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Systematic Review

Maternal respiratory syncytial virus vaccination for infant protection: updated systematic review and meta-analysis of efficacy, effectiveness, and safety

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A B S T R A C T

Background: Respiratory syncytial virus (RSV) is a major cause of severe illness in infants and young children.
Methods: We updated this systematic review to explore the efficacy, effectiveness and safety of authorised maternal RSV prefusion F (RSVpreF) vaccine for infant protection. We searched MEDLINE, Cochrane Library/Central, Embase and grey literature from 2000 to June 2025. We included randomised controlled trials (RCTs) and non-randomised studies of interventions (NRSIs).
Results: Meta-analyses of RCTs showed high certainty of evidence that maternal RSVpreF vaccine lowered medically attended RSV-related lower respiratory tract infections (RSV-LRTI) with vaccine efficacy of 68% (relative risk (RR) 0.32; 95% confidence interval (CI) 0.13 to 0.77, 2 trials; 7656 participants), severe RSV-LRTI with a vaccine efficacy of 84% (RR 0.16; 95% CI 0.07 to 0.36, 2 trials; 7656 participants) and RSV-related hospitalisations with a vaccine efficacy of 70% (RR 0.30; 95% CI 0.15 to 0.61, 1 trial; 7148 participants) in infants. Within the limited evidence base available, there may be little to no difference in RSV-related mortality, all-cause mortality, vaccine-related serious adverse events, and intensive care admission. Requirements for invasive ventilation and duration of hospitalisation due to RSV disease were not reported by any trials. NRSIs suggested effectiveness of 72% (RR 0.28; 95% CI: 0.17 to 0.46, 3 NRSIs; 1229 participants) against hospitalisation, but certainty was very low.
Interpretation: Maternal RSVpreF vaccination reduced medically attended and severe RSV-LRTI and RSV-related hospitalisation in infants. No safety signals were identified. Further research is required to clarify the long-term effectiveness of the authorised vaccine.

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1. Background

Respiratory syncytial virus (RSV) is a highly contagious pathogen that can cause a wide range of respiratory illnesses, from mild infections to severe disease [1]. Most individuals are infected during early childhood and may experience repeated infections throughout life. In 2019, RSV was estimated to cause approximately 33 million lower respiratory tract infections in children under five globally, leading to 3.6 million hospitalisations and around 101,000 deaths. Infants aged 0–6 months experienced the greatest burden, accounting for an estimated 6.6 million illnesses, 1.4 million hospitalisations, and 46,000 deaths [2]. The WHO similarly estimates that RSV causes around 3.6 million hospitalisations and 100,000 deaths annually among children under five, with nearly half of deaths occurring in infants younger than six months [3]. RSV seasonality in Europe, traditionally characterised by winter outbreaks, was disrupted during the COVID-19 pandemic, with subsequent seasons showing variations in timing, geographic patterns, and epidemic duration compared with pre-pandemic trends [4].

Since its discovery in 1956 [5], RSV vaccine development has been a major research priority, with a focus on maternal vaccination to protect infants. Clinical trials have evaluated maternal RSV vaccines for safety, immunogenicity, and efficacy. Currently, RSV vaccination strategies include maternal immunisation as an important approach to protecting infants from RSV lower respiratory tract disease during early life. Among authorised RSV vaccines, Abrysvo by Pfizer [6] is authorised for maternal immunisation during pregnancy to prevent RSV lower respiratory tract disease in infants and for those aged 18 years and older who are at increased risk of RSV disease. Other authorised RSV vaccines, including Arexvy by GSK [7] and mResvia by Moderna [8], are indicated for those aged 18 years and older. Understanding how these vaccines perform, including safety and effectiveness, is important for guiding immunisation policies, particularly for high-risk populations.

We published a systematic review to assess the efficacy, effectiveness, and safety of RSV vaccines compared with placebo, no intervention, other vaccines targeting different respiratory pathogens, alternative RSV vaccines, or specific RSV monoclonal antibodies (MAbs) across all human populations [1]. The published review covered studies from 2000 to April 2024, and the search was later updated in December 2024 and again in June 2025.

In this manuscript, we describe the updated evidence on maternal RSV prefusion F (RSVpreF) vaccination to protect infants.

2. Methods

This is an update of a published systematic review. The overall systematic review included human populations without restrictions based on age, sex, ethnicity, comorbidities, or geographic location. This manuscript specifically reports findings from randomised controlled trials (RCTs) and non-randomised studies of interventions (NRSIs) evaluating maternal RSV vaccination. The detailed methodology is described in the published systematic review [1]; here, we present a concise summary. We conducted a comprehensive literature search, screened studies according to predefined eligibility criteria, extracted data from included trials, performed meta-analyses that incorporated any newly identified studies, assessed the risk of bias for relevant outcomes, and evaluated the certainty of the evidence.

