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RESEARCH ARTICLE

Impact and Effectiveness of Universal Respiratory Syncytial Virus Vaccination During Pregnancy on Infant Hospitalizations in Buenos Aires: A Retrospective Cohort Study

[version 1]

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Abstract

Background

Respiratory syncytial virus (RSV) is a major cause of hospitalizations and mortality in young infants worldwide. The RSVpreF maternal immunization (MI) has been recently introduced in Argentina.

Methods

To assess the impact of RSVpreF MI on RSV hospitalizations due to ALRTI we used a Poisson model. We compared pre-implementation years with the first cold season following the vaccine introduction in 2024, utilizing data from a multicenter, retrospective cohort study at three hospitals in Buenos Aires, Argentina. Additionally, a nested test-negative case-control study was conducted to estimate the vaccine effectiveness (VE) against RSV-related ALRTI hospitalizations, pediatric intensive care (PICU) admissions, and extended hospital stays in infants. The eligible population for VE analysis included all ALRTI-hospitalized infants under 6 months, tested for RSV, whose mothers were eligible for MI.

Findings

RSVpreF MI reduced RSV-ALRTI hospitalizations in infants under 6 months by 33.6% (95%CI 29.5-37.2) compared to expected cases from previous years. The number needed to immunize to prevent an RSV-related hospitalization was 83·9 (95%CI 65·9 – 185·4). The VE was 66.1% (95% CI 30.1-83.8) for infants under 6 months and 80.8% (95%CI 62.8-90.5) for infants under 3 months, adjusted for age, sex, comorbidities, and epidemiological weeks (when possible). The adjusted VE for PICU admission was 87.2% (95%CI 52.6-97.0) and 88.6% (95%CI 62.3-97.1) for extended hospital stays in infants under 6 months.

Interpretation

MI averted one-third of RSV-related hospitalizations and reduced the odds of ALRTI hospitalizations in infants under 6 months.

Keywords
Respiratory syncytial virus, vaccine effectiveness, vaccine impact, maternal vaccination

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Summary
The study evaluates the impact and effectiveness of RSVpreF maternal immunization. It demonstrates a significant reduction in RSV-related hospitalizations in infants under six months, highlighting the robust vaccine's effectiveness in preventing severe RSV-ALRTI in this age group.

Introduction
Respiratory syncytial virus (RSV) is a major public health threat worldwide.[1] Every year, millions of young infants are hospitalized, and thousands succumb to the virus, predominantly in low- and middle-income countries (LMICs) where structural poverty limits access to timely and adequate medical treatments.[2,3] Annual RSV epidemics overwhelm emergency services, pediatric wards, and intensive care units, leading to delayed elective and chronic care, unsafe staffing levels, and underutilized resources during off-peak periods.[4,5]

In Argentina, RSV is estimated to cause nearly 250,000 clinical visits, 30,000 hospitalizations, over 450 deaths, and healthcare costs exceeding US$ 25 million annually in children under five.[6,7] Respiratory failure and in-hospital deaths from RSV predominantly affect term infants, with poor outcomes often linked to low-quality medical care.[8] However, the vast majority of RSV-related deaths occur at home or outside health facilities, often after families seek prior medical assistance.[9,10] Many of these home fatalities are misdiagnosed as sudden infant death syndrome, underestimating the virus's real impact for years.[9]

For decades, RSV immunization has been eagerly awaited to improve infant respiratory health.[11] Two products—Nirsevimab (AstraZeneca, and Sanofi), a long-acting monoclonal antibody for infants, and Bivalent Prefusion F (RSVpreF) vaccine (Pfizer) for pregnant individuals—completed phase 3 clinical trials, were licensed in over 53 countries and were recommended for national implementation by the World Health Organization's Strategic Advisory Group of Experts on Immunization (WHO SAGE).[11–15] Maternal immunization (MI) enhances immunity during pregnancy, transferring antibodies to the baby for lasting protection, while nirsevimab, given at birth, provides passive immunity, offering early-life protection.[13,14] Despite both interventions being authorized by Argentina's National Administration of Drugs, Food and Medical Devices (ANMAT), Argentina is the first country to introduce the RSVpreF maternal vaccine as the primary intervention in a national RSV immunization program in March 2024.[11]

The universal maternal vaccination strategy, implemented for the first time in Argentina, was conducted between 1st March and 31st August 2024, encompassing the period before and during the RSV season of high hospitalizations.[8,16,17] This strategy was incorporated into the National Vaccination Schedule, which provides free vaccinations for pregnant women between 32 and 36.6 weeks of gestation.[11,15] The RSVpreF MI coverage in the Metropolitan Area of Buenos Aires (MABA) was 55.3% and overall in Argentina 62%.[11,15]

The RSV impact and effectiveness of maternal immunization (RIMA) study is a hospital-based, multicenter, retrospective cohort study aimed at evaluating the impact and effectiveness of RSVpreF MI against RSV-related acute lower respiratory tract infection (ALRTI) hospitalizations, critical RSV-related ALRTI, and RSV-attributed deaths in infants aged 6 months or younger. This study also seeks to estimate the number of averted cases, and the number needed to immunize (NNI) to prevent one RSV-related ALRTI hospitalization. Here, we report the first-year results of RSVpreF implementation in the Metropolitan Area of Buenos Aires (MABA), Argentina's most densely populated region.[18]

