Q1 (quintile 1) indicates least deprived; Q2, slightly deprived; Q3, moderately deprived; Q4, highly deprived; Q5, most deprived.

nirsevimab immunization under real-world conditions, which addresses a critical evidence gap because these immunization strategies are being implemented internationally.

Limitations

This study has several limitations. First, because the RSVpreF vaccine became available in September and matching was performed on birth date, infants were by design born later in the RSV season. Consequently, infants born earlier in the RSV season may be underrepresented, which could limit generalizability to that group, although RSV activity was very limited before November.

Second, this study was conducted during the first season of maternal RSVpreF vaccination in France when eligibility was limited to 32 to 36 weeks' gestation (as in the US and Canada[47,48]), whereas the World Health Organization recommends vaccination beginning at 28 weeks' gestation. These findings reflect early national experience in France and should be reevaluated in future studies and settings.

Third, follow-up was limited to a single RSV season, precluding assessment of the durability of protection. Fourth, administrative data did not permit analysis by RSV subtype.

Fifth, the subgroup analyses were not stratified beyond 60 days of follow-up, limiting assessment of longer-term differences between the 2 preventive strategies. Sixth, unmeasured confounding (such as the health-seeking behavior of the parents, household smoking, or day care attendance) could not be excluded.

Conclusions

Compared with maternal vaccination with the RSVpreF vaccine, passive infant immunization with nirsevimab was associated with lower risks of RSV-related hospitalization and severe outcomes. These findings reflect the first RSV season with use of these immunization strategies in mainland France; their use should be reevaluated in future studies.

ARTICLE INFORMATION

Accepted for Publication: November 17, 2025.

Published Online: December 22, 2025. doi:10.1001/jama.2025.24082

Author Contributions: Dr Jabagi and Ms Bertrand 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.
Concept and design: All authors.
Acquisition, analysis, or interpretation of data: Jabagi, Bertrand, Gabet, Olié, Zureik.
Drafting of the manuscript: Jabagi, Zureik.
Critical review of the manuscript for important intellectual content: Bertrand, Gabet, Kolla, Olié, Zureik.
Statistical analysis: Jabagi, Bertrand, Gabet, Zureik.
Supervision: Jabagi, Gabet, Olié, Zureik.

Conflict of Interest Disclosures: None reported.

Funding/Support: This study was funded by the French National Agency for Medicines and Health Products Safety and the French National Health Insurance.

Role of the Funder/Sponsor: The funders/sponsors had a role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Data Sharing Statement: See Supplement 2.

Additional Contributions: We thank Nicolas Minier, MPH, PhD (French National Agency for Medicines and Health Products Safety and French National Health Insurance [EPI-PHARE]), for his assistance in preparing the graphical figures. Mr Minier did not receive any compensation for his contribution.

REFERENCES

1. Li Y, Wang X, Blau DM, et al; Respiratory Virus Global Epidemiology Network; RESCEU Investigators. Global, regional, and national disease burden estimates of acute lower respiratory infections due to respiratory syncytial virus in children younger than 5 years in 2019: a systematic analysis. *Lancet*. 2022;399(10340):2047-2064. doi:10.1016/S0140-6736(22)00478-0

2. Shi T, McAllister DA, O'Brien KL, et al; RSV Global Epidemiology Network. Global, regional, and national disease burden estimates of acute lower respiratory infections due to respiratory syncytial virus in young children in 2015: a systematic review and modelling study. *Lancet*. 2017;390(10098):946-958. doi:10.1016/S0140-6736(17)30938-8

3. European Medicines Agency. Beyfortus. Published 2022. Accessed September 2, 2025. https://www.ema.europa.eu/en/medicines/human/EPAR/beyfortus

4. US Food and Drug Administration. FDA approves new drug to prevent RSV in babies and toddlers. Published 2024. Accessed September 2, 2025. https://www.fda.gov/news-events/press-announcements/fda-approves-new-drug-prevent-rsv-babies-and-toddlers

5. US Food and Drug Administration. FDA approves first vaccine for pregnant individuals to prevent RSV in infants. Published 2024. Accessed September 2, 2025. https://www.fda.gov/news-events/press-announcements/fda-approves-first-vaccine-pregnant-individuals-prevent-rsv-infants

