McMaster University | Health Forum

Rapid evidence synthesis

Efficacy and effectiveness of respiratory syncytial virus vaccines and monoclonal antibodies against lower respiratory tract disease in older adults and infants

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Context

- Respiratory syncytial virus (RSV) is a common respiratory virus that causes mild symptoms in most people; however, it can manifest as serious lower respiratory tract disease (LRTD)/lower respiratory tract infection (LRTI) in infants and older adults with underlying conditions or weakened immune systems.
- RSV is one of the most significant causes of excess morbidity and mortality in older adults (1) and is associated with 52.7 hospitalizations per 100,000 people over the age of 65 years annually.(2)
- Adults with certain underlying chronic conditions are at increased risk of RSV-associated LRTD/ LRTI, with 9.5% of U.S. adults 18 to 49 years and 24.3% of those 50 to 64 years at risk.(3; 4)
- In Canada, RSV also has a greater impact on infant and child populations.
  - While high-risk infants face a greater risk of severe outcomes, healthy term infants contribute most to the overall healthcare burden.(5)
  - Nationally, about 1% of Canadian infants are hospitalized with RSV in their first year.(6)
  - Children in remote northern communities face a disproportionate burden of RSV hospitalization, with rates ranging from 20 to 50% of all live births in some areas.(6)
- AREXVY™ (RSVPreF3) by GlaxoSmithKline, ABRYSVO™ (RSVpreF) by Pfizer, and mRESVIA™ by Moderna are vaccines that are authorized in Canada to prevent LRTD/LRTI caused by RSV in adults.
- For infant protection, Health Canada has authorized the monoclonal antibody BEYFORTUS™ (nirsevimab) by Sanofi and SYNAGIS® (palivizumab), as well as the ABRYSVO™ (RSVpreF) vaccine by Pfizer, which provides passive immunity.
  - The National Advisory Committee on Immunization (NACI) currently recommends nirsevimab for immunization programs while they await more data on RSVpreF.(6)
- Monitoring vaccine performance through efficacy and effectiveness studies is crucial for understanding and improving vaccination benefits, and for evaluating how circulating and evolving RSV types affect vaccine performance in both clinical settings and real-world conditions, while also considering various outcomes and populations.
- The Public Health Agency of Canada aims to monitor the efficacy, post-market effectiveness, and impact of RSV vaccines over time to support vaccine policy, enhance situational awareness, inform routine briefings, and ultimately protect Canadians from severe illness.
- This living evidence synthesis has been requested to inform these efforts.

Questions

Primary research questions

1) What is the efficacy of RSV vaccines against LRTD/ LRTI, medically attended LRTD/ LRTI, and severe LRTD/ LRTI in the general population (all ages), older adults aged ≥60 years, and newborn infants and young children <2 years old (RSVpreF only)?
2) What is the effectiveness of RSV vaccines against LRTD/ LRTI, medically attended LRTD/ LRTI, and severe LRTD/ LRTI in the general population (all ages), older adults aged ≥60 years, and newborn infants and young children <2 years old (RSVpreF only)?

Secondary research questions

1) How effective are RSVPreF3 and RSVpreF against LRTD/ LRTI, medically attended LRTD/ LRTI, and severe LRTD/ LRTI over multiple RSV seasons and time?
2) What is the effectiveness of nirsevimab against hospitalization in infants and children less than 2 years of age?
3) How effective are RSV vaccines against LRTD/ LRTI, medically attended LRTD/ LRTI, and severe LRTD/ LRTI in high-risk adults aged 18–59 years (for future update)?

High-level summary of key findings

Evidence identified

- We identified 1,913 articles, and after removing 143 duplicates, we screened 1,799 titles and abstracts.
- We reviewed 102 full-text articles and included 35 articles published between 2020 and 2024:
  - 13 studies were randomized clinical trials
  - 22 were non-randomized clinical studies (e.g. test-negative case-control, prospective cohort study, retrospective cohort study).
- The risk of bias results were as follows:
  - in randomized studies (RoB 2), the risk of bias was assessed as low (n = 10) and some concerns (n = 3)
  - in non-randomized clinical studies (ROBINS-I), the risk of bias was assessed as low (n = 2), moderate (n = 16) and serious (n = 4).

Key findings for RSV immunization product efficacy

- Nirsevimab monoclonal antibody (BEYFORTUS™) demonstrates high efficacy (70–86%) in preventing RSV infections and hospitalizations in infants, with consistent results across multiple studies.
- Maternal RSVpreF vaccination (ABRYSVO™) provides significant protection to infants (51–100% efficacy), with strongest effects in the first 90 days of life and against severe disease.
- For adults ≥60 years, GSK's RSVPreF3 (AREXVY™) and Pfizer's RSVpreF (ABRYSVO™) vaccines show strong efficacy (67–94% and 59–86%, respectively) against RSV-related respiratory illness.