Methods
Study design and population
As mentioned, the RIMA study is a multicenter, retrospective cohort, and hospital-based aimed at analyzing the impact and effectiveness of universal RSVpreF vaccination in pregnant individuals to prevent infant hospitalizations due to RSV-ALRTI in the MABA. We collected clinical, epidemiological, and etiological data from all infants aged 0 to 18 months—capturing those susceptible during their first and second RSV seasons—who were diagnosed with ALRTI and admitted to three public tertiary-level hospitals in the MABA region between January 1, 2018, and November 30, 2024. The study gathered information on hospitalization ALRTI episodes, and specific diagnoses coded according to International Classification of Diseases (ICD)-10 standards.[19] Data were collected on the following characteristics: sex, age, gestational age, comorbidities, health care insurance, and home location.[19] Inclusion criteria were a clinical diagnosis of ALRTI at admission and having at least one virological test done within 48 hours of hospitalization.[13] Patients were excluded if they did not undergo a molecular diagnosis test, were discharged within 24 hours of hospital admission, received Palivizumab, or resided outside the catchment area.[16] Maternal vaccination status was obtained from vaccination certificates or the Nominalized Federal Vaccination Registry platform.[11,16,20]

A nested test-negative case-control study was conducted to estimate the effectiveness of the RSVpreF MI in preventing RSV-related ALRTI hospitalizations in their infants, compared to infants of unvaccinated pregnant individuals.[21] The eligible population for vaccine effectiveness (VE) analysis included all ALRTI-hospitalized infants younger than 6 months born between 1st March and 9th November 2024, excluding those born before 32 weeks of gestational age or those whose gestational age had not reached at least 32 weeks during the vaccination campaign, as outlined in the table of dates and gestational weeks. Cases were defined as infants 6 months old or younger, whose mothers were eligible for vaccination, were hospitalized with a diagnosis of ALRTI, and had a laboratory-confirmed RSV-positive test. Controls were defined as infants 6 months old or younger, whose mothers were eligible for vaccination and were hospitalized with a diagnosis of ALRTI and a laboratory-confirmed RSV-negative test. The exclusion criteria for the VE analysis were as follows: 1) only the first RSV-related ALRTI hospitalization or the earliest non-RSV hospitalization was included in the analysis, with subsequent episodes excluded; 2) infants whose mothers were not immunized within the recommended timeframe (at least 14 days before birth) for the vaccine to be effective; and 3) patients with nosocomial RSV infections were excluded.[21]

Molecular diagnosis

Nasal swabs or aspirates were obtained from all hospitalized infants with ALTRI and tested for RSV, human rhinovirus (hRV), influenza A viruses (Flu-A), human metapneumovirus (hMPV), Parainfluenza virus type 3 (PIV3), human adenovirus (HAdV), and since 2020 for coronavirus (SARS-CoV-2), using standardized multiplex real-time polymerase chain reaction (RT-PCR) in each hospital and reported by a certified laboratory staff.[8,16]

Ethical considerations

Since the study utilizes a retrospective cohort design and relies on information from medical records, informed consents were not obtained. This decision was made in accordance with the approval and support of the Institutional Review Board of the participating hospitals (Comité de Ética e Investigación del Hospital de Niños Pedro de Elizalde code 6828 approved on March 15, 2022, Comité Institucional de Revisión de Protocolos de Investigación del Hospital de Niños Sor María Ludovica approved on October 28, 2021, Comité de Ética e Investigación de Hospital Nacional Prof. Alejandro Posadas approved on September 8 2022). There is no personal identification data in the study, all individuals were allocated to the study with a unique anonymous identifier. Researchers were trained in good clinical practice and adhere to the Helsinki declaration.

Statistical analysis

For comparisons of variables between groups and the univariable analysis, Pearson's χ^2 test was applied to categorical variables, and Student's t-test or Wilcoxom's test to continuous variables, with a p-value < 0.05 considered statistically significant. All variables were analyzed for missing data, and none exhibited more than 10% missing values.[22]

The impact of RSVpreF MI on RSV cases among ALTRI-related hospitalizations was assessed using a model with Poisson regression.[23] To estimate the weekly hospitalization rates among infants aged ≤ 6 months during their first RSV season (Group 1) we used the weekly hospitalization rates of infants within their second RSV season (aged 12 to 18 months, Group 2) as an offset[19,24] We used data between epidemiological weeks 15 and 40 from the 2018, 2019, and 2023 RSV seasons, ensuring that Group 1 participants in 2024 were already within the period when vaccinated individuals were recorded To estimate the number of RSV averted cases, among ALTRI hospitalizations directly prevented by the immunization campaign, cumulative hospitalization rates were calculated using a corrected week approach based on deciles of cumulative incidence within the specified epidemiological weeks.[25] This adjustment allowed for better comparability of epidemic timing across seasons. Thus, for 2024, we assumed that Group 2 hospitalization rates reflected the natural dynamics of RSV in the absence of vaccination.[19,24] This assumption was based on Group 2 experiencing its second RSV season during both the vaccination campaign and the RSV season, making it a suitable reference for the unvaccinated scenario.[19] To estimate the expected number of RSV cases among ALRTI hospitalizations in 2024 in the absence of vaccination, we used predicted values from the Poisson model for Group 1 based on historical trends.[26–29]

To assess the VE of RSVpreF MI in preventing RSV-ALRTI hospitalizations in infants 6 months of age or younger, a test-negative case-control study required a sample of 270 participants to achieve 90% power and a significance level of 0.05, assuming an expected VE of 60%. This calculation assumes an estimated 35% overall vaccine coverage during the vaccination season in the catchment region. Multiple logistic regression was applied to estimate the adjusted Odds Ratio (aOR) and 95% Confidence Interval (CI). The models were adjusted by age in months, sex, and comorbidities. Univariate analysis was performed to evaluate the effect of potential confounding such as prematurity, epidemiological week of hospital admission, and health insurance; those variables with p-values <0.20 were included in the multivariate analysis. Only if aOR was modified were at least 10% of these confounders retained in the final models.[19,21] The RSVpreF adjusted

VE was estimated as: aVE=(1-aOR)*100. A natural cubic spline with 1 knot was applied to capture non-linear relationships between the epidemiological week and vaccine effectiveness. All statistical analyses were performed using R Studio software (R version 4.2.2), and data curation was done using STATA (version 17), and Python (version 3.13.0) software.