2.1. Search methods

The original search covered studies published between 2000 and April 2024. It was later updated in December 2024 and again in June 2025, with the final search capturing evidence from 2000 through June 2025. The search timeframe was chosen to capture recent developments in RSV vaccine technology and immunology. As these vaccines were only recently authorised, it was important to include newly published trials and observational studies to provide up-to-date evidence base and to support ongoing monitoring of vaccine safety and effectiveness as RSV vaccination programmes expand. Our search encompassed the following databases: Medline (via Ovid), Cochrane Library/Central (via Wiley), Embase (via Embase. com/Elsevier), ClinicalTrials.gov (www.clinicaltrials.gov), and the International Clinical Trials Registry Platform (ICTRP). Additionally, the review team identified supplementary references through forward citation tracking.

2.2. Selection criteria

In the overall systematic review, we included all human populations without restrictions on age, sex, ethnicity, comorbidities, or geographic location. In this manuscript, we present the findings specifically from trials and non-randomised studies evaluating maternal RSV vaccines. The intervention focused on maternal RSV vaccines, including their efficacy, effectiveness, and safety in infants. Eligible comparisons were placebo or no intervention; one RSV vaccine versus another RSV vaccine or another type of vaccine; the same RSV vaccine at different dosages or schedules; or MAbs. Primary outcomes were RSV illness confirmed by laboratory tests, hospitalisation due to RSV disease confirmed by laboratory tests, mortality from illness caused by RSV, all-cause mortality, intensive care unit (ICU) admission, and serious adverse events related to vaccination. We considered both RCTs and NRSIs.

2.3. Data collection and analysis

We followed the standard method for citation screening at the title, abstract, and full-text stages, data extraction on the study and participant characteristics, and risk of bias assessment, with at least two independent review authors performing the tasks. We assessed the risk of bias using the Cochrane Risk of Bias 2 tool for RCTs [9] and the ROBINS-I (The Risk Of Bias In Non-randomised Studies – of Interventions) tool for the NRSIs [10]. Additionally, we assessed the certainty of the evidence using the GRADE approach [11]. The GRADE assessment was conducted by one author and cross-checked by another.

When appropriate, we performed a random-effects model meta-analysis. This model allows for the possibility that the true effect size may vary across studies due to differences in study populations, interventions, or methodologies. It provides a more conservative estimate of the effect size and its uncertainty, which is particularly appropriate when there is potential heterogeneity among the included studies.

We calculated risk ratio (RR) and obtained pooled effect estimates across strata using the Cochran-Mantel-Haenszel method. We synthesised RCTs and NRSIs separately. In NRSIs, we used adjusted data. Different types of heterogeneity (owing to varying clinical characteristics, methodological diversity, or small study effects) were evaluated and statistically quantified using I^2 and the chi-square test.

Using the random-effects model, we calculated 95% confidence intervals (95% CI) for meta-analyses. Subgroup analyses (for different clinical characteristics, including different populations, interventions and comparators) were planned irrespective of the measured statistical heterogeneity. We could perform subgroup analyses by vaccine type. In this manuscript, we present results solely for authorised vaccine, while the supplementary summary of findings table includes results for both authorised and unauthorised vaccines. We initially planned to conduct sensitivity analyses for the RCTs and NRSIs separately, based on risk-of-bias ratings. Although the risk of bias assessment varied across RCTs and NRSIs, a risk-of-bias-based sensitivity analysis was not feasible because all RCTs were judged to have the same risk of bias for each outcome, and similarly, all NRSIs were judged to have the same risk of bias for each outcome.

2.3.1. Results

We included three RCTs (two evaluating the authorised RSVpreF vaccine [12–15] and one evaluating an unauthorised RSV F-protein nanoparticle vaccine [16]) and four NRSIs evaluating RSVpreF in

routine practice [17–20]. This is based on the initial published systematic review and the updated analyses, with searches covering evidence from 2000 to June 2025. The RCTs provided data on vaccine efficacy and safety, while the NRSIs contributed with evidence on real-world effectiveness and safety.

Among the RCTs, two evaluated the authorised RSVpreF vaccine (Abrysvo by Pfizer), and one assessed an unauthorised recombinant RSV F protein nanoparticle vaccine developed by Novavax. In this manuscript, we report the findings from trials evaluating authorised RSV vaccine. A supplementary summary of findings table is also provided, presenting the combined results for both authorised and unauthorised vaccines. The two RCTs with authorised vaccine included 7656 participants and were conducted across 18 countries. Most participants were from the United States (45%), followed by South Africa (13%), Argentina (12%), and Japan (6%). Other participating countries included Taiwan, Spain, The Gambia, Finland, the Netherlands, Chile, New Zealand, the Philippines, Mexico, Brazil, Denmark, Canada, Australia, and South Korea. One trial was conducted in the United States, Chile, Argentina, and South Africa, but the currently available interim results include only US data. NRSIs suggested similar effectiveness against hospitalisation, but certainty was very low. The NRSIs included 14,003 participants and were conducted at 12 hospitals and four paediatric hospitals in Argentina, as well as at sites in the United States and the United Kingdom.