6. European Medicines Agency. First RSV vaccine to protect infants up to 6 months of age and older adults. Published 2023. Accessed September 2, 2025. https://www.ema.europa.eu/en/news/first-rsv-vaccine-protect-infants-6-months-age-and-older-adults

7. Griffin MP, Yuan Y, Takas T, et al; Nirsevimab Study Group. Single-dose nirsevimab for prevention of RSV in preterm infants. *N Engl J Med*. 2020;383(5):415-425. doi:10.1056/NEJMoa1913556

8. Hammitt LL, Dagan R, Yuan Y, et al; MELODY Study Group. Nirsevimab for prevention of RSV in healthy late-preterm and term infants. *N Engl J Med*. 2022;386(9):837-846. doi:10.1056/NEJMoa2110275

9. Drysdale SB, Cathie K, Flamein F, et al; HARMONIE Study Group. Nirsevimab for prevention of hospitalizations due to RSV in infants. *N Engl J Med*. 2023;389(26):2425-2435. doi:10.1056/NEJMoa2309189

10. Sumsuzzman DM, Wang Z, Langley JM, Moghadas SM. Real-world effectiveness of nirsevimab against respiratory syncytial virus disease in infants: a systematic review and meta-analysis. *Lancet Child Adolesc Health*. 2025;9(6):393-403. doi:10.1016/S2352-4642(25)00093-8

11. Jabagi MJ, Cohen J, Bertrand M, Chalumeau M, Zureik M. Nirsevimab effectiveness at preventing RSV-related hospitalization in infants. *NEJM Evid*. 2025;4(3):EVIDoa2400275. doi:10.1056/EVIDoa2400275

12. Ares-Gómez S, Mallah N, Santiago-Pérez MI, et al; NIRSE-GAL Study Group. Effectiveness and impact of universal prophylaxis with nirsevimab in infants against hospitalisation for respiratory syncytial virus in Galicia, Spain: initial results of a population-based longitudinal study. *Lancet Infect Dis*. 2024;24(8):817-828. doi:10.1016/S1473-3099(24)00215-9

13. Moline HL, Toepfer AP, Tannis A, et al; New Vaccine Surveillance Network Collaborators. Respiratory syncytial virus disease burden and nirsevimab effectiveness in young children from 2023-2024. *JAMA Pediatr*. 2025;179(2):179-187. doi:10.1001/jamapediatrics.2024.5572

14. Kampmann B, Madhi SA, Munjal I, et al; MATISSE Study Group. Bivalent prefusion F vaccine in pregnancy to prevent RSV illness in infants. *N Engl J Med*. 2023;388(16):1451-1464. doi:10.1056/NEJMoa2216480

15. Marc GP, Vizzotti C, Fell DB, et al; BERNI Study Working Group. Real-world effectiveness of RSVpreF vaccination during pregnancy against RSV-associated lower respiratory tract disease leading to hospitalisation in infants during the 2024 RSV season in Argentina (BERNI study): a multicentre, retrospective, test-negative, case–control study. *Lancet Infect Dis*. 2025;25(9):1044-1054. doi:10.1016/S1473-3099(25)00156-2

16. Santé Publique France (French National Health Data System). Documentation du SNDS and SNDS OMOP. Accessed October 21, 2025. https://documentation-snds.health-data-hub.fr/snds/formation_snds/sante_publique_france.html

17. Semenzato L, Le Vu S, Botton J, et al. Long-term prognosis of patients with myocarditis attributed to COVID-19 mRNA vaccination, SARS-CoV-2 infection, or conventional etiologies. *JAMA*. 2024;332(16):1367-1377. doi:10.1001/jama.2024.16380

18. Boutin S, Bertrand M, Cohen JF, Zureik M, Chalumeau M, Jabagi MJ. Sociodemographic characteristics of infants receiving nirsevimab. *JAMA Netw Open*. 2025;8(4):e254341. doi:10.1001/jamanetworkopen.2025.4341

19. Domachowske J, Madhi SA, Simões EAF, et al; MEDLEY Study Group. Safety of nirsevimab for RSV in infants with heart or lung disease or prematurity. *N Engl J Med*. 2022;386(9):892-894. doi:10.1056/NEJMc2112186

