Impact and effectiveness of RSV maternal immunization on infant hospitalizations in Buenos Aires: a hospital-based, multicentre, retrospective surveillance cohort study

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Summary

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

Methods This study assessed the impact of RSVpreF MI on RSV-related acute lower respiratory tract infections (ALRTI) hospitalizations through a hospital-based, multicentre, retrospective surveillance cohort study, and measured vaccine effectiveness (VE) using a nested test-negative case–control study. Data of hospitalized infants under 18 months of age was collected and analysed within seven years from three Argentine tertiary hospitals. VE analysis included ALRTI-hospitalized infants who were born between March 1 and November 9, 2024, were under 6 months of age when tested for RSV, and whose mothers were eligible for prenatal RSV immunization. Expected RSV-ALRTI hospitalizations were compared with observed cases using a Poisson model. We estimated the VE of RSVpreF MI against RSV-ALRTI hospitalizations, paediatric intensive care unit (PICU) admissions, and extended hospital stays by comparing these rates in vaccinated and unvaccinated under 3 and 6 months.

Findings A total of 3373 participants were included in the impact analysis, fromof whom 323 were born during the vaccination period and were eligible for the VE analysis. The VE of RSVpreF MI was 80·8% (95% CI: 62·8–90·5%), and 66·1% (95% CI 30·1–83·8) for infants under 3 and 6 months, respectively, adjusted for age, sex, comorbidities, and epidemiological weeks. 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. The vaccine reduced RSV-ALRTI hospitalizations in infants under 6 months by 33·6% (95% CI 29·5–37·2) in 2024 compared to expected cases from previous years. The number needed to immunize to prevent one RSV-related hospitalization was 83·9 (95% CI 65·9–185·4).

Interpretation RSVpreF MI significantly reduced RSV-ALRTI hospitalizations, averting one-third of such hospitalizations in infants under 6 months. These findings provide valuable evidence for policymakers and health authorities.

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Keywords: Respiratory syncytial virus; Vaccine effectiveness; Vaccine impact; Maternal vaccination

Research in context

Evidence before this study

A bivalent RSV prefusion F (RSVpreF) protein–based maternal vaccine, containing stabilized pre-F proteins from both RSV A and B antigenic subgroups, demonstrated a favorable safety profile and significant efficacy in preventing RSV-confirmed medically attended (MA) acute lower respiratory tract infections (ALRTI) in infants. In a phase 3 randomized clinical trial (RCT), the MATISSE study, the RSVpreF maternal vaccine demonstrated significant protection against the risk of RSV-confirmed MA-ALRTI by 51·3% (95·8% CI 29·4–66·8) and provided even stronger protection against severe cases, lowering the risk by 82·4% (95% CI 57·5–93·9) within the first 90 days of life and by 70·0% (95% CI 50·6–82·5) up to 180 days after birth. By September 2023, the RSVpreF maternal vaccine had received market authorization in several countries, including Argentina, the United States, England, Japan, Canada, Australia, and Brazil. Argentina became the first country to incorporate RSVpreF into a national RSV immunization program as a universal, free-of-charge primary intervention, launching the initiative in March 2024. The first year of the immunization campaign began on March 1 and ended on August 31, 2024, and included all pregnant women between weeks 32 and 36·6 of gestation.

On May 28, 2025, we conducted a PubMed search using the terms (respiratory syncytial virus AND RSVpreF AND (effectiveness OR impact)), applying no date or language restrictions and filtering for ages 0–23 months. Our objective was to identify preliminary studies providing real-world evidence on RSVpreF vaccine effectiveness. The search yielded two test-negative case–control studies from Argentina that assessed RSVpreF vaccine effectiveness: Lancet Infect Dis (2025 May 5; S1473-3099(25)00156-2. https://doi.org/10.1016/S1473-30992500156-2) and Pediatr Infect Dis J (2025 May 28. https://doi.org/10.1097/INF.0000000000004878). In the first study, Pérez Marc G et al. analyzed data from 505 patients, reporting a 71·3% effectiveness (95% CI: 53·3–82·3) in preventing hospitalizations due to RSV-associated acute lower respiratory tract infection (ALRTI) during the first six months of life. In contrast, Gentile A et al. found in 187 infants under 6 months an effectiveness of 68·2% (95% CI: 33·1–84·9%). However, no data are currently available regarding the program's impact on hospital admissions.