Box 1: Approach and supporting materials

We retrieved candidate studies by searching: 1) Medline, 2) Embase via OVID, 3) Preprint Citation Index (e.g. bioRiv, medRxiv); and 4) ClinicalTrials.gov. We also included studies identified by subject-matter experts who reviewed the protocols and final report. Searches were conducted for studies reported in English, French, Spanish, Portuguese, Arabic, and Chinese conducted with humans and published since database inception until 20 January 2025. Our detailed search strategy is included in Appendix 1.

For efficacy/effectiveness outcomes, any experimental design such as interventional trials or observational designs including cohort, test-negative case-control, before-after studies, interrupted time-series, and case series were considered for inclusion. For all outcomes, evidence syntheses were tracked, and any relevant primary studies from them were pulled out for our analysis. A full list of included studies is provided in Appendices 2 and 3. Studies excluded at the last stages of reviewing are provided in Appendix 4.

Population of interest: Older adults aged ≥60 years, children less than 2 years of age (for secondary question 2), and adults aged 18–59 years (for secondary question 3).

Intervention and control/comparator: Intervention: three RSV vaccines named AREXVY™ (RSVPreF3), ABRYSVO™ (RSVpreF), and mRESVIA™(mRNA-1345) as well as the monoclonal antibody BEYFORTUS™ (nirsevimab); Control: Unvaccinated individuals or individuals receiving placebo.

Primary outcomes: 1) lower respiratory tract disease (LRTD)/ lower respiratory tract infection (LRTI); 2) medically attended LRTD/LRTI; and 3) severe LRTD/LRTI.

Secondary outcomes: 1) acute respiratory infection/acute respiratory disease; and 2) any of the following outcomes associated with RSV due to a) hospitalization; b) emergency department visits; c) ICU admission; d) deaths; and e) outpatient visits.

Data extraction: Data extraction was conducted by one team member.

Critical appraisal: The risk of bias (ROB) of individual studies was assessed using validated ROB tools. For randomized controlled trials, we used RoB-2, and for observational studies, we used ROBINS-I. Judgments for the domains within these tools were decided by one reviewer and details are provided in Appendices 5 and 6. A PRISMA flow diagram is provided in Appendix 7.

Summaries: We summarized the evidence by presenting narrative evidence profiles across studies by outcome measure.

- Moderna's mRNA-1345 (mRESVIA™) demonstrates approximately 84% efficacy against RSV-LRTD in older adults, with better protection against RSV-A (92%) than RSV-B (69%).

Key findings for RSV immunization product effectiveness

- Nirsevimab demonstrated high effectiveness in infants, providing 80–90% protection against RSV-related hospitalizations across studies, 85–95% protection against severe disease requiring intensive care, and 70–80% protection against medically attended RSV infection in primary care settings, though effectiveness wanes over time.
- Effectiveness of nirsevimab varies by setting and disease severity, with highest protection against severe outcomes (hospitalization, ICU admission, oxygen support) and comparatively lower protection against milder presentations like emergency department visits and outpatient cases.
- Both RSV vaccines for older adults (GSK's Arexvy and Pfizer's Abrysvo) show robust effectiveness (75–83%) against RSV-associated hospitalizations in adults ≥60 years, with somewhat higher effectiveness for Arexvy (83%) compared to Abrysvo (73%), and evidence of waning protection beyond 60 days post-vaccination.
- No effectiveness studies were identified for maternal RSVpreF vaccine (Abrysvo) in preventing infant RSV or for Moderna's mRESVIA vaccine in older adults.

Background

Respiratory syncytial virus (RSV) presents a significant and variable public-health challenge in Canada, particularly affecting infants, young children, and older adults. Recent data highlights the scope of this issue:

- RSV is associated with 52.7 hospitalizations per 100,000 people over the age of 65 years annually (2)
- among U.S. adults, 9.5% of those aged 18 to 49 years and 24.3% of those aged 50 to 64 years are at risk of severe RSV disease due to underlying conditions (3; 7)
- in Canada, about 1% of Canadian infants are hospitalized with RSV in their first year of life (6)
- in some remote northern communities of Canada, hospitalization rates for children range from 20 to 50% of all live births.(6)

This growing public-health concern has intensified the focus on more effective RSV prevention strategies, particularly for high-risk and disproportionately affected groups. Recently authorized vaccines and immunization products offer new possibilities for RSV prevention:

- AREXVY™ and ABRYSVO™ are authorized vaccines in Canada to prevent LRTD/LRTI caused by RSV in individuals 60 years and older
- a monoclonal antibody called nirsevimab (BEYFORTUS™) and a vaccine called RSVpreF (ABRYSVO™) are authorized to protect infants using passive immunity.

