NIHR | National Institute for Health and Care Research

PROSPERO
International prospective register of systematic reviews

Effectiveness and immunogenicity of respiratory syncytial virus vaccine (RSVpreF from Pfizer) for pregnant persons: A living systematic review and meta-analysis

Agustina Mazzoni, Ariel Bardach, Mabel Berrueta, Agustin Ciapponi, Karen Klein, Martin Brizuela, Carolina Nigri, Jamile Ballivian, Juan Manuel Sambade, Katharina Stegelmann, Divya Patel, Jessica Atwell, Jennifer Deese, Deshayne Fell, Sarah Cox, Xu Xiong, Andy Stergachis, Flor Munoz, Pierre Buekens

Citation 1 change

Agustina Mazzoni, Ariel Bardach, Mabel Berrueta, Agustin Ciapponi, Karen Klein, Martin Brizuela, Carolina Nigri, Jamile Ballivian, Juan Manuel Sambade, Katharina Stegelmann, Divya Patel, Jessica Atwell, Jennifer Deese, Deshayne Fell, Sarah Cox, Xu Xiong, Andy Stergachis, Flor Munoz, Pierre Buekens. Effectiveness and immunogenicity of respiratory syncytial virus vaccine (RSVpreF from Pfizer) for pregnant persons: A living systematic review and meta-analysis. PROSPERO 2025 CRD420251077829. Available from https://www.crd.york.ac.uk/PROSPERO/view/CRD420251077829.

REVIEW TITLE AND BASIC DETAILS

Review title

Effectiveness and immunogenicity of respiratory syncytial virus vaccine (RSVpreF from Pfizer) for pregnant persons: A living systematic review and meta-analysis

Condition or domain being studied 1 change

Respiratory Syncytial Virus Infection; Vaccine; Pregnancy ; Vaccine Immunogenicity; Clinical effectiveness

RSV A and B (all strains)

Rationale for the review 1 change

Globally, respiratory syncytial virus (RSV) is the leading cause of lower respiratory tract disease (LRTD) in infants and children under 5 years of age, leading to considerable morbidity, mortality, and economic burden. The first vaccine for the prevention of RSV in infants, RSVpreF (ABRYSVO), has been licensed by the United States Food and Drug Administration, the European Medicines Agency, and many other regulatory agencies.

RSVpreF is indicated for active immunization of pregnant individuals for the prevention of lower respiratory tract disease (LRTD) and severe LRTD caused by RSV in infants from birth through 6 months. The earliest gestational age at which RSVpreF is approved for administration is 24 weeks; some countries have licensed or recommended the vaccine for use later in pregnancy (e.g., from 28 or 32 weeks gestational age).

Clinical trials demonstrated the safety and efficacy profile of RSVpreF among more than 7,000 mothers and their infants across 18 countries, however, additional data are needed from post-licensure studies to evaluate effectiveness across diverse geographic settings and demographic groups, against additional outcomes beyond RSV associated LRTD in infants 0-6 months of age, and among key subgroups and stratifications crucial for informing vaccine policy, implementation guidelines and maximizing public health impact.

As post licensure data are generated, this living systematic review aims to capture and analyze this information and provide reliable, up-to-date global evidence to describe the effectiveness and immunogenicity of RSVpreF vaccination in pregnancy.

Review objectives 1 change

Primary review questions

- What is the efficacy/effectiveness of maternal RSVpreF vaccination during pregnancy in preventing RSV-specific and all-cause respiratory illness in infants?
- What is the immune response associated with maternal RSVpreF vaccination and how long does it last in individuals vaccinated during pregnancy?
- What is the efficacy/effectiveness of maternal RSVpreF vaccination during pregnancy in preventing RSV-specific and all-cause respiratory illness in pregnant and postpartum people?

Secondary review questions

- Does maternal RSVpreF immunogenicity or efficacy/effectiveness vary by gestational timing at vaccination, time from vaccination to birth, gestational age at birth, or by other maternal/ infant factors?