Added value of this study

We conducted a retrospective cohort surveillance study to generate real-world evidence on the RSVpreF maternal vaccine in Argentina, the first country to implement this intervention as a nationwide, free-of-charge, universal immunisation programme.

Using a nested test-negative case–control analysis within our surveillance system, we estimated the adjusted vaccine effectiveness (aVE) of RSVpreF against RSV-related acute lower respiratory tract infection (ALRTI) hospitalisations to be 80·8% (95% CI 62·8–90·5) within the first three months of life and 66·1% (95% CI 30·1–83·8) up to six months of age. Additionally, the aVE for paediatric intensive care unit admission was 87·2% (95% CI 52·6–97·0), while for extended hospital stays in infants under six months of age, it was 88·6% (95% CI 62·3–97·1).

The immunisation programme led to a 33·6% (95% CI 29·5–37·2) reduction in RSV-ALRTI hospitalisations among infants under age six months in 2024, compared to expected cases from previous years (2018, 2019, and 2023). The estimated number needed to immunise (NNI) to prevent one RSV-related ALRTI hospitalisation was 83·9 (95% CI 65·9–185·4).

Implications of all the available evidence

The landscape of RSV disease, a major global public health threat, is evolving with the introduction of safe and effective preventive interventions. Our findings demonstrate that RSVpreF maternal immunisation significantly reduces the odds of RSV-related hospitalisations, PICU admissions, and prolonged hospital stays. Additionally, we observed a decline in hospitalisations due to severe RSV disease in young infants.

These results align with the World Health Organization Strategic Advisory Group of Experts recommendation for the RSVpreF maternal vaccine implementation, the findings of the MATISSE study, real-world studies, and predictive impact models. However, given the availability of two preventive strategies, governments, scientific advisory panels, stakeholders, and public health decision-makers must carefully assess the implementation of one or both interventions based on robust scientific evidence.

The findings presented in this study provide valuable data to inform cost-effectiveness analyses and health technology assessments, supporting future policy decisions. While this study generates high-quality evidence, its results should be complemented by future real-world studies across diverse populations and settings to further validate and refine these findings.

Introduction

Respiratory syncytial virus (RSV) is a major public health threat worldwide.[1] Every year, millions of young infants are hospitalized with RSV, with thousands of them unfortunately dying as a consequence of the infection. This has predominantly occurred in low- and

middle-income countries (LMICs) where structural poverty limits access to timely and adequate medical treatment.[2,3] Annual RSV epidemics overwhelm emergency services, paediatric wards, and intensive care units, leading to delayed elective and chronic care, unsafe staffing ratios, and underutilized resources during off-peak periods.[4]

In Argentina, RSV is estimated to cause nearly 250,000 clinical visits, 30,000 hospitalizations, and over 450 deaths in children under the age of five.[5] Healthcare costs associated with these RSV cases have exceeded US$ 25 million annually in the country.[5,6] Respiratory failure and in-hospital deaths from RSV predominantly affect term infants, with poor outcomes often linked to low-quality medical care.[7] However, the vast majority of RSV-related deaths occur at home or outpatient health facilities, often after families seek prior medical assistance.[8] Many of these home fatalities are misdiagnosed as sudden unexpected death in infancy (SUDI), underestimating RSV's devastating impact for years.[8]