2.3.1.1. Risk of bias in RCTs. The overall risk of bias across all trials in each outcome was assessed as low. Detailed risk-of-bias assessments for RCTs involving maternal vaccination with infant benefit are presented in Supplementary Fig. 1.

2.3.1.2. Risk of bias in NRSIs. All four NRSIs on maternal vaccination for infant benefit (17-20) were assessed as having a serious risk of bias for each outcome, with concerns related to confounding (2 NRSIs), missing data (3 NRSIs), and measurement of outcomes (4 NRSIs). Detailed risk-of-bias assessments for NRSIs involving maternal vaccination with infant benefit are presented in Supplementary Fig. 2.

Although risk of bias differed across the included trials and NRSIs, sensitivity analyses based on risk of bias could not be conducted because all RCTs, and separately all NRSIs, received the same risk-of-bias rating (low risk of bias for RCTs and serious risk of bias for NRSIs) for each outcome.

2.4. Comparison 1: efficacy and safety of authorised maternal RSVpreF vaccine versus placebo in infants

In a meta-analysis of 2 trials [12–15] involving 7656 participants, the efficacy and safety of RSVpreF vaccine were assessed compared to placebo.

2.4.1. Primary outcomes

2.4.1.1. Medically attended RSV-associated lower respiratory tract infection in infants. The meta-analysis showed that maternal immunisation with an authorised RSVpreF vaccine reduced medically attended RSV-related lower respiratory tract infection in infants, demonstrating a vaccine efficacy of 68% up to 90 days after birth (anticipated absolute effect 6 per 1000 vs 17 per 1000; RR: 0.32; 95% CI: 0.13 to 0.77; $I^2 = 44\%$; 2 trials; 7656 participants; high-certainty evidence) (Fig. 1).

2.4.1.2. Medically attended RSV-associated severe lower respiratory tract illness in infants. The meta-analysis showed that maternal immunisation with an authorised RSVpreF vaccine reduced medically attended severe RSV-related lower respiratory tract infection in infants, demonstrating a vaccine efficacy of 84% up to 90 days after birth (anticipated absolute effect 2 per 1000 vs 10 per 1000; RR 0.16; CI: 0.07 to 0.36; $I^2 = 0\%$; 2 trials; 7656 participants, high certainty of evidence) (Fig. 2).

2.4.1.3. Hospitalisation due to RSV disease. Maternal immunisation with an authorised RSVpreF vaccine reduced hospitalisation due to RSV disease in infants, demonstrating a vaccine efficacy of 70% (anticipated absolute effect 3 per 1000 vs 9 per 1000; RR 0.30; CI: 0.15 to 0.61; I^2=N/A; 1 trial; 7148 participants, high certainty of evidence).

2.4.1.4. Mortality from illness caused by laboratory-confirmed RSV disease. One trial with the authorised vaccine reported one RSV-related death in the placebo group. We concluded that maternal RSVpreF vaccine may result in little to no difference in mortality from illness caused by RSV (RR 0.33; CI: 0.01 to 8.13; anticipated absolute effect 0 per 1000 vs 0 per 1000; I^2=N/A; 1 trial; 7148 participants; low certainty of evidence).

2.4.1.5. All-cause mortality. One trial with authorised vaccine reported eight deaths in the vaccinated group and 14 in the placebo group. We concluded that maternal RSVpreF vaccine may result in little to no difference in all-cause mortality (RR 0.57; CI: 0.24 to 1.35; anticipated absolute effect 2 per 1000 vs 4 per 1000; I^2=N/A; 1 trial; 7148 participants; low certainty of evidence).

2.4.1.6. Admission to an ICU. One trial with authorised vaccine reported six ICU admissions in the vaccine group and seven in the placebo group. We concluded that maternal RSVpreF vaccine may result in little to no difference in ICU admission due to RSV disease in infants (RR 1.63; CI: 0.57 to 4.66; anticipated absolute effect 86 per 1000 with RSV vaccination vs 53 per 1000 with placebo; I^2=N/A; 1 trial; 203 participants; low certainty of evidence). This outcome was reported in a subset of infants with RSV disease (n = 203); absolute risks are conditional on that subset.

2.4.1.7. Serious adverse events (SAEs) related to vaccination. Two trials with authorised vaccine reported three maternal SAEs related to vaccination in the vaccinated group and one in the placebo group. We concluded that the maternal RSVpreF vaccine may result in little to no difference in SAEs related to vaccination (RR 2.98; CI: 0.31 to 28.65; anticipated absolute effect 1 per 1000 vs 0 per 1000; I^2=N/A; 2 trials; 7554 participants; low certainty of evidence).

Both trials reported that none of the infant SAEs were related to the vaccination.