- Does maternal RSVpreF immunogenicity or efficacy/effectiveness vary with administration with other routinely recommended vaccines during pregnancy or by RSV subtype?
- Does maternal RSVpreF immunogenicity or efficacy/effectiveness vary by country income-level, region, or seasonal pattern?
- What RSV-specific immune factors, and in what quantities, are transferred from RSVpreF vaccinated pregnant individuals to their fetuses/newborns through the placenta, what variables affect the presence, quantity and transfer of those factors, and how long are immune factors sustained in pregnant/postpartum people/infants?
- What RSV-specific immune factors, and in what quantities, are present in human milk, what variables affect the presence and quantity of those factors, and how long are immune factors sustained in human milk?

Keywords
RSV vaccine; Effectiveness; Immunogenicity; Pregnancy; Living systematic review

Country
Argentina; United States of America

ELIGIBILITY CRITERIA

Population 1 change

Included
Pregnant persons, postpartum persons, newborns and infants.

Intervention(s) or exposure(s)

Included
Bivalent, non-adjuvanted, RSVpreF vaccine for pregnant persons.

Comparator(s) or control(s) 1 change

Included
Any control group will be considered whether it involves standard care, no intervention, placebo, or a different preventive strategy (e.g. monoclonal antibodies). Additionally, non-comparative studies will be included. The presence of a control group will not be a requirement.

Study design 1 change
Both randomized and nonrandomized study types will be included.

Included
We will include randomized controlled trials (phase 2/3 RCT) and phase 4 post-licensure studies (e.g., ecologic, quasi-experimental, before and after), and observational studies (e.g., cohort, case-control, test-negative study design, screening method, cross-sectional, case series, etc.), publication year, and language.

Excluded
We will exclude narrative reviews, editorials, commentaries, case reports, preprints, and modeling studies.

Context 1 change
Setting: Studies to be included will be those which evaluate immunogenicity and efficacy/effectiveness of RSVpreF vaccination of pregnant persons in pregnant and post-partum persons and their infants. Eligible studies will include randomized and post-licensure observational studies reporting efficacy or effectiveness outcomes with sample sizes of at least 50 participants, and immunogenicity outcomes with at least 10 participants.

TIMELINE OF THE REVIEW

Date of first submission to PROSPERO
03 July 2025

Review timeline 1 change
Start date: 30 September 2025. End date: 1 March 2028.

Date of registration in PROSPERO
07 July 2025

AVAILABILITY OF FULL PROTOCOL

Availability of full protocol
A full protocol has not been written.

SEARCHING AND SCREENING

Search for unpublished studies
Both published and unpublished studies will be sought.

Main bibliographic databases that will be searched 1 change

The main databases to be searched are *CENTRAL - Cochrane Central Register of Controlled Trials*, *Embase.com*, *LILACS - Latin American and Caribbean Health Sciences Literature*, *MEDLINE*, *PubMed* and *SCI - Science Citation Index*.

Other important or specialist databases that will be searched

Science Citation Index Expanded (SCI-EXPANDED), China Network Knowledge Information (CNKI), Chinese Biomedical Literature Database (CBM), Chinese Science Journal Database (CSDC). Grey literature published by national health agencies since August 2023 will also be included as data sources. All ongoing RCTs will be tracked in clinical trial registries.

Search language restrictions

There are no language restrictions.

Search date restrictions 1 change

Databases will be searched for articles published from 1 January 2023 and before by 1 March 2028.

Other methods of identifying studies 1 change

Other studies will be identified by: *looking through all the articles that cite the papers included in the review ("snowballing")*, *reference list checking* and *searching trial or study registers*.

Link to search strategy

A full search strategy has been uploaded to PROSPERO. The PDF may be accessed through this link https://www.crd.york.ac.uk/PROSPEROFILES/b5abfa237c2d8df348ca601e0e75bc45.pdf.