Two immunization products, nirsevimab (AstraZeneca, and Sanofi), a long-acting monoclonal antibody for infants, and Bivalent Prefusion F (RSVpreF) vaccine (Pfizer) for pregnant individuals, have been licensed globally and endorsed by the World Health Organization (WHO) for universal use.[9–13] Maternal immunization (MI) transfers protective antibodies to newborns, while nirsevimab offers passive immunity at birth.[11,12] 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 MI as the primary intervention in a national RSV immunization program in March 2024, while nirsevimab was not available in that year.[9]

The universal maternal vaccination strategy, implemented for the first time in Argentina, was conducted between March 1 and August 31 of 2024, encompassing the period before and during the season of high RSV hospitalizations.[7,14] This strategy was incorporated into the National Vaccination Schedule, which provides free vaccinations for pregnant women between 32 and 36·6 weeks of gestation.[9,13] The RSVpreF MI coverage in the Metropolitan Area of Buenos Aires (MABA) was 55·3% and overall in Argentina 62%.[9,13]

The RSV impact and effectiveness of maternal immunization (RIMA) study is a hospital-based, multicentre, retrospective surveillance 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.[15]

Methods

Study design and population

We collected clinical, epidemiological, and etiological data from all infants aged 0–18 months, capturing those susceptible during their first and second RSV seasons, who were diagnosed with ALRTI and admitted to three public tertiary-level hospitals (Hospital de Niños Pedro Elizalde, Hospital Nacional Alejandro Posadas, and Hospital de Niños Sup Sor María Ludovica) in the MABA region between January 1, 2018, and November 30, 2024 (Fig. 1a). All the hospitals' Institutional Review Boards approved the study accordingly (Hospital de Niños Pedro Elizalde approval date May 7, 2024; Hospital Nacional Alejandro Posadas approval number 654EMP1S0/24(22)ren; Hospital de Niños Sup Sor María Ludovica approval date May 23, 2024). Informed consent was waived as the study was observational, retrospective, and only anonymized data were used. The study gathered information on hospitalization ALRTI episodes and specific diagnoses coded according to International Classification of Diseases (ICD)-10 standards (Supplementary Materials).[16] Data was collected on the following characteristics: sex, age, gestational age, comorbidities, health insurance status, and home location.[16] Inclusion criteria were a clinical diagnosis of ALRTI (Supplementary Materials) during hospitalization and having at least one virological test done.[11] Patients were excluded if they did not undergo a molecular diagnosis test, received Palivizumab, or resided outside the catchment area.[14] Maternal vaccination status was obtained from vaccination certificates or the Nominalized Federal Vaccination Registry platform.[9,14,17]

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.[18] The eligible population for vaccine effectiveness (VE) analysis included all ALRTI-hospitalized infants younger than 6 months old who were born between March 1st and November 9th 2024. We excluded babies born before 32 weeks 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 (Supplementary Table 1). Cases were defined as infants 6 months old or younger who were hospitalized with ALRTI and laboratory-confirmed RSV infection, and whose mothers were eligible for prenatal vaccination. Controls were defined as infants 6 months old or younger who were hospitalized with ALRTI and laboratory-confirmed lack of RSV infection, and whose