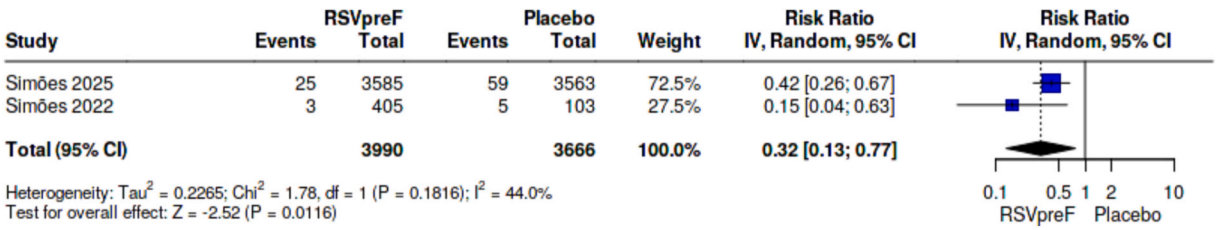

Fig. 1. Efficacy of authorised maternal RSVpreF vaccine vs placebo for medically attended RSV-associated lower respiratory tract infection in infants.

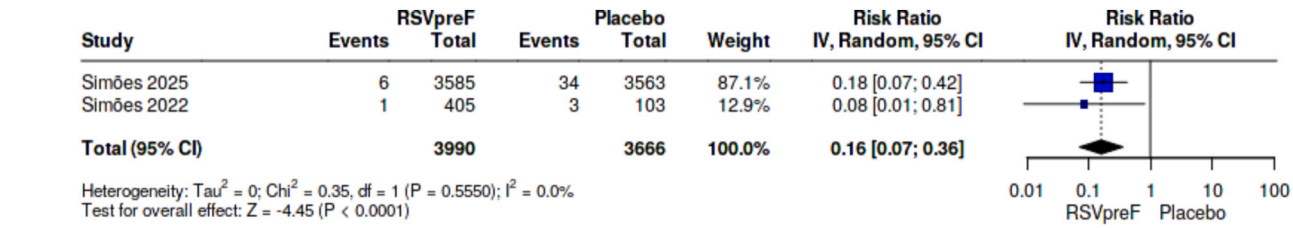

Fig. 2. Efficacy of authorised maternal RSVpreF vaccine vs placebo for medically attended severe RSV-associated lower respiratory tract infection in infants.

2.4.1.8. Primary outcomes that were not measured by any trials. Requirements for invasive ventilation and the duration of hospitalisation were not measured in any of the trials.

2.4.2. Secondary outcomes

2.4.2.1. Acute otitis media in children. One trial with an authorised vaccine reported one case of otitis media in infants, occurring in the vaccine group.

2.4.2.2. Development of asthma in children. One trial with an authorised vaccine reported 33 cases of diagnosed asthma or asthma-related symptoms in infants in the vaccine group and 44 cases in the placebo group.

2.4.2.3. Unsolicited adverse events (spontaneously reported/other adverse events). All trials reported unsolicited adverse events, with no notable differences between the vaccine and control groups. Lymphadenopathy and injection site bruising were recorded as unsolicited adverse events but occurred at similar rates in both groups.

2.4.2.4. Adverse events of special interest (AESI). One trial using the authorised vaccine, maternal AESI included premature delivery and SARS-CoV-2 infection, while infant AESI comprised developmental delay, low birthweight, SARS-CoV-2 infection, and prematurity. The occurrence of these events was similar between the vaccine and control groups.

2.4.2.5. Solicited adverse events. All trials reported data on solicited adverse events. The most frequently observed local reactions included pain, swelling, and redness at the injection site, while the most common systemic reactions were fever, fatigue, headache, muscle pain, vomiting, and diarrhoea. Systemic reactions occurred more often in participants who received the vaccine.

2.4.2.6. Secondary outcomes that were not measured by any trials. No trials measured symptomatology, antibiotic use, duration of ICU stay, or duration of protection.

2.5. Comparison 2: effectiveness of authorised maternal RSVpreF vaccine versus no vaccination in infants

Four NRSIs [17,20] involving 14,003 participants, three of which used a test-negative design, and one used a cohort study design, evaluated the effectiveness of authorised maternal RSVpreF vaccine. Three NRSIs reported hospitalisation due to laboratory-confirmed RSV disease, two NRSIs reported mortality from illness caused by laboratory-confirmed RSV disease, one NRSI reported admission to an intensive care unit due to RSV disease, two NRSIs reported requirement of mechanical ventilation, one NRSI reported duration of hospitalisation, one NRSI reported antibiotic use, one NRSI reported duration of ICU admission, and one NRSI reported adverse events of special interest.

2.5.1. Hospitalisation due to laboratory-confirmed RSV disease

Effectiveness of authorised maternal RSVpreF vaccine on hospitalisation due to RSV disease, is very uncertain with a vaccine effectiveness of 72% (RR 0.28; CI: 0.17 to 0.46; I^2 = 44.6%; 3 NRSIs; 1229 participants, very low certainty of evidence) (Fig. 3).

2.5.2. Mortality from illness caused by RSV

One NRSI reported three infant deaths among those with unvaccinated mothers (n = 235), with no deaths in the vaccinated group (n = 51). Another NRSI reported no RSV-related deaths.