Results

Impact of RSVpreF maternal vaccine

Throughout seven years of surveillance, 8,407 infants aged ≤18 months were enrolled after being hospitalized with ALRTI. Of these, 2,498 were excluded as they were born during the COVID-19 pandemic years (2020–2022), which affected RSV circulation.[16] Between epidemiological weeks 15 and 40, 4,807 ALTRI hospitalizations were recorded. After excluding infants aged 6–12 months and rehospitalization cases (n=1,434), 3,373 cases were included for impact analysis.

In a scenario without RSVpreF MI, an estimated 397 RSV hospitalizations (95% CI 374–420) would be expected among infants 0-6 months during epidemiological weeks 15–40 of 2024. The vaccination strategy prevented an estimated 133 cases (95% CI 110–156), equivalent to 215.71 (178.44–252.56) averted RSV cases per 1,000 infants with ALRTI-related hospitalizations (Table 1). The estimated reduction in 2024 was 33.57% (95% CI 29.48–37.17) in RSV cases relative to the expected number (Table 1). The NNI to prevent one RSV-ALRTI hospitalization was calculated at 83.87 (95% CI 65.91–185.38). Interestingly, the predicted cumulative incidence for past RSV seasons closely aligned with observed cases, whereas during the vaccination period, it significantly declined compared to predictions (Figure 1).

RSV maternal vaccine effectiveness

From January 1st to November 30th 2024, 647 infants 6 months old or younger were hospitalized, and 399 were born between March 1 and November 9, 2024, to pregnant individuals who were candidates for vaccination, and vaccination status was available. Twenty-three excluded cases were born within the first 14 days after vaccination, not ensuring a significant transplacental transfer of antibodies. After excluding 53 rehospitalizations, 323 infants were incorporated in the VE analysis, with no recorded cases of palivizumab administration found in the study.

Among the 323 infants, sex and age were evenly distributed between the vaccinated and unvaccinated groups (p=0.442 and p=0.095, respectively). Overall, 58.2% were male, the median age was 2.7 months (IQR 1.7 to 3.8 months), 57.6% were younger than 3 months, and 42.4% were between 3 and 6 months old (Table 2). Prematurity was significantly more common in the unvaccinated group (p=0.007), with 18.1% of infants born preterm, compared to 7.1% in the vaccinated group (Table 2). Comorbidities were present in 8.7% of infants, with no significant differences found according to RSV vaccination status (p=0.610) (Table 2). Since the study was conducted among a vulnerable population, only 8.4% had private health insurance, with no significant difference observed between the two groups (p=0.537). Regional differences were observed in the infants' origins, highlighting disparities in vaccination coverage (p = 0.013). Across the RSV season, 69.5% of the unvaccinated group were hospitalized due to ALRTI compared to 43.4% in the vaccinated group, with a statistically significant difference (p < 0.001).

Viral pathogens were tested in all participants, resulting in an overall positive rate of 74.5%. The most detected pathogen was RSV (40.6%), followed by hMPV (17.3%), PIV3 (10.2%), hRV (4.3%), SARS-CoV-2 (2.5%), Influenza A or B (2.5%), and HAdV (0.9%). Other viral pathogens were detected in 4.3% of cases. RSV detection showed a statistically significant difference between the two groups, with a positive rate of 17.7% in the vaccinated group compared to 52.9% in the unvaccinated group (p < 0.001) (Table 2 and Figure 2). Parainfluenza virus was more frequently found in the vaccinated group compared with the unvaccinated group. Coinfections were identified in 3.5% of the vaccinated group and 12.9% of the unvaccinated group, also showing a statistically significant difference (p=0.007). Overall, 20.7% of hospitalized infants were admitted to PICU, without a significant difference between the two groups (p=0.066) (Table 2). However, PICU admission rates differed significantly between cases (n=45, 34.3%) and controls (n=22, 11.4%).

Table 1. Summary of the impact of the 2024 vaccination campaign on RSV-related ALRI hospitalizations.

Measure	Value	95% CI
Observed cases	264.00	
Averted cases	133.39	110.35-156.18
Averted cases over expected (% relative reduction)	33.57	29.48-37.17
Averted number of cases per 1000	215.71	178.44-252.56
The number needed to immunize	83.87	65.91 – 185.38