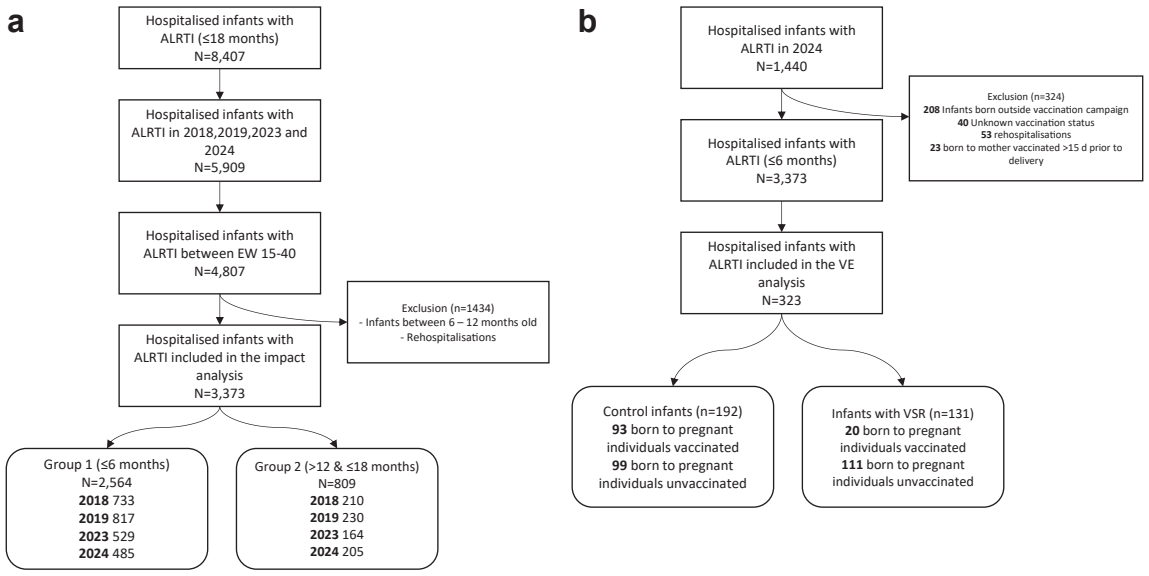


Fig. 1: Selection flowchart for the definition of the impact and vaccine effectiveness analysis. Flow chart of the study population selection for the vaccine impact (a) and effectiveness (b) analysis.

mothers were eligible for prenatal vaccination. The exclusion criteria for the VE analysis were as follows: 1) only the first infant 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 (Fig. 1b).[18]