While these products show potential for RSV prevention, uncertainty persists about their effectiveness across different populations and RSV types.(8-12) Factors such as age, health status, and the match between vaccine strains and circulating viruses can influence vaccine efficacy and effectiveness.

To inform ongoing efforts to update and refine vaccine recommendations, there is a critical need for high-quality, routinely updated syntheses of the best-available evidence, which is why this living evidence synthesis has been requested. Monitoring vaccine performance through efficacy and effectiveness studies is crucial for understanding and improving vaccination benefits, and for evaluating how circulating and evolving RSV affect vaccine performance in both clinical settings and real-world conditions.

Our primary research questions were the following:

1) What is the efficacy of RSV vaccines against LRTD/LRTI, medically attended LRTD/LRTI, and severe LRTD/LRTI in in the general population (all ages), older adults aged ≥60 years, and newborn infants and young children <2 years old (RSVpreF only)?

2) What is the effectiveness of RSV vaccines against LRTD/ LRTI, medically attended LRTD/ LRTI, and severe LRTD/ LRTI in the general population (all ages), older adults aged ≥60 years, and newborn infants and young children <2 years old (RSVpreF only)?

Our secondary research questions were the following:
1) How effective are RSVPreF3 and RSVpreF against LRTD/ LRTI, medically attended LRTD/ LRTI, and severe LRTD/ LRTI over multiple RSV seasons and time?
2) What is the effectiveness of nirsevimab against hospitalization in infants and children less than 2 years of age?
3) How effective are RSV vaccines against LRTD/ LRTI, medically attended LRTD/ LRTI, and severe LRTD/ LRTI in high-risk adults aged 18–59 years (for future update)?

What we found

Key findings

We identified 1,943 articles, and after removing 143 duplicates, we screened 1,799 titles and abstracts. We reviewed 102 full-text articles and included 35 articles published between 2020 and 2024. Data from Papi (2023) (10) and Ison (2024) (13) are from a single trial (AReSVi-006) testing GSK's RSVPreF3 OA vaccine. Similarly, Walsh (2023) (12) and Walsh (2024) (14) report data from the same RENOIR trial testing Pfizer's bivalent RSVpreF vaccine, with the 2024 publication providing extended two-season efficacy results. Additionally, Otsuki (2024) presented a Japan subset analysis of Kampmann's (2023) study (MATISSE).(15) To avoid duplicate data, we only included Ison (2024), Walsh (2024), and Kampmann (2023) in our analysis.

These studies included the following:
- 13 randomized clinical trials
  - the risk of bias in the randomized studies was low in eight; there were some concerns in three of the included studies
- 22 non-randomized clinical studies (e.g., test-negative case-control, prospective cohort, retrospective cohort study)
  - the risk of bias (ROBINS-I) in the non-randomized studies was low in two, moderate in 16, and serious in four
- the 35 studies spanned multiple geographic regions:
  - South (Argentina, Brazil, Chile) and North America (U.S., Canada)
  - Europe (Spain, France, Germany, U.K., Netherlands, Finland, Belgium)
  - Asia (Japan, Philippines, South Korea)
  - Africa (South Africa, Gambia)
  - Australasia (Australia, New Zealand).

A summary of the characteristics of the individual studies included, such as its population, study design, type of vaccine and efficacy/effectiveness outcomes assessed, is represented in Table 1 (efficacy studies) and Table 2 (effectiveness studies). In general, the studies analyze similar outcomes, namely RSV-related LRTD/LRTI, RSV-related acute respiratory infection/disease (ARI/ARD), RSV-related bronchiolitis outcomes, and RSV-related outcomes without specifically classifying them as LRTD/ LRTI, ARI or bronchiolitis outcomes. We extracted the outcomes explicitly following what authors reported in their original articles. The diagnostic criteria varied slightly between studies; for details of the definition of each outcome, please refer to each study.