2.5.3. Admission to an intensive care unit due to RSV disease

One NRSI reported 10 (20%) ICU admissions (>4 h) in infants born to vaccinated mothers (n = 51) and 59 (25%) ICU admission in infants born to unvaccinated mothers (n = 235).

2.5.4. Requirement for mechanical ventilation

One NRSI reported that seven infants (14%) in the maternal vaccination group (n = 51) and 38 (16%) in the unvaccinated group (n = 235) required mechanical ventilation. Another NRSI reported that 2 infants (16.7%) in the maternal vaccination group (n = 12) and 14 (17.6%) in the unvaccinated group (n = 79) required assisted mechanical ventilation.

2.5.5. Duration of hospital admission

One NRSI reported that the hospital admission duration was 5 days (IQR 3-9) in infants in the maternal vaccination group (n = 51) and 7 days (IQR 4-11) in infants born to unvaccinated mothers (n = 235).

2.5.6. Use of antibiotics

One NRSI reported that 25 infants in the maternal vaccination group (n = 51) and 111 in the unvaccinated group (n = 235) used any antibiotics.

2.5.7. Duration of ICU admission

One NRSI reported the duration of ICU admission was 10 days (IQR 6-19) in the maternal vaccination group (n = 51) and 10 days (IQR 8-13) in the unvaccinated group (n = 235).

2.5.8. Adverse events of special interest

One NRSI reported adverse events of special interest. The NRSI reported 449 preterm births among the maternal vaccination group (n = 6385) and 444 among the unvaccinated group (n = 6387) with an RR of 1.01 (95% CI: 0.89 to 1.15). There were 525 small-for-gestational-age births in the maternal vaccination group (n = 6385) and 570 in the unvaccinated group (n = 6387), with a RR of 0.92 (95% CI: 0.82 to 1.03). There were 520 large for gestational age among the maternal vaccination group (n = 6385) and 489 among the unvaccinated group (n = 6387) with an RR 1.06 (95% CI: 0.95 to 1.20).

We have provided the characteristics of the included trials and NRSIs in Supplementary Tables 1–6.

3. Discussion

The results of maternal RSVpreF vaccine for infant benefit showed

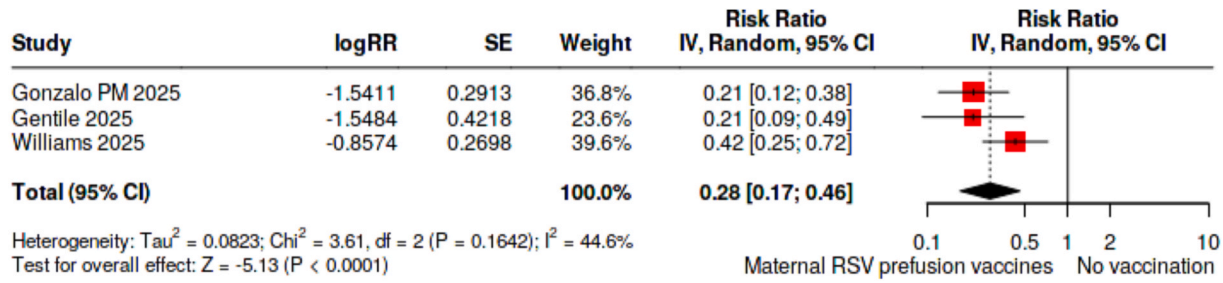

Fig. 3. Effectiveness of authorised maternal RSVpreF vaccine vs no vaccination for hospitalisation due to laboratory-confirmed RSV disease in infants.

that the authorised maternal RSVpreF vaccine reduces medically attended RSV-associated lower respiratory tract infections, medically attended RSV-associated severe lower respiratory tract infections, and RSV–related hospitalisation in infants. Authorised maternal RSVpreF vaccine may result in little to no difference in SAEs related to vaccination. The evidence from RCTs is supplemented by findings from real-world data derived from NRSIs. Vaccine effectiveness against hospitalisation from NRSIs was comparable to efficacy estimates from RCTs, further strengthening the evidence for vaccine-induced protection against RSV-related hospitalisation; however, the certainty of the evidence in NRSIs is very low due to methodological limitations and imprecision (see Summary of findings Table 1 and Summary of findings Table 2).

In the analysis of RCTs, we downgraded the certainty of evidence for mortality from RSV-related illness, all-cause mortality, vaccine-related serious adverse events and admission to an intensive care unit due to RSV disease due to imprecision arising from the small number or absence of events. It is to be noted that the available evidence is insufficient to determine the direction or magnitude of effect for the outcomes mortality from RSV-related illness, vaccine-related serious adverse events and admission to an intensive care unit due to RSV disease because of very wide confidence intervals in the effect estimate. The findings should be interpreted with caution as the evidence base is limited for these outcomes. In the analysis of NRSIs, we downgraded the

Summary of findings Table 1
Efficacy of authorised maternal RSVpreF vaccine vs placebo in infants.