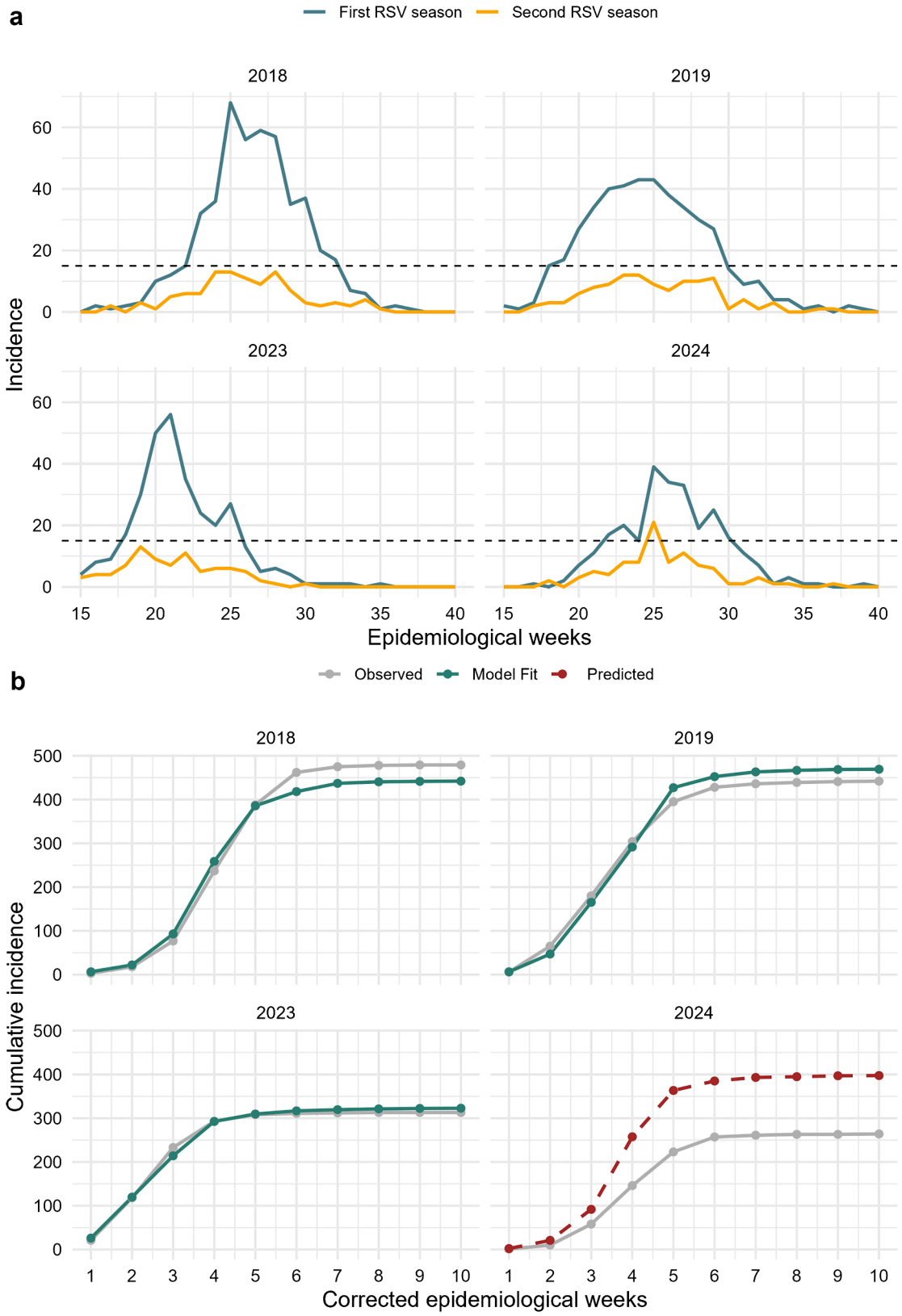
Molecular diagnosis

Nasal swabs or aspirates were obtained from all hospitalized infants with ALTRI and were tested for RSV, human rhinovirus (hRV), influenza A (Flu-A) and B (Flu-B) viruses, 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 (Allplex™ RV Essential Assay by Seegene). Results were reported by certified laboratory staff.[7,14]

Statistical analysis

For comparisons of variables between groups and the univariable analysis, Pearson's $\chi 2$ test was applied to categorical variables, and Student's t-test or Wilcoxon's rank-sum test to continuous variables, with a p-value <0·05 considered statistically significant. All variables were analysed for missing data, and none exhibited more than 10% missing values.

The impact of RSVpreF MI on RSV cases among ALTRI-related hospitalizations was assessed using a model with Poisson regression.[19] 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 12–18 months, Group 2) as a reference (Suppl. material, *Poisson model specification*).[16,20] 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 (Fig. 2 and Supplementary Figure 1). In Argentina, lockdown measures were enforced for much of 2020 and throughout the 2021 winter season.[14] Due to pandemic-related disruptions, RSV hospitalization patterns varied significantly in 2020, 2021, and 2022, leading to the exclusion of these years from the impact analysis (Supplementary Table 2).[14,16] To estimate the number of RSV cases among ALRTI hospitalizations that were 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. 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.[16,20] 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.[16] 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 (Suppl.


a
First RSV season
Second RSV season
2018
2019
2023
2024
Incidence
0
20
40
60
15
20
25
30
35
40
Epidemiological weeks
b
Observed
Model Fit
Predicted
Cumulative incidence
0
100
200
300
400
500
1
2
3
4
5
6
7
8
9
10
Corrected epidemiological weeks

Material, *Parametric bootstrap for CI* and *Estimated impact and results*).