Selection process

Studies will be screened independently by at least two people (or person/machine combination) with a process to resolve differences.

Other relevant information about searching and screening

Pairs of reviewers will independently screen each title and abstract and any potentially relevant full-text studies and reports will be retrieved. These will be independently selected, and any exclusion criteria will be documented for ineligible studies, in both study phases. Any disagreements will be resolved through review team discussions and documented. This process will be performed using the web-based software Nested Knowledge (https://nested-knowledge.com/).

DATA COLLECTION PROCESS

Data extraction from published articles and reports 1 change

Data will be extracted independently by at least two people (or person/machine combination) with a process to resolve differences.

Authors will not be contacted for further information.

Study risk of bias or quality assessment

Risk of bias will be assessed using: *Cochrane RoB-2* and *ROBINS-I*

For non-comparative studies, we will use the NIH Quality Assessment Tool.

Data will be assessed independently by at least two people (or person/machine combination) with a process to resolve differences.

Additional information will **not** be sought from study investigators if required information is unclear or unavailable in the study publications/reports.

Reporting bias assessment

Risk of bias due to missing results will not be assessed

Certainty assessment

Certainty of findings will not be assessed

OUTCOMES TO BE ANALYSED

Main outcomes 1 change

Effectiveness outcomes of RSVpreF may be measured as:

1. In infants (birth through 12 months) and pregnant and post-partum people (from RSVpreF vaccination through 1 year):

• RSV detection

• RSV acute respiratory illness [ARI, lower respiratory tract illness (LRTI) or disease (LRTD)]

• RSV hospitalization

• RSV LRTI/LRTD hospitalization

• All-cause LRTI/LRTD

• All-cause LRTI/LRTD hospitalization (does not require confirmation of etiology)

• Asymptomatic RSV infection

2. In infants (birth through 12 months):

• RSV complications including secondary bacterial infection, respiratory failure, multiorgan failure, death [including case fatality rate (CFR)]

• Antibiotic use in infants with RSV infection

Immunogenicity outcomes of RSVpreF may be measured as:

1. Humoral immune responses (quantity and durability) including RSV-A and RSV-B antibody titers and cellular immune responses, in infant umbilical cord blood at delivery, infant peripheral blood at delivery, maternal/infant transplacental transfer ratios, maternal serum at delivery, and maternal breastmilk.
2. RSV viral load inlcuding infant blood at time of illness, infant respiratory sample at time of illness, maternal blood at time of illness, and maternal respiratory sample at time of illness.

Additional outcomes 1 change

There are no additional outcomes.

PLANNED DATA SYNTHESIS

Strategy for data synthesis 1 change

Detailed methodology for summary and statistical analyses of data collected in this study will be documented in a statistical analysis plan (SAP), which will be dated, filed, and maintained by the sponsor. The SAP may modify the plans outlined in the protocol; any major modifications of primary endpoint definitions or their analyses would be reflected in a protocol amendment.

The final data set of pooled data is then summarized and mapped using PowerBI to create an interactive dashboard for data visualization, programmed by the IECS team and based on this protocol. This platform will allow users to explore maternal and neonatal effectiveness and immunogenicity outcomes through various figures, tables, and maps.

Finally, meta-analyses will be performed using RShiny, incorporating random-effects models and proportional meta-analyses to synthesize the data based on algorithms that select and automatically calculate the meta-analyses in the shiny app.

Provided that data are available and methodologically suitable, aggregate meta-analyses will be performed for each comparison in accordance with the Cochrane Handbook of Systematic Reviews of Interventions, employing random-effects meta-analysis for primary analyses.