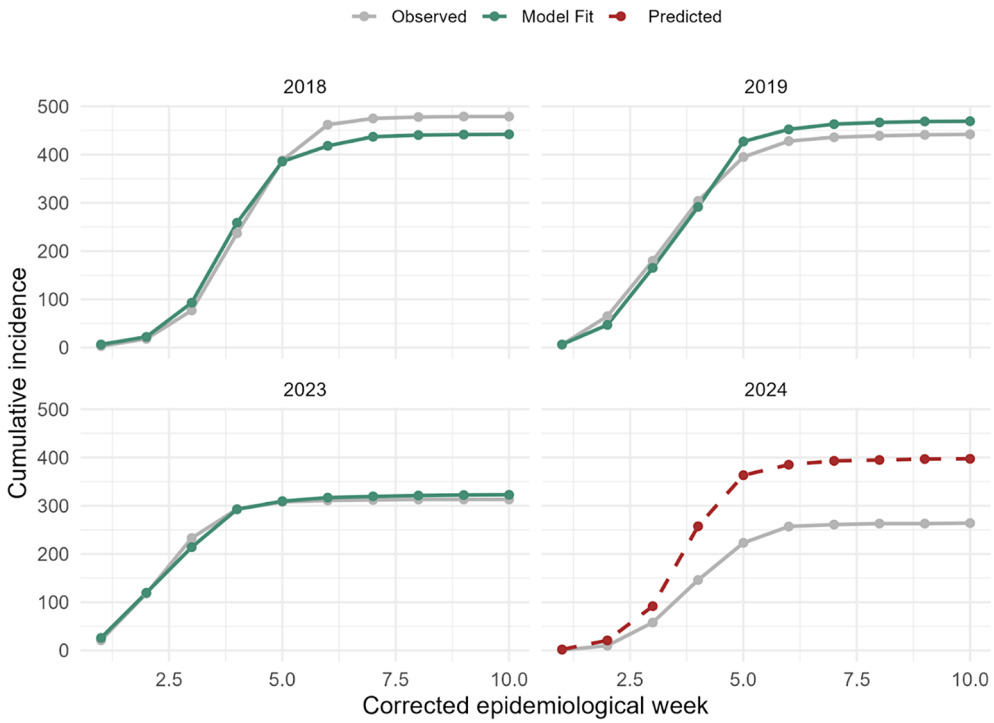

Figure 1. Model fit and predictions for cumulative RSV-related ALRI hospitalizations across seasons for infants during their first RSV season (2018, 2019, 2023, and 2024). The solid gray line represents the observed cumulative RSV incidence for infants during their first RSV season (aged 0–6 months, Group 1), while the solid green line shows the model fit for the same group in 2018, 2019, and 2023. As shown in Figure 1, the model demonstrates a reasonable fit to the cumulative training data for these years. The dashed red line corresponds to the model's prediction for the 2024 season, showing a marked divergence from the observed cumulative data for Group 1.

Table 2. Descriptive analysis of the population by vaccination status.

	Overall	Gestational vaccinated status n (%)		*p* value
		Unvaccinated	Vaccinated	
	(N=323)	(n=210)	(n =113)	
Male	188 (58.2)	119 (56.7)	69 (61.1)	.442
Median (IQR) age, months	2.7 (1.7-3.8)	2.9 (1.8-3.8)	2.7 (1.5-3.7)	.095
Age groups				.354
0-3 months	186 (57.6)	117 (55.7)	69 (61.1)	
3-6 months	137 (42.4)	93 (44.3)	44 (38.9)	
Preterm birth (born at <37 weeks gestation)	46 (14.2)	38 (18.1)	8 (7.1)	**.007**
Comorbidities	28 (8.7)	17 (8.1)	11 (9.8)	.610
Health insurance	27 (8.4)	19 (9.0)	8 (7.1)	.537
Residential area				**.013**
South	150 (46.4)	85 (40.5)	65 (57.5)	
Center	113 (34.4)	80 (38.1)	31 (27.4)	
West	62 (19.2)	45 (21.4)	17 (15.0)	
RSV season hospitalizations	195 (60.4)	146 (69.5)	49 (43.4)	**< .001**
ALRTI without a viral diagnosis	82 (25.5)	42 (20.1)	40 (35.7)	**.002**

Table 2. *Continued*

	Overall	Gestational vaccinated status n (%)		*p* value
		Unvaccinated	Vaccinated	
	(N=323)	(n=210)	(n =113)	
Viral agent				
Respiratory Syncytial Virus	131 (40.6)	111 (52.9)	20 (17.7)	**< .001**
Metapneumovirus	56 (17.3)	34 (16.2)	22 (19.5)	.458
Parainfluenza Virus	33 (10.2)	14 (6.7)	19 (16.8)	**.004**
Human Rhinovirus	14 (4.3)	9 (4.3)	5 (4.4)	.953
Sars-Coronavirus 2	8 (2.5)	4 (2.0)	4 (3.6)	.394
Influenza	8 (2.5)	6 (2.9)	2 (1.8)	.549
Human Adenovirus	3 (0.9)	2 (1.0)	1 (0.9)	.952
Others	14 (4.3)	12 (5.7)	2 (1.8)	.097
Coinfections	31 (9.6)	27 (12.9)	4 (3.5)	**.007**
PICU admission	67 (20.7)	50 (23.8)	17 (15.0)	.066