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 analyses were 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 variables such as prematurity, epidemiological week of hospital admission, and health insurance. Variables with p-values <0·20 were included in the multivariate analysis, and if they had at least 10% confounding effect, they were included in the final models.[16,18] The RSVpreF adjusted VE was estimated by the following calculation 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. Our supplemental materials detail the methods used to determine the optimal cut-off points evaluating VE in the context of the interval between vaccination and birth (Supplementary Figure 2), the onset of RSV season (Supplementary Figure 3, and Supplementary Table 2), and prolonged hospital stays (Supplementary Table 3).[21,22] All statistical analyses were performed using R Studio software (R version 4 2 2). 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, 8407 infants aged ≤18 months were enrolled after being hospitalized with ALRTI (Fig. 1a). Of these, 2498 were excluded as they were born during the COVID-19 pandemic years (2020–2022), which affected RSV circulation (Supplementary Figure 4 and Supplementary Table 2).[14] Between epidemiological weeks 15 and 40, 4807 ALTRI hospitalizations were recorded. After excluding infants aged 6–12 months and rehospitalization cases (n = 1434), 3373 cases were included for impact analysis (Supplementary Table 4). Descriptive comparisons between the years of surveillance are shown in Supplementary Tables 5 and 6

In the absence of RSVpreF MI, an estimated 397 RSV hospitalizations (95% CI 374–420) would be expected among infants aged 0–6 months during epidemiological weeks 15–40 of 2024 (Supplementary Table 7). The implementation of the vaccination strategy prevented an estimated 133 cases of RSV (95% CI 110–156), equivalent to 215·71 (178·44–252·56) per 1000 infants with ALRTI-related hospitalizations (Table 1). The estimated reduction of RSV cases in 2024 was 33·6% (95% CI 29·5–37·2) relative to the expected number (Table 1). The NNI to prevent one RSV-ALRTI hospitalization was calculated at 83·9 (95% CI 65·9–-185·4). 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 (Fig. 2a–b, Supplementary Figures 1 and 5).

RSV maternal vaccine effectiveness

From January 1st to November 30th, 2024, 647 infants aged 6 months or younger were hospitalized, 399 were born between March 1 and November 9, 2024, to pregnant individuals who were candidates for vaccination (Fig. 1b). 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 (Fig. 1b), 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 (such as cardiological diseases, Down Syndrome, congenital respiratory diseases, neurological diseases, and others) were present in 8·7% of infants, with no significant differences found according to RSV vaccination status (p = 0·610)

Fig. 2: Model fit and predictions for incidence and cumulative incidence RSV-related ALRI hospitalizations across seasons for infants during their first RSV season (2018, 2019, 2023, 2024). (a) The solid teal line represents the incidence for infants during their first RSV season (0–6 months), while the solid gold line corresponds to infants during their second RSV season (12–18 months). The dashed horizontal line provides a contextual threshold for comparison. In 2024, the cumulative trend for Group 2 remains consistent with other years, while the incidence for Group 1 appears to decrease, narrowing the gap between the two groups. (b) The solid grey 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 Fig. 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.

Measure	Value	95% CI
Observed cases	264·0	
Averted cases	133·4	110·4–156·2
Averted cases over expected (% relative reduction)	33·6	29·5–37·2
Averted number of cases per 1000	215·7	178·4–252·6
The number needed to immunize	83·9	65·9–185·4

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

(Table 2). The study was conducted with an underinsured population, with only 8·4% of patients having private health insurance. There was no significant difference observed based on insurance status (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 between March and November (cold season), resulting in an overall positive rate of 74·5% between these months. 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 Supplementary Figure 6). 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 vaccinated or unvaccinated groups (p = 0·066) (Table 2). However, PICU admission rates differed significantly between cases (n = 45, 34·3%) and controls (n = 22, 11·4%) (Supplementary Table 8).