Proportional meta-analyses will be performed to summarize frequencies from 1-sample studies. R statistical software will be used to analyze the data. Meta, Metafor and Tidyverse are the main packages selected for data analysis. Hazard ratios, risk ratios, or odds ratios along with their corresponding 95% confidence intervals (CI) will be computed for dichotomous outcomes, whereas mean

differences or standardized mean differences will be determined for continuous outcomes. Additionally, proportions with 95% CI will be determined for non-comparative studies. For reporting efficacy/effectiveness outcomes, measures will be converted into vaccine efficacy whenever feasible. Adjusted effect measures will be prioritized (e.g., by age, region, etc) over unadjusted estimates. Heterogeneity will be explored through subgroup analyses.

Subgroup analysis: the following pre-specified subgroup analyses will be performed if data on subgroups are available in the included studies:

- Country income level (high or low- and middle-income country).
- Region (based on the Institute for Health Metrics and Evaluation categorization).
- Study design
- Gestational age at time of vaccination (e.g., 24-28 weeks, 28-32 weeks, 32-37 weeks)
- Gestational age at birth
- Seasonality (yes or no)
- Infant risk status (high -risk vs. not high- risk)
- Maternal risk status (high- risk vs. not high -risk)
- RSV subtype (A or B).

Publication bias will be formally assessed by funnel plots and Egger and Begg tests.

Sensitivity analysis will be undertaken by excluding high-risk bias studies.

CURRENT REVIEW STAGE

Stage of the review at this submission

Review stage	Started	Completed
Pilot work		
Formal searching/study identification		
Screening search results against inclusion criteria		
Data extraction or receipt of IPD		
Risk of bias/quality assessment		
Data synthesis		

Review status
The review is currently planned or ongoing.

Publication of review results
Results of the review will be published.

REVIEW AFFILIATION, FUNDING AND PEER REVIEW

Review team members 1 change
Dr Agustina Mazzoni (review guarantor and contact) ORCID: 0000-0003-3328-2705. Institute for Clinical Effectiveness and Health Policy. Argentina.

No conflict of interest declared.

Dr Ariel Bardach. Institute for Clinical Effectiveness and Health Policy. Argentina.

No conflict of interest declared.

Dr Mabel Berrueta. Institute for Clinical Effectiveness and Health Policy. Argentina.

No conflict of interest declared.

Dr Agustin Ciapponi. Institute for Clinical Effectiveness and Health Policy. Argentina.

No conflict of interest declared.

Dr Karen Klein. Institute for Clinical Effectiveness and Health Policy. Argentina.

No conflict of interest declared.

Dr Martin Brizuela. Institute for Clinical Effectiveness and Health Policy. Argentina.

No conflict of interest declared.

Ms Carolina Nigri. Institute for Clinical Effectiveness and Health Policy. Argentina.

No conflict of interest declared.

Dr Jamile Ballivian. Institute for Clinical Effectiveness and Health Policy. Argentina.

No conflict of interest declared.

Dr Juan Manuel Sambade. Institute for Clinical Effectiveness and Health Policy. Argentina.

No conflict of interest declared.

Dr Katharina Stegelmann. Institute for Clinical Effectiveness and Health Policy. Argentina.

No conflict of interest declared.

Ms Divya Patel. Pfizer. United States of America.

Conflict of interest
Employee of Pfizer and may hold stock or stock options

Dr Jessica Atwell. ORCID: 0000-0003-1169-6456. Pfizer. United States of America.

Conflict of interest
Employee of Pfizer and may hold stock or stock options

Dr Jennifer Deese. ORCID: 0000-0003-1535-1076. Pfizer. United States of America.

Conflict of interest
Employee of Pfizer and may hold stock or stock options

Dr Deshayne Fell. ORCID: 0000-0002-5548-3228. Pfizer. United States of America.

Conflict of interest
Employee of Pfizer and may hold stock or stock options

Dr Sarah Cox. ORCID: 0000-0002-2447-0504. Pfizer. United States of America.

Conflict of interest

Employee of Pfizer and may hold stock or stock options

Dr Xu Xiong. ORCID: 0000-0001-9292-5059. Tulane University, Celia Scott Weatherhead School of Public Health. United States of America.