1. Efficacy of RSV immunization products

1.1 Infants and children aged <2 years

1.1.1 Nirsevimab monoclonal antibody (BEYFORTUS™)

RSV-related LRTI/LRTD outcomes

Multiple randomized, double-blind, placebo-controlled trials have demonstrated the efficacy of nirsevimab in preventing RSV-related infections in infants. Simões (2023) conducted a comprehensive evaluation of nirsevimab efficacy, reporting a 79.5% relative risk reduction (95% CI 65.9–87.7) for the primary endpoint of medically attended RSV-related LRTD/LRTI. The study also demonstrated a 41.9% relative risk reduction (95% CI 25.7–54.6) for LRTI/LRTD outpatient visits.(16) Similarly, Griffin (2020) focused on preterm infants with gestational age at birth of 29 weeks 0 days to 34 weeks 6 days, showing a 70.1% lower incidence (95% CI 52.3–81.2, p<0.001) of medically attended RSV-related LRTI/LRTD compared to placebo.(17)

For RSV-related LRTI/LRTD requiring hospitalization, Simões found a 77.3% relative risk reduction (95% CI 50.3–89.7) and Griffin demonstrated a 78.4% lower incidence (95% CI 51.9–90.3) compared to placebo.(16; 17) Drysdale (2023) conducted a pragmatic, phase 3b, open-label, two-group, randomized trial across 235 sites in France, Germany, and the United Kingdom that included healthy infants 12 months or younger born at gestational age ≥29 weeks. This study reported an 83.2% efficacy (95% CI 67.8–92.0, p<0.001) for RSV-related LRTD/LRTI hospitalization. Country-specific efficacy against hospitalization for RSV-related LRTD/LRTI in the Drysdale study showed consistent results across regions: France (89.6%, adjusted 95% CI 58.8–98.7), Germany (74.2%, adjusted 95% CI 27.9-92.5), and United Kingdom (83.4%, adjusted 95% CI 34.3–97.6).(18)

Regarding severe RSV-related LRTI/LRTD, Simões (2023) reported an 86.0% relative risk reduction (95% CI 62.5–94.8).(16) Drysdale (2023) reported an efficacy of 75.7% (95% CI 32.8–92.9, p=0.004) with 5 infants (0.1%) in the nirsevimab group versus 19 infants (0.5%) in the standard-care group.(18)

1.1.2 Maternal RSVpreF vaccine (ABRYSVO™) and Maternal RSVPreF3 vaccine

Several randomized, double-blind, placebo-controlled trials have demonstrated the efficacy of maternal RSVpreF vaccine in preventing RSV infections in infants. For medically attended RSV-related LRTD/LRTI. Kampmann (2023) reported 57.1% efficacy (99.5% CI 14.7–79.8) within 90 days after birth and 51.3% efficacy (97.58% CI 29.4–66.8) within 180 days after birth in the MATISSE trial, which included 7,358 pregnant women at 24–36 weeks' gestation across 18 countries, with 3,570 infants whose mothers received RSVpreF and 3,558 infants whose mothers received placebo.(19)

Dieussaert (2024) reported 65.5% efficacy (95% CI 37.5–82.0) for any medically assessed RSV-related LRTI/LRTD from birth to 6 months of age in a phase 3 trial of maternal RSVPreF3-Mat (by GlaxoSmithKline) that included 5,328 pregnant women with 3,426 infants in the vaccinated group and 1,711 in the placebo group.(9) However, it is important to note that this vaccine is not approved for use, and enrollment and vaccination were stopped prematurely due to a higher risk of preterm birth observed in the vaccine group compared to the placebo group.

Regarding RSV-related hospitalization, Kampmann (2023) showed 67.7% efficacy (99.17% CI 15.9-89.5) within 90 days after birth and 56.8% efficacy (99.17% CI 10.1–80.7) within 180 days after birth.(19)

For severe medically attended RSV-related LRTI/LRTD, Kampmann (2023) reported 81.8% efficacy (99.5% CI 40.6-96.3) within 90 days after birth and 69.4% efficacy (97.58% CI 44.3–84.1) within 180 days after birth.(19) Dieussaert (2024) reported 69.0% efficacy (95% CI 33.0–87.6) for severe medically assessed RSV-associated LRTD.(9)

1.2 Older adults aged ≥60 years

1.2.1 RSVPreF3 vaccine (AREXVY™)

Multiple phase 3 trials have been conducted to evaluate the efficacy of RSVPreF3 vaccine in adults ≥60 years. For RSV-related LRTI/LRTD, Curran (2024) showed 87.5% efficacy (95% CI 58.9–97.6) against RSV-confirmed LRTI/LRTD with medically attended visits in an observer-blind, multi-country, randomized trial.(20) Ison (2024) reported 67.2% efficacy (97.5% CI 48.2–80.0) for one dose over 2 RSV seasons in the AReSVi-006 phase 3 trial conducted across 17 countries.(13) For severe RSV-related LRTD, Ison (2024) reported 78.8% efficacy (95% CI 52.6–92.0%) for one dose over 2 RSV seasons