The aVE estimate of RSVpreF MI against RSV-related ALTRI hospitalizations in infants 6 months old or younger was 66·1% (95% CI 30·1–83·8%) when adjusted for age, sex, comorbidities, and epidemiological week of hospital admission (Table 3). In infants 3

	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)	0·442
Median (IQR) age, months	2·7 (1·7–3·8)	2·9 (1·8–3·8)	2·7 (1·5–3·7)	0·095
Age groups				0·354
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)	**0·007**
Comorbidities	28 (8·7)	17 (8·1)	11 (9·8)	0·610
Health insurance	27 (8·4)	19 (9·0)	8 (7·1)	0·537
Residential area				**0·013**
South	150 (46·4)	85 (40·5)	65 (57·5)	
Centre	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)	**<0·001**
ALRTI without a viral diagnosis	82 (25·5)	42 (20·1)	40 (35·7)	**0·002**
Viral agent				
Respiratory Syncytial Virus	131 (40·6)	111 (52·9)	20 (17·7)	**<0·001**
Metapneumovirus	56 (17·3)	34 (16·2)	22 (19·5)	0·458
Parainfluenza Virus	33 (10·2)	14 (6·7)	19 (16·8)	**0·004**
Human Rhinovirus	14 (4·3)	9 (4·3)	5 (4·4)	0·953
Sars-Coronavirus 2	8 (2·5)	4 (2·0)	4 (3·6)	0·394
Influenza	8 (2·5)	6 (2·9)	2 (1·8)	0·549
Human Adenovirus	3 (0·9)	2 (1·0)	1 (0·9)	0·952
Others	14 (4·3)	12 (5·7)	2 (1·8)	0·097
Coinfections	31 (9·6)	27 (12·9)	4 (3·5)	**0·007**
PICU admission	67 (20·7)	50 (23·8)	17 (15·0)	0·066

Bold indicates statistical significance (p < 0·05).

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

months old or younger, the effectiveness estimate was 80·8% (95% CI: 62·8–90·5%), when adjusted by age, sex, and comorbidities. RSVpreF MI showed protection against RSV-related PICU admissions with an effectiveness estimate of 87·2 (95% CI 52·6–97·0) and against RSV related-prolonged hospital stays (≥11 days) with an effectiveness estimate of 88·6% (95% CI: 62·3–97·1%), both estimations adjusted for age, sex, and comorbidities. No deaths were recorded among these infants (Table 3).

No significant differences were found (p = 0·594) in aVE when comparing vaccination occurring 15–27 days before delivery (62·2%, 95% CI 2·0–85·8) with vaccination occurring at least 27 days before delivery (73·1%, 95% CI 29·4–90·4), after adjusting for age, sex, comorbidities, and epidemiological week (Supplementary Table 9).

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 of age. The effectiveness was greatest among infants younger than 3 months old and for those admitted to the PICU or with prolonged hospital stays.

The results are consistent with the MATISSE phase 3 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.[23] The study VE results are similar with findings from two published studies in the country. Pérez Marc et al. reported a 71·3% VE (95% CI: 53·3–82·3) in preventing hospitalizations due to RSV-associated lower respiratory tract infection (RSV-ALRTI), while Gentile et al. found a 68·2% VE (95% CI: 33·1–84·9%).[24,25] Additionally, these findings align with earlier modelling estimates that projected a 20–40% reduction in RSV-related hospitalizations, underscoring the transformative potential of maternal vaccination in public health.[5,26] This evidence strongly reinforces the WHO SAGE recommendation and position paper for countries to implement MI strategies to protect young infants from severe RSV disease.[27]

Outcomes	Vaccinated pregnant individuals, n/N (%)		RSVpreF vaccine effectiveness	
	RSV-related ALRTI hospitalizations	non-RSV-related ALRTI hospitalizations	aVE%	95% CI
RSV-ALRTI hospitalization				
≤6 months old[a]	20/131 (15·3)	93/192 (51·8)	66·1	30·1–83·8
≤3 months old[b]	16/88 (18·2)	53/98 (54·1)	80·8	62·8–90·5
RSV-PICU admission				
≤6 months old[b]	6/45 (13·3)	11/22 (50·0)	87·2	52·6–97·0
Prolonged hospital stays[b]	6/54 (11·1)	14/36 (39·9)	88·6	62·3–97·1

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

Table 3: **RSVpreF vaccine effectiveness in reducing RSV-Related ALRI hospitalizations in infants.**