20. Hall CB. Respiratory syncytial virus and parainfluenza virus. *N Engl J Med*. 2001;344(25):1917-1928. doi:10.1056/NEJM200106213442507

21. Carroll KN, Gebretsadik T, Griffin MR, et al. Increasing burden and risk factors for bronchiolitis-related medical visits in infants enrolled in a state health care insurance plan. *Pediatrics*. 2008;122(1):58-64. doi:10.1542/peds.2007-2087

22. Glezen WP, Paredes A, Allison JE, Taber LH, Frank AL. Risk of respiratory syncytial virus infection for infants from low-income families in relationship to age, sex, ethnic group, and maternal antibody level. *J Pediatr*. 1981;98(5):708-715. doi:10.1016/S0022-3476(81)80829-3

23. Rey G, Jougla E, Fouillet A, Hémon D. Ecological association between a deprivation index and mortality in France over the period 1997-2001: variations with spatial scale, degree of urbanicity, age, gender and cause of death. *BMC Public Health*. 2009;9:33. doi:10.1186/1471-2458-9-33

24. Pornet C, Delpierre C, Dejardin O, et al. Construction of an adaptable European transnational ecological deprivation index: the French version. *J Epidemiol Community Health*. 2012;66(11):982-989. doi:10.1136/jech-2011-200311

25. Lassalle M, Zureik M, Dray-Spira R. Proton pump inhibitor use and risk of serious infections in young children. *JAMA Pediatr*. 2023;177(10):1028-1038. doi:10.1001/jamapediatrics.2023.2900

26. Meyer A, Marty L, Drouin J, Weill A, Carbonnel F, Dray-Spira R. Risks of 75 major congenital malformations after in utero exposure to thiopurines and anti-TNF for maternal inflammatory bowel disease. *Clin Gastroenterol Hepatol*. 2025;23(12):2292-2305.e12. doi:10.1016/j.cgh.2025.01.008

27. Hernán MA, Robins JM. Using big data to emulate a target trial when a randomized trial is not available. *Am J Epidemiol*. 2016;183(8):758-764. doi:10.1093/aje/kwv254

28. Xu S, Ross C, Raebel MA, Shetterly S, Blanchette C, Smith D. Use of stabilized inverse propensity scores as weights to directly estimate relative risk and its confidence intervals. *Value Health*. 2010;13(2):273-277. doi:10.1111/j.1524-4733.2009.00671.x

29. Harder VS, Stuart EA, Anthony JC. Propensity score techniques and the assessment of measured covariate balance to test causal associations in psychological research. *Psychol Methods*. 2010;15(3):234-249. doi:10.1037/a0019623

30. Therneau TM, Grambsch PM. *Modeling Survival Data: Extending the Cox Model*. Springer; 2000. doi:10.1007/978-1-4757-3294-8

31. Xu H, Aparicio C, Wats A, et al. Estimated effectiveness of nirsevimab against respiratory syncytial virus. *JAMA Netw Open*. 2025;8(3):e250380. doi:10.1001/jamanetworkopen.2025.0380

32. Moreno-Pérez D, Korobova A, Croche-Santander FB, et al. Nirsevimab prophylaxis for reduction of respiratory syncytial virus complications in hospitalised infants: the multi-centre study during the 2023-2024 season in Andalusia, Spain (NIRSEGRAND). *Vaccines (Basel)*. 2025;13(2):175. doi:10.3390/vaccines13020175

33. Vazquez-Lopez P, Rivas-Garcia A, Luaces-Cubells C, et al. Changes in care in Spanish pediatric emergency departments after the first immunization with nirsevimab. *Pediatr Emerg Care*. 2025;41(5):365-371. doi:10.1097/PEC.0000000000003339

34. McLachlan I, et al. Vaccine effectiveness of the maternal RSVpre-F vaccine against severe disease in infants in Scotland, UK: national population-based case-control and cohort analyses. *medRxiv*. Posted August 6, 2025. doi:10.1101/2025.08.01.25332515

35. Williams TC, Marlow R, Cunningham S, et al; PERUKI & BronchStart Collaboration. Bivalent prefusion F vaccination in pregnancy and respiratory syncytial virus hospitalisation in infants in the UK: results of a multicentre, test-negative, case-control study. *Lancet Child Adolesc Health*. 2025;9(9):655-662. doi:10.1016/S2352-4642(25)00155-5