No conflict of interest declared.

Professor Andy Stergachis. ORCID: 0000-0003-0057-6627. University of Washington. United States of America.

No conflict of interest declared.

Dr Flor Munoz. ORCID: 0000-0002-0457-7689. Baylor College of Medicine. United States of America.

Conflict of interest
Member of DSMB Pfizer vaccines

Investigator (site PI) Pfizer COVID vaccines

Professor Pierre Buekens. ORCID: 0000-0002-4294-8559. Tulane University, Celia Scott Weatherhead School of Public Health and Tropical Medicine. United States of America.

No conflict of interest declared.

Named contact

Dr Agustina Mazzoni (amazzoni@iecs.org.ar). ORCID: 0000-0003-3328-2705. Institute for Clinical Effectiveness and Health Policy. Argentina.

Review affiliation

Institute for Clinical Effectiveness and Health Policy

Funding source

Pfizer.

Peer review

There has been no peer review of this planned review.

ADDITIONAL INFORMATION

Review conflict of interest 1 change

Declared individual interests are recorded under team member details. This review is funded by a commercial organisation. Six review team members have declared a potential conflict of interest.This review also notes the following interests:

Declared individual interests are recorded under team member details. This review is funded by a commercial organisation. Six review team members have declared a potential conflict of interest. No additional interests are recorded for this review.

Medical Subject Headings

Female; Fetus; Gestational Age; Humans; Immunity; Immunologic Factors; Infant; Infant, Newborn; Milk, Human; Placenta; Postpartum Period; Pregnancy; Respiratory Syncytial Virus Vaccines; Respiratory Syncytial Virus, Human; Seasons; Vaccination; Vaccines, Combined

Revision note 1 change

Based on the work carried out by the team, several modifications were made to the systematic review. Specifically, within the population criteria, we included postpartum individuals in addition to pregnant persons, newborns, and infants, as they are also

considered part of the maternal population. Regarding the eligibility criteria for the studies, we decided to exclude narrative reviews, editorials, commentaries, case reports, preprints, and modeling studies. We also agreed to exclude certain sources of information related to these study types, as we considered that they would not contribute substantial value to the review. We changed the start date for the review to September 30th. In relation to databases to be searched, we have added grey literature published by national health agencies and clinical trial registries, as these sources may provide valuable additional data. The outcomes were reorganized to present the information more clearly. Finally, we added a more detailed version of Planned Data Synthesis.

SIMILAR REVIEWS

Check for similar records already in PROSPERO

PROSPERO identified a number of existing PROSPERO records that were similar to this one (last check made on 20 June 2025). These are shown below along with the reasons given by that the review team for the reviews being different and/or proceeding.

- Safety, immunogenicity, and effectiveness of respiratory syncytial virus vaccines for pregnant persons: A living systematic review and meta-analysis [published 11 March 2023] [CRD42023404261]. The review was judged **not to be similar**
- Systematic Review and Meta-Analysis of Efficacy and Safety of Maternal Respiratory Syncytial Virus (RSV) Vaccination in Preventing Severe Neonatal Infection and Associated Outcomes. [published 8 April 2025] [CRD420251014636]. The review was judged **not to be similar**
- Safety, immunogenicity, and effectiveness of Lassa vaccines in pregnant persons: A protocol for a living systematic review and meta-analysis [published 20 June 2024] [CRD42024554330]. The review was judged **not to be similar**

PROSPERO version history 1 change

- Version 2.0, published 14 Oct 2025
- Version 1.0, published 07 Jul 2025

Disclaimer

The content of this record displays the information provided by the review team. PROSPERO does not peer review registration records or endorse their content.

PROSPERO accepts and posts the information provided in good faith; responsibility for record content rests with the review team. The guarantor for this record has affirmed that the information provided is truthful and that they understand that deliberate provision of inaccurate information may be construed as scientific misconduct.