Our research revealed a 48% vaccination coverage among control individuals—slightly below the regional average and significantly lower than the national benchmark.[9,13] This disparity likely highlights unequal access to vaccination across various population sectors.[28] To address this gap, targeted efforts to raise awareness and improve access are critical.[29] Enhancing community outreach programs and engaging local healthcare providers can play a pivotal role in boosting vaccination rates within underserved groups.[29] Furthermore, with recent RCTs and surveillance reports confirming the vaccine's safety, re-evaluating the optimal vaccination window during pregnancy is essential.[11,23,30,31] Identifying the most cost-effective timing will maximize the intervention's benefits and ensure maternal and infant safety while optimizing healthcare resources.[32,33]

Our study has some limitations. To assess the impact of RSV vaccination 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.[16,34] The model's predictions are closely aligned with observed case counts in previous seasons, however, there is a possibility that this model does not exactly align with population-level data of the 2024 RSV season in Buenos Aires. Another challenge we faced was estimating the exposed population to calculate important metrics such as the number of averted cases per 1000 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.[16,20] Our cohort's high RSV prevalence and low vaccination coverage likely influenced these estimations.[9,35] Future studies should focus on narrower geographic areas with robust population data to improve accuracy and address these limitations.[14] A higher sample size may provide an adequate power to explore protective role of RSVpreF MI in protecting of PICU admissions in those RSV negative individuals. Finally, confounding variables impacting vaccine effectiveness estimates, such as seasonality, narrow vaccination window, the concentration of cases in infants under 3 months old 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.[14,23]

While Argentina introduced RSVpreF MI during the full RSV season in 2024, Spain adopted nirsevimab in 2023.[16] Since then, nirsevimab has demonstrated over 80% effectiveness against RSV-ALRTI hospitalizations in Spain, Chile, the United States, among other countries, aligning with findings from the MELODY and HARMONIE studies.[12,20,36–38] Despite both strategies relying on passive immunization, differences in implementation may influence their effectiveness and impact.[9,26,35] The success of the NIRSE-GAL or NIRSE-CL programs, with over 90% coverage, highlights the importance of timely immunization and rapid uptake.[20,37] The 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.[9,16,37] This strategy achieved a median reduction of 89·2% in RSV-ALRTI hospitalizations overall and 95·2% in the seasonal cohort in Galicia.[20] Given MI's potentially lower impact and nirsevimab's higher cost, combining both strategies or adopting a future infant vaccination approach, similar to that for pertussis or influenza, may offer greater benefits in Argentina.[39] However, assessing the cost-effectiveness of such combined strategies and compared with different scenarios is essential for a sustainable implementation.[40]

This study provides strong real-world evidence that RSVpreF MI is highly effective in reducing RSV-related hospitalizations, PICU admissions, and hospital stays for infants under six months of age. Furthermore, the vaccination strategy has led to a measurable decline in hospital admissions compared to previous years, reinforcing its public health benefits. These findings present a compelling case for policymakers and health authorities to accelerate the global adoption of RSV maternal immunization, driving meaningful progress in protecting vulnerable infant populations.

Contributors

JD, GG, and MTC conceptualised the study. JLR, CG, JD, and MTC developed the methodology. ES and JLR cleaned the data. JLR, JD, DP, and GS analysed the data. JLR, GG, DP, GS, JD, and MTC interpreted the data. JLR wrote the first draft with inputs from GG, DP, GS, JD, and MTC. JLR, JD, and MTC reviewed the initial manuscript. The rest of the authors contributed to data collection, and query resolution, and reviewed the manuscript. All authors have read and agreed to the published version of the manuscript. JLR, GG, ES, JD, and MTC had access to raw data and verified the data. JD and MTC were responsible for the decision to submit the manuscript.

Data sharing statement

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.

AI use statement

Artificial intelligence tools were not used in writing or analysis for this manuscript.

Declaration of interests

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Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.lana.2025.101296.

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