Outcome No of participants (studies)	Vaccine efficacy (95% CI) Relative Risk (RR) (95% CI)	Anticipated absolute effects (95% CI)			Certainty	Comment
		With placebo	With RSVpreF vaccination	Difference		
Medically attended RSV-associated lower respiratory tract infection in infants No of participants: 7656 (2 RCTs)	**Vaccine efficacy 68%** (23% to 87%) **RR 0.32** (0.13 to 0.77)	17 per 1000	**6 per 1000** (2 to 13)	**12 fewer per 1000** (15 fewer to 4 fewer)	⨁⨁⨁⨁ High	Authorised maternal RSVpreF vaccine reduced medically attended RSV-associated lower respiratory tract infection in infants.
Medically attended severe RSV-associated lower respiratory tract infection in infants No of participants: 7483 (2 RCTs)	**Vaccine efficacy 84%** (64% to 93%) **RR 0.16** (0.07 to 0.36)	10 per 1000	**2 per 1000** (1 to 4)	**8 fewer per 1000** (9 fewer to 6 fewer)	⨁⨁⨁⨁ High	Authorised maternal RSVpreF vaccine reduced medically attended severe RSV-associated lower respiratory tract infection in infants.
Hospitalisation due to RSV disease No of participants: 7148 (1 RCT)	**Vaccine efficacy 70%** (29% to 85%) **RR 0.30** (0.15 to 0.61)	9 per 1000	**3 per 1000** (1 to 6)	**6 fewer per 1000** (8 fewer to 4 fewer)	⨁⨁⨁⨁ High	Authorised maternal RSVpreF vaccine reduced hospitalisation due to RSV disease in infants.
Mortality from illness caused by RSV No of participants: 7148 (1 RCT)	**RR 0.33** (0.01 to 8.13)	0 per 1000	**0 per 1000** (0 to 2)	**0 fewer per 1000** (0 fewer to 2 more)	⨁⨁◯◯ Low[a]	Authorised maternal RSVpreF vaccine may result in little to no difference in mortality from illness caused by RSV in infants.
All-cause mortality No of participants: 7148 (1 RCT)	**RR 0.57** (0.24 to 1.35)	4 per 1000	**2 per 1000** (1 to 5)	**2 fewer per 1000** (3 fewer to 1more)	⨁⨁◯◯ Low[a]	Authorised maternal RSVpreF vaccine may result in little to no difference in all-cause mortality in infants.
Maternal serious adverse events (SAEs) related to vaccination No of participants: 7554 (2 RCTs)	**RR 2.98** (0.31 to 28.65)	0 per 1000	**1 per 1000** (0 to 8)	**1 more per 1000** (0 fewer to 8 more)	⨁⨁◯◯ Low[a]	Authorised maternal RSVpreF vaccine may result in little to no difference in maternal serious adverse events (SAEs) related to vaccination.
Serious adverse events (SAEs) related to vaccination in infants No of participants: 7554 (2 RCTs)	not estimable	-	-	-	-	Not estimable as there are no events in either arm.
Admission to an intensive care unit due to RSV disease No of participants: 203 (1 RCT)	**RR 1.63** (0.57 to 4.66)	53 per 1000	**86 per 1000** (30 to 245)	**33 more per 1000** (23 fewer to 193 more)	⨁⨁◯◯ Low[a]	Authorised maternal RSVpreF vaccine may result in little to no difference in admission to ICU due to RSV disease in infants.
Requirement for invasive ventilation due to RSV disease	-	-	-	-	-	Not measured
Duration of hospitalisation due to RSV disease	-	-	-	-	-	Not measured

CI: confidence interval.
Explanations.
[a] Imprecision: downgraded for few events and CI crossing the threshold (downgraded x 2 level).

Summary of findings Table 2
Effectiveness of authorised maternal RSVpreF vaccine vs no vaccination in infants.

Outcome No of participants (studies)	Vaccine effectiveness (95% CI) Relative Risk (RR) (95% CI)	Certainty	Comment
Frequency of laboratory-confirmed RSV illness	-	-	Not measured
Hospitalisation due to RSV disease No of participants: 1229 (3 NRSIs)	**Vaccine effectiveness 72%** (54% to 83%) **RR 0.28** (0.17 to 0.46)	⨁◯◯◯ Very low [a,b]	The effectiveness of the authorised maternal RSVpreF vaccine is very uncertain for hospitalisation due to RSV disease.
Mortality from illness caused by RSV No of participants: 692 (2 NRSIs)	Not estimable	Not estimable	Not estimable
All-cause mortality	-	-	Not measured
Serious adverse events (SAEs) related to vaccination	-	-	Not measured
Admission to an intensive care unit due to RSV disease No of participants: 286 (1 NRSI)	Not estimable	Not estimable	Not estimable
Requirement for invasive ventilation due to RSV disease No of participants: 286 (1 NRSI)	Not estimable	Not estimable	Not estimable
Duration of hospitalisation due to RSV disease No of participants: 286 (1 NRSI)	Not estimable	Not estimable	Not estimable

CI: confidence interval; *RSV: Respiratory Syncytial Virus*.
Explanations.
[a] Risk of bias: downgraded due to serious risk of bias in all included studies (downgraded x 2 levels).
[b] Imprecision: downgraded due to very few events (downgraded x 1 level).

certainty of the evidence for the outcome hospitalisation due to RSV disease, given methodological limitations and imprecision. However, these real-world studies offer useful information on how well the vaccine work in everyday healthcare settings, support the findings from clinical trials, and help address gaps where randomised studies are unavailable or cannot be conducted.