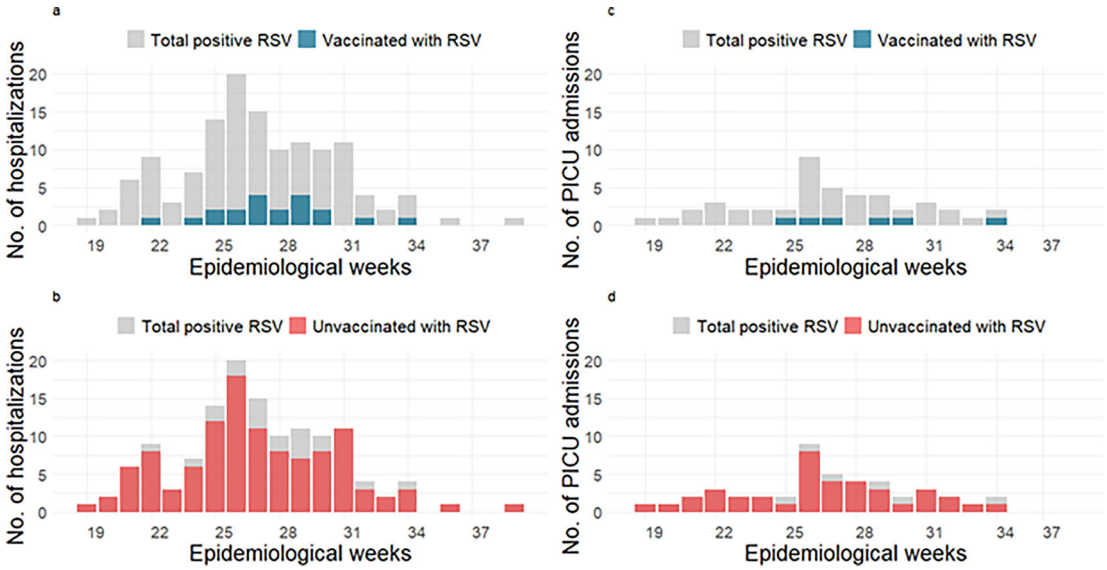

Figure 2. Comparisons of RSV-related ALTRI hospitalizations and PICU admissions between vaccination status. a) Comparison of Total RSV-related ALTRI Hospitalizations and RSV-related ALTRI Hospitalizations in Children of Gestationally Vaccinated Individuals with the PreF Vaccine, by epidemiological week. b) Comparison of Total RSV-related ALTRI Hospitalizations and RSV-related ALTRI Hospitalizations in Children of Gestationally Unvaccinated Individuals, by epidemiological week. c) Comparison of Total RSV-related ALTRI PICU admissions and RSV-related ALTRI PICU admissions in Children of Gestationally Vaccinated Individuals with the PreF Vaccine, by epidemiological week. d) Comparison of Total RSV-related PICU admissions and RSV-related ALTRI PICU admissions in Children of Gestationally Unvaccinated Individuals, by epidemiological week.

The aVE estimates of RSVpreF MI against RSV-related ALTRI hospitalizations in infants 6 months old or younger, was 66.10% (95% CI 30.13-83.83%) when adjusted for age, sex, comorbidities, and epidemiological week of hospital admission (Table 3). In infants 3 months old or younger, the effectiveness estimate was 80.77% (95% CI: 62.76-90.48%), when adjusted by age, sex, and comorbidities. RSVpreF MI showed protection against RSV-related PICU admissions with an effectiveness estimate of 87.21 (95%CI 52.62-97.01) and against RSV related-long hospital stays (≥11 days) with an effectiveness estimate of 88.64% (95%CI: 62.27-97.09%), both estimations adjusted for age, sex, and comorbidities. No deaths were recorded among these infants (Table 3).

Table 3. **RSVpreF vaccine effectiveness in reducing RSV-related ALRI hospitalizations in infant.**

Outcomes	Vaccinated pregnant individuals, n/N (%)		RSVpreF vaccine effectiveness	
	RSV-related ALRTI hospitalizations	non-RSV-related ALRI hospitalizations	aVE%	95%IC
RSV-ALRTI hospitalization				
≤ 6 months old†	20/131 (15.27)	93/192 (51.83)	66.10	30.13-83.83
≤3 months old*	16/88 (18.18)	53/98 (54.08)	80.77	62.76-90.48
RSV-PICU admission				
≤ 6 months old*	6/45 (13.33)	11/22 (50.00)	87.21	52.62-97.01
Long hospital stays*	6/54 (11.11)	14/36 (39.89)	88.64	62.27-97.09

RSV: respiratory syncytial virus; ALRTI: acute lower respiratory tract infection; aVE: adjusted vaccine effectiveness.
†Adjusted by sex, age in months, comorbidities, and epidemiological weeks.
*Adjusted by sex, age in months, and comorbidities.

No significant differences were found (p=0.594) in aVE when comparing vaccination occurring 15 to 27 days before delivery (62.21%, 95%CI 2.01-85.80) with vaccination occurring at least 27 days before delivery (73.08%, 95% 29.43-90.39), after adjusting for age, sex, comorbidities, and epidemiological week.

Discussion

Argentina's pioneering free universal vaccination for pregnant individuals in 2024 enabled real-world evaluation of RSVpreF across an entire RSV season in 2024. Our findings reveal a significant protective effect of RSVpreF MI against RSV-ALRTI hospitalizations, PICU admissions, and prolonged hospital stays. Maternal vaccination with RSVpreF reduced hospitalizations due to RSV-ALRTI by one-third and was associated with reduced odds of RSV-related ALRTI hospitalizations in infants younger than 6 months. The effectiveness was greatest among infants younger than 3 months and for those admitted to the PICU or with long hospital stays.

The results are consistent with the Matisse phase 3 randomized clinical trial (RCT), where the RSVpreF vaccine showed protective efficacy—82.4% within 90 days and 70.0% within 180 days—against severe RSV-associated medically attended ALRTI.[30] This evidence strongly reinforces the WHO SAGE recommendation for countries to implement MI strategies to protect young infants from severe RSV disease.[31] Additionally, these findings align with earlier modeling estimates that projected a 20 to 40% reduction in RSV-related hospitalizations, underscoring the transformative potential of maternal vaccination in public health.[6,32–34]

Our research revealed a 48% vaccination coverage among control individuals—slightly below the regional average and significantly lower than the national benchmark.[11,15] This disparity likely highlights unequal access to vaccination across various population sectors.[35,36] To address this gap, targeted efforts to raise awareness and improve access are critical.[37] Enhancing community outreach programs and engaging local healthcare providers can play a pivotal role in boosting vaccination rates within underserved groups.[37] Furthermore, with recent RCTs confirming the vaccine's safety, re-evaluating the optimal vaccination window during pregnancy is essential.[13,30,38] Identifying the most cost-effective timing will maximize the intervention's benefits and ensure maternal and infant safety while optimizing healthcare resources.[39,40]