36. Jasset OJ, Lopez Zapana PA, Bahadir Z, et al. Enhanced placental antibody transfer efficiency with longer interval between maternal respiratory syncytial virus vaccination and birth. *Am J Obstet Gynecol*. 2025;232(6):554.e1-554.e15. doi:10.1016/j.ajog.2024.10.053

37. Gomme J, Wanlapakorn N, Ha HTT, Leuridan E, Herzog SA, Maertens K. The impact of timing of pertussis vaccination during pregnancy on infant antibody levels at birth: a multi-country analysis. *Front Immunol*. 2022;13:913922. doi:10.3389/fimmu.2022.913922

38. Ocana de Sentuary C, Testard C, Lagrée M, et al. Acceptance and safety of the RSV-preventive treatment of newborns with nirsevimab in the maternity department: a prospective longitudinal cohort study in France. *EClinicalMedicine*. 2024;79:102986. doi:10.1016/j.eclinm.2024.102986

39. US Centers for Disease Control and Prevention. Infant protection against respiratory syncytial virus (RSV) by maternal RSV vaccination or receipt of nirsevimab, and intent for nirsevimab receipt, United States. Published 2025. Accessed October 21, 2025. https://www.cdc.gov/rsvvaxview/dashboard/nirsevimab-coverage-infants.html

40. Núñez O, Olmedo C, Moreno-Perez D, et al; Nirsevimab Effectiveness Study Collaborators. Effectiveness of catch-up and at-birth nirsevimab immunisation against RSV hospital admission in the first year of life: a population-based case-control study, Spain, 2023/24 season. *Euro Surveill*. 2025;30(5):2400596. doi:10.2807/1560-7917.ES.2025.30.5.2400596

41. Fourati S, Reslan A, Bourret J, et al; POLYRES Investigators. Genotypic and phenotypic characterisation of respiratory syncytial virus after nirsevimab breakthrough infections: a large, multicentre, observational, real-world study. *Lancet Infect Dis*. 2025;25(3):301-311. doi:10.1016/S1473-3099(24)00570-X

42. Zar HJ. New advances in RSV: is prevention attainable? *Pediatr Pulmonol*. 2025;60(suppl 1):S120-S122. doi:10.1002/ppul.27310

43. Walsh EE, Pérez Marc G, Zareba AM, et al; RENOIR Clinical Trial Group. Efficacy and safety of a bivalent RSV prefusion F vaccine in older adults. *N Engl J Med*. 2023;388(16):1465-1477. doi:10.1056/NEJMoa2213836

44. Falsey AR, Walsh EE, Scott DA, et al. Phase 1/2 randomized study of the immunogenicity, safety, and tolerability of a respiratory syncytial virus prefusion F vaccine in adults with concomitant inactivated influenza vaccine. *J Infect Dis*. 2022;225(12):2056-2066. doi:10.1093/infdis/jiab611

45. Blauvelt CA, Zeme M, Natarajan A, et al. Respiratory syncytial virus vaccine and nirsevimab uptake among pregnant people and their neonates. *JAMA Netw Open*. 2025;8(2):e2460735. doi:10.1001/jamanetworkopen.2024.60735

46. Gabet A, Bertrand M, Jabagi MJ, Kolla E, Olié V, Zureik M. Maternal and neonatal outcomes after respiratory syncytial virus prefusion F protein vaccination during pregnancy: analysis from the 2024-2025 immunization campaign in France. *Obstet Gynecol*. Published online November 13, 2025. doi:10.1097/AOG.0000000000006121

47. Public Health Agency of Canada. Respiratory syncytial virus (RSV) vaccines: Canadian immunization guide. Published 2023. Accessed October 21, 2025. https://www.canada.ca/en/public-health/services/publications/healthy-living/canadian-immunization-guide-part-4-active-vaccines/respiratory-syncytial-virus.html

48. US Centers for Disease Control and Prevention. RSV vaccine guidance for pregnant women. Published 2025. Accessed October 21, 2025. https://www.cdc.gov/rsv/hcp/vaccine-clinical-guidance/pregnant-people.html