In this updated systematic review, we have presented findings from both RCTs and NRSIs. The recently published Cochrane review on RSV vaccines [1] included only RCT evidence for maternal RSV vaccine. This paper complements those findings by incorporating additional data from NRSIs.

Current evidence from both RCTs and NRSIs does not suggest an increased risk of prematurity associated with maternal RSV vaccination with an authorised vaccine. Although no safety signals were identified in the RCTs or NRSIs evaluating authorised vaccine, large-scale post-marketing studies are needed to further assess the safety of RSV vaccine. Ongoing safety monitoring through post-marketing surveillance should receive particular attention. Studies with longer follow-up periods are also required to evaluate both the direct and indirect long-term effects, as well as the sustained effectiveness of the vaccine. Such research should include populations from various geographical regions, especially low- and middle-income countries. International collaboration will be vital for collecting comprehensive data on RSV vaccine performance worldwide, and efforts to strengthen global surveillance networks and standardised monitoring protocols would be highly valuable.

As the RCTs provide high-certainty evidence that authorised maternal RSVpreF vaccine reduce medically attended RSV-associated lower respiratory tract infections, severe RSV-associated lower respiratory tract infections, and RSV-related hospitalisation in infants, and as findings from NRSIs complement these results by providing effectiveness estimates from routine practice, guideline developers may consider this evidence through an evidence-to-decision process. This may support clinical decision-making in the long term. Future research priorities include understanding the duration of immunity provided by RSV vaccine, assessing the effects of co-administering RSV vaccine with other vaccines, and evaluating the cost-effectiveness of vaccination programmes across healthcare settings. Additional areas of interest involve determining the need for revaccination in future pregnancies, examining how maternal immunisation influences infants' responses to monoclonal antibodies in subsequent pregnancies, studying how waning maternal antibodies affect protection throughout the RSV season (particularly for late-season births), and comparing the effectiveness of maternal RSV vaccination with monoclonal antibody strategies for protecting infants.

A limitation of the systematic review is the restriction to articles published in English, which may have led to the exclusion of studies published in other languages. Additional limitations include limited follow-up during the period of protection, and sparse data for rare outcomes.

4. Conclusions

In infants, maternal vaccination with authorised RSVpreF vaccine reduced RSV-associated lower respiratory tract infections, including severe infections and hospitalisation due to RSV disease. Authorised maternal RSVpreF vaccine may result in little to no difference in mortality from illness caused by RSV, all-cause mortality, maternal and infantile SAEs related to vaccine, and admission to ICU due to RSV diseases; however, the evidence base is limited for these outcomes and should be interpreted with caution. No safety signals were identified. More post-marketing observational and surveillance studies are needed to evaluate the effectiveness and safety of authorised maternal RSV vaccine across diverse pregnant women and settings.

CRediT authorship contribution statement

KM Saif-Ur-Rahman: Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing. **Catherine King:** Data curation, Formal analysis, Investigation, Writing – review & editing. **Sean Whelan:** Data curation, Formal analysis, Investigation, Writing – review & editing. **Matthew Blair:** Data curation, Formal analysis, Investigation, Writing – review & editing. **Sean Donohue:** Data curation, Formal analysis, Investigation, Writing – review & editing. **Caoimhe Madden:** Data curation, Formal analysis, Investigation, Writing – review & editing. **Kavita Kothari:** Data curation, Investigation, Methodology, Resources, Software, Writing – review & editing. **Isolde Sommer:** Formal analysis, Investigation, Methodology, Validation, Writing – review & editing. **Thomas Harder:** Formal analysis, Investigation, Methodology, Validation, Writing – review & editing. **Nicolas Dauby:** Formal analysis, Investigation, Validation, Writing – review & editing. **Simona Maria Ruta:** Formal analysis, Investigation, Validation, Writing – review & editing. **Julie Frère:** Formal analysis, Investigation, Validation, Writing – review & editing. **Viktoria Schönfeld:** Formal analysis, Investigation, Methodology, Validation, Writing – review & editing. **Eero Poukka:** Formal analysis,

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Data availability

Available from the corresponding author on request.

Declaration of competing interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.nmni.2026.101831.