Our study has some limitations. Our non-population-based design made estimating denominators challenging. Therefore, to assess RSV vaccination impact on ALRTI hospitalizations, we used a Poisson model with individual-level data, adjusting for RSV rates in the second group as a proxy for intergroup ratios.[19,41,42] The model's predictions are closely aligned with observed case counts in previous seasons. Another challenge we faced was estimating the exposed population to calculate important metrics such as the number of averted cases per 1,000 infants and NNI. To tackle this, we estimated the incidence of RSV-ALRTI hospitalizations in both exposed and non-exposed populations using available population data.[19,24] Our cohort's high RSV prevalence and low vaccination coverage likely influenced these estimations.[11,32,34] Future studies should focus on narrower geographic areas with robust population data to improve accuracy and address these limitations.[16] Finally, seasonality also influenced the vaccine's effect however, factors like the narrow vaccination window, the concentration of cases in infants under 3 months during the RSV season, and limited case numbers restricted further subgroup analyses. Future research should refine the timing of maternal vaccination, considering RSV seasonality post-COVID-19, infant age during the RSV season, and gestational age at vaccination to optimize outcomes.[16,30,43]

While Argentina introduced RSVpreF MI during the full RSV season in 2024, Galicia, Spain, adopted nirsevimab in 2023.[19,44] Nirsevimab demonstrated 81.6% effectiveness (95% CI: 65.1–90.3) against RSV-ALRTI hospitalizations, aligning with findings from the MELODY and HARMONIE studies.[14,24,45,46] Despite both strategies relying on passive immunization, differences in implementation may influence their effectiveness and impact.[11,32,33,47] The success of the NIRSE-GAL program, with over 90% coverage, highlights the importance of timely immunization and rapid uptake.[24] Its comprehensive approach includes infants born during the campaign, catch-up vaccination for those under six months, and high-risk groups aged 6–24 months with high-risk factors.[11,19,44] This strategy achieved a median reduction of 89.2% in RSV-ALRTI hospitalizations overall and 95.2% in the seasonal cohort.[24] Given MI's potentially lower impact and nirsevimab's higher cost, combining both strategies or adopting a future infant vaccination approach, like for pertussis or influenza, may offer greater benefits.[48,49] However, assessing the cost-effectiveness of such combined strategies is essential for sustainable implementation.[50]

Conclusions

This study demonstrates that RSVpreF MI is effective and significantly reduces RSV-related hospitalizations in infants under six months of age. These findings offer policymakers and health authorities compelling real-world evidence to support the adoption of RSV maternal immunization.

Data availability

Underlying data

The data collected for this study will be made available upon request. Data will be shared with researchers after signing a data access agreement. The data will be accessible through: https://github.com/cimetunsam/rsv-dinamicas.

Bibliography

1. Wildenbeest JG, Billard MN, Zuurbier RP, *et al.*: **The burden of respiratory syncytial virus in healthy term-born infants in Europe: a prospective birth cohort study.** *Lancet Respir. Med.* 2023; **11**(4): 341–353.
PubMed Abstract | Publisher Full Text | Free Full Text

2. Li Y, Wang X, Blau DM, *et al.*: **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.
PubMed Abstract | Publisher Full Text | Free Full Text

3. Mazur NI, Löwensteyn YN, Willemsen JE, *et al.*: **Global Respiratory Syncytial Virus–Related Infant Community Deaths.** *Clin. Infect. Dis.* 2021; **73**(Supplement_3): S229–S237.
PubMed Abstract | Publisher Full Text | Free Full Text

4. Wang X, Li Y, Vazquez Fernandez L, *et al.*: **Respiratory Syncytial Virus–Associated Hospital Admissions and Bed Days in Children <5 Years of Age in 7 European Countries.** *J. Infect. Dis.* 2022; **226** (Supplement_1): S22–S28.
PubMed Abstract | Publisher Full Text

5. Bouckaert N, Lefèvre M, Van den Heede K, *et al.*: **RSV Burden and Its Impact on Pediatric Inpatient Bed Occupancy in Belgium: An Analysis of National Hospital Claims Data.** *Pediatr. Infect. Dis. J.* 2023; **42**(10): 857–861.
PubMed Abstract | Publisher Full Text

6. Guiñazú G, Dvorkin J, Mahmud S, *et al.*: **Evaluation of the potential impact and cost-effectiveness of respiratory syncytial virus (RSV) prevention strategies for infants in Argentina.** *Vaccine.* 2024; **42**(23): 126234.
PubMed Abstract | Publisher Full Text | Free Full Text

7. Dvorkin J, Sosa E, Vodicka E, *et al.*: **Cost of illness due to respiratory syncytial virus acute lower respiratory tract infection among infants hospitalized in Argentina.** *BMC Public Health.* 2024; **24**(1): 427.
PubMed Abstract | Publisher Full Text | Free Full Text

8. Geoghegan S, Erviti A, Caballero MT, *et al.*: **Mortality due to Respiratory Syncytial Virus. Burden and Risk Factors.** *Am. J. Respir. Crit. Care Med.* 2017; **195**(1): 96–103.
Publisher Full Text

9. Caballero MT, Bianchi AM, Grigaites SD, *et al.*: **Community Mortality Due to Respiratory Syncytial Virus in Argentina: Population-based Surveillance Study.** *Clin. Infect. Dis.* 2021; **73**(Supplement_3): S210–S217.
PubMed Abstract | Publisher Full Text | Free Full Text

10. Caballero MT, Bianchi AM, Nuño A, *et al.*: **Mortality Associated With Acute Respiratory Infections Among Children at Home.** *J. Infect. Dis.* 2019; **219**(3): 358–364.
PubMed Abstract | Publisher Full Text | Free Full Text

11. Pecenka C, Sparrow E, Feikin DR, *et al.*: **Respiratory syncytial virus vaccination and immunoprophylaxis: realising the potential for protection of young children.** *Lancet.* 2024; **404**: 1157–1170.
PubMed Abstract | Publisher Full Text

12. Respiratory Syncytial Virus (RSV) Immunization Products: Accessed December 3, 2024.
Reference Source

13. Kampmann B, Madhi SA, Munjal I, *et al.*: **Bivalent Prefusion F Vaccine in Pregnancy to Prevent RSV Illness in Infants.** *N. Engl. J. Med.* 2023; **388**(16): 1451–1464.
PubMed Abstract | Publisher Full Text

14. Muller WJ, Madhi SA, Seoane Nuñez B, *et al.*: **Nirsevimab for Prevention of RSV in Term and Late-Preterm Infants.** *N. Engl. J. Med.* 2023; **388**(16): 1533–1534.
PubMed Abstract | Publisher Full Text

15. *Department of Immunization, Vaccines and Biologicals (IVB). Strategic Advisory Group of Experts on Immunization SAGE Meeting; September 23-26, 2024; Hybrid Meeting, Geneva, Switzerland.* World Health Organization; Accessed January 27, 2025.
Reference Source

16. Dvorkin J, Sosa E, Guiñazú G, *et al.*: **Dynamic Patterns of Seroprevalence and Severity of Rsv-Associated Disease in Young Children in Buenos Aires Before and after the COVID-19 Pandemic: A Multicentre Retrospective Cohort Study.** December 5, 2024.
Publisher Full Text

17. Gentile Á, Lucion MF, Juárez MDV, *et al.*: **Respiratory syncytial virus in preterm infants: 19 years of active epidemiological surveillance in a children's hospital.** *Arch. Argent. Pediatr.* 2020; **118**(6): 386–392.
PubMed Abstract | Publisher Full Text

18. Ministerio de Salud de la Nación: **Peso poblacional del AMBA.** 2023.
Reference Source

19. Ares-Gómez S, Mallah N, Santiago-Pérez MI, *et al.*: **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.
PubMed Abstract | Publisher Full Text

20. Ministry of Health Argentina: **Introduction to Registro Federal de Vacunación Nominalizado (NOMIVAC).**
Reference Source

21. van Roekel C, Poukka E, Turunen T, *et al.*: **Effectiveness of Immunization Products Against Medically Attended Respiratory Syncytial Virus Infection: Generic Protocol for a Test-Negative Case-Control Study.** *J. Infect. Dis.* 2024; **229** (Supplement_1): S92–S99.
PubMed Abstract | **Publisher Full Text**

22. Jakobsen JC, Gluud C, Wetterslev J, *et al.*: **When and how should multiple imputation be used for handling missing data in randomised clinical trials – a practical guide with flowcharts.** *BMC Med. Res. Methodol.* 2017; **17**(1): 162.
PubMed Abstract | **Publisher Full Text** | **Free Full Text**

23. Ovbude LJ, Grassano L, Cheuvart B, *et al.*: **Statistical Inference for Vaccine Efficacy: A Re-Randomization Procedure to Analyse Poisson Outcomes under Covariate-Adaptive Randomization.** *Stat. Biopharm. Res.* October 1, 2024; **16**: 491–497. Accessed January 21, 2025.
Publisher Full Text,

24. Mallah N, Pardo-Seco J, Pérez-Martínez O, *et al.*: **Full 2023–24 season results of universal prophylaxis with nirsevimab in Galicia, Spain: the NIRSE-GAL study.** *Lancet Infect. Dis.* 2024; **25**: e62–e63.
PubMed Abstract | **Publisher Full Text**

25. Zhang MJ, Fine J: **Summarizing differences in cumulative incidence functions.** *Stat. Med.* 2008; **27**(24): 4939–4949.
PubMed Abstract | **Publisher Full Text** | **Free Full Text**

26. Mendes D, Alves C, Batel-Marques F: **Number needed to treat (NNT) in clinical literature: an appraisal.** *BMC Med.* 2017; **15**: 112.
PubMed Abstract | **Publisher Full Text** | **Free Full Text**

27. Karageorgou E, Samanidou V: **Youden test application in robustness assays during method validation.** *J. Chromatogr. A.* 2014; **1353**: 131–139.
PubMed Abstract | **Publisher Full Text**

28. Midgley CM, Haynes AK, Baumgardner JL, *et al.*: **Determining the Seasonality of Respiratory Syncytial Virus in the United States: The Impact of Increased Molecular Testing.** *J. Infect. Dis.* 2017; **216** (3): 345–355.
PubMed Abstract | **Publisher Full Text** | **Free Full Text**

29. Wollny K, Pitt T, Brenner D, *et al.*: **Predicting prolonged length of stay in hospitalized children with respiratory syncytial virus.** *Pediatr. Res.* 2022; **92**(6): 1780–1786.
PubMed Abstract | **Publisher Full Text**

30. Simões EAF, Pahud BA, Madhi SA, *et al.*: **Efficacy, Safety, and Immunogenicity of the MATISSE (Maternal Immunization Study for Safety and Efficacy) Maternal Respiratory Syncytial Virus Prefusion F Protein Vaccine Trial.** *Obstet. Gynecol.* 2025; **145**(2): 157–167.
PubMed Abstract | **Publisher Full Text** | **Free Full Text**

31. World Health Organization: **Strategic Advisory Group of Experts on Immunization (WHO SAGE). Recommendations for Maternal Vaccination and Monoclonal Antibody Administration for RSV Prevention.** Published September 2024. Accessed January 12, 2025.
Reference Source

32. Hogan AB, Campbell PT, Blyth CC, *et al.*: **Potential impact of a maternal vaccine for RSV: A mathematical modelling study.** *Vaccine.* 2017; **35**(45): 6172–6179.
PubMed Abstract | **Publisher Full Text**