References

[1] Saif-Ur-Rahman KM, King C, Whelan SO, Blair M, Donohue S, Madden C, et al. Efficacy and safety of respiratory syncytial virus vaccines. Cochrane Database Syst Rev 2025 Sep 29;9(9):CD016131. https://doi.org/10.1002/14651858.CD016131.

[2] Li Y, Wang X, Blau DM, Caballero MT, Feikin DR, Gill CJ, 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):2047–64. https://doi.org/10.1016/S0140-6736(22)00478-0.

[3] WHO. Respiratory syncytial virus (RSV). https://www.who.int/news-room/fact-sheets/detail/respiratory-syncytial-virus-(rsv). [Accessed 15 December 2025].

[4] European Centre for Disease Prevention and Control. Rapid scientific advice on protecting infants against respiratory syncytial virus disease for the European 2025/26 winter season – november 2025. Stockholm: ECDC; 2025. [Accessed 15 December 2025].

[5] Peeples ME, Thongpan I. Nirsevimab-resistant respiratory syncytial virus strains are rare but there. Lancet Infect Dis 2023;23(7):773–4. https://doi.org/10.1016/S1473-3099(23)00137-8.

[6] European Medical Agency. Abrysvo. https://www.ema.europa.eu/en/medicines/human/EPAR/abrysvo. [Accessed 15 December 2025].

[7] European Medical Agency. Arexvy. https://www.ema.europa.eu/en/medicines/human/EPAR/arexvy. [Accessed 15 December 2025].

[8] European Medical Agency. mResvia. https://www.ema.europa.eu/en/medicines/human/EPAR/mresvia. [Accessed 15 December 2025].

[9] Sterne JA, Savović J, Page MJ, Elbers RG, Blencowe NS, Boutron I, et al. RoB 2: a revised tool for assessing risk of bias in randomised trials. Br Med J 2019;366:l4898.

[10] Sterne JA, Hernán MA, Reeves BC, Savović J, Berkman ND, Viswanathan M, et al. ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions. Br Med J 2016;12(355):i4919.

[11] Guyatt G, Oxman AD, Akl EA, Kunz R, Vist G, Brozek J, et al. GRADE guidelines: 1. Introduction-GRADE evidence profiles and summary of findings tables. J Clin Epidemiol 2011;64(4):383–94.

[12] Madhi SA, Kampmann B, Simões EAF, Zachariah P, Pahud BA, Radley D, et al. Preterm birth frequency and associated outcomes from the MATISSE (maternal immunization study for safety and efficacy) maternal trial of the bivalent respiratory syncytial virus prefusion F protein vaccine. Obstet Gynecol 2025 Feb 1;145(2):147–56. https://doi.org/10.1097/AOG.0000000000005817.

[13] Simões EAF, Pahud BA, Madhi SA, Kampmann B, Shittu E, Radley D, 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 Feb 1;145(2):157–67. https://doi.org/10.1097/AOG.0000000000005816.

[14] Kampmann B, Madhi SA, Munjal I, Simões EAF, Pahud BA, Llapur C, et al. Bivalent prefusion F vaccine in pregnancy to prevent RSV illness in infants. N Engl J Med 2023 Apr 20;388(16):1451–64. https://doi.org/10.1056/NEJMoa2216480.

[15] Simões EAF, Center KJ, Tita ATN, Swanson KA, Radley D, Houghton J, et al. Prefusion F protein-based respiratory syncytial virus immunization in pregnancy. N Engl J Med 2022 Apr 28;386(17):1615–26. https://doi.org/10.1056/NEJMoa2106062.

[16] Madhi SA, Polack FP, Piedra PA, Munoz FM, Trenholme AA, Simões EAF, et al. Respiratory syncytial virus vaccination during pregnancy and effects in infants. N Engl J Med 2020 Jul 30;383(5):426–39. https://doi.org/10.1056/NEJMoa1908380.

[17] Pérez Marc G, Vizzotti C, Fell DB, Di Nunzio L, Olszevicki S, Mankiewicz SW, et al. 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 Sep;25(9):1044–54. https://doi.org/10.1016/S1473-3099(25)00156-2.

[18] Gentile A, Juárez MDV, Lucion MF, Gregorio G, López O, Fernández T, et al. Maternal immunization with RSVpreF vaccine: effectiveness in preventing respiratory syncytial virus-associated hospitalizations in infants under 6 months in Argentina: Multicenter case-control study. Pediatr Infect Dis J 2025 Oct 1;44(10):988–94. https://doi.org/10.1097/INF.0000000000004878.

[19] Hsieh TYJ, Wei JC, Collier AR. Investigation of maternal outcomes following respiratory syncytial virus vaccination in the third trimester: insights from a real-world United States electronic health records database. Am J Obstet Gynecol 2025 May 3. https://doi.org/10.1016/j.ajog.2025.04.067. S0002-9378(25)00298-4.

[20] Williams TC, Marlow R, Cunningham S, Drysdale SB, Groves HE, Hunt S, et al. 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 Sep;9(9):655–62. https://doi.org/10.1016/S2352-4642(25)00155-5.