33. Du Z, Pandey A, Moghadas SM, *et al.*: **Impact of RSVpreF vaccination on reducing the burden of respiratory syncytial virus in infants and older adults.** *Nat. Med.* January 9, 2025; **31**: 647–652.
PubMed Abstract | **Publisher Full Text** | **Free Full Text**

34. Hodgson D, Wilkins N, van Leeuwen E, *et al.*: **Protecting infants against RSV disease: an impact and cost-effectiveness comparison of long-acting monoclonal antibodies and maternal vaccination.** *Lancet Reg. Health Eur.* 2024; **38**: 100829.
PubMed Abstract | **Publisher Full Text** | **Free Full Text**

35. Gentile Á, Torres-Torreti JP, López-López P, *et al.*: **Epidemiologic changes and novelties on vaccination against Bordetella pertussis in Latin America.** *Rev. Chilena Infectol.* 2021; **38**(2): 232–242.
PubMed Abstract | **Publisher Full Text**

36. Facciolà A, Visalli G, Orlando A, *et al.*: **Vaccine hesitancy: An overview on parents' opinions about vaccination and possible reasons of vaccine refusal.** *J. Public Health Res.* 2019; **8**(1): 1436.
PubMed Abstract | **Publisher Full Text** | **Free Full Text**

37. Zarekar M, Al-Shehabi H, Dörner R, *et al.*: **The impact of information and communication technology on immunisation and immunisation programmes in low-income and middle-income countries: a systematic review and meta-analysis.** *EBioMedicine.* 2025; **111**: 105520.
PubMed Abstract | **Publisher Full Text** | **Free Full Text**

38. Otsuki T, Akada S, Anami A, *et al.*: **Efficacy and safety of bivalent RSVpreF maternal vaccination to prevent RSV illness in Japanese infants: Subset analysis from the pivotal randomized phase 3 MATISSE trial.** *Vaccine.* 2024; **42**(22): 126041.
PubMed Abstract | **Publisher Full Text**

39. Fleming JA, Baral R, Higgins D, *et al.*: **Value profile for respiratory syncytial virus vaccines and monoclonal antibodies.** *Vaccine.* 2023; **41**: S7–S40.
PubMed Abstract | **Publisher Full Text**

40. Baral R, Fleming J, Khan S, *et al.*: **Inferring antenatal care visit timing in low- and middle-income countries: Methods to inform potential maternal vaccine coverage.** *PLoS One.* 2020; **15**(8): e0237718.
PubMed Abstract | **Publisher Full Text** | **Free Full Text**

41. Jain V, Serisier A, Lorgelly P: **The Real-World Impact of Vaccination on COVID-19 Cases During Europe's Fourth Wave.** *Int. J. Public Health.* 2022; **67**: 1604793.
PubMed Abstract | **Publisher Full Text** | **Free Full Text**

42. Xu S, Zeng C, Newcomer S, *et al.*: **Use of Fixed Effects Models to Analyze Self-Controlled Case Series Data in Vaccine Safety Studies.** *J. Biom. Biostat.* 2012; **Suppl 7**: 006.
PubMed Abstract | **Publisher Full Text**

43. Sahni LC, Olson SM, Halasa NB, *et al.*: **Maternal Vaccine Effectiveness Against Influenza-Associated Hospitalizations and Emergency Department Visits in Infants.** *JAMA Pediatr.* 2024; **178**(2): 176–184.
PubMed Abstract | **Publisher Full Text** | **Free Full Text**

44. Martinón-Torres F, Mirás-Carballal S, Durán-Parrondo C: **Early lessons from the implementation of universal respiratory syncytial virus prophylaxis in infants with long-acting monoclonal antibodies, Galicia, Spain, September and October 2023.** *Eurosurveillance.* 2023; **28**(49): 2300606.
PubMed Abstract | **Publisher Full Text** | **Free Full Text**

45. Hammitt LL, Dagan R, Yuan Y, *et al.*: **Nirsevimab for Prevention of RSV in Healthy Late-Preterm and Term Infants.** *N. Engl. J. Med.* 2022; **386**(9): 837–846.
PubMed Abstract | **Publisher Full Text**

46. Griffin MP, Yuan Y, Takas T, *et al.*: **Single-Dose Nirsevimab for Prevention of RSV in Preterm Infants.** *N. Engl. J. Med.* 2020; **383**(5): 415–425.
PubMed Abstract | **Publisher Full Text**

47. Terstappen J, Hak SF, Bhan A, *et al.*: **The respiratory syncytial virus vaccine and monoclonal antibody landscape: the road to global access.** *Lancet Infect. Dis.* 2024; **24**(12): e747–e761.
PubMed Abstract | **Publisher Full Text**

48. Sobanjo-ter Meulen A, Duclos P, McIntyre P, *et al.*: **Assessing the Evidence for Maternal Pertussis Immunization: A Report From the Bill & Melinda Gates Foundation Symposium on Pertussis Infant Disease Burden in Low- and Lower-Middle-Income Countries.** *Clin. Infect. Dis.* 2016; **63**(Suppl 4): S123–S133.
PubMed Abstract | **Publisher Full Text** | **Free Full Text**

49. Ludvigsson JF, Ström P, Lundholm C, *et al.*: **Maternal vaccination against H1N1 influenza and offspring mortality: population based cohort study and sibling design.** *BMJ.* 2015; **351**: h5585.
PubMed Abstract | **Publisher Full Text** | **Free Full Text**

50. Shoukat A, Abdollahi E, Galvani AP, *et al.*: **Cost-effectiveness analysis of nirsevimab and maternal RSVpreF vaccine strategies for prevention of Respiratory Syncytial Virus disease among infants in Canada: a simulation study.** *Lancet Reg. Health Am.* 2023; **28**: 100629.
PubMed Abstract | **Publisher Full Text** | **Free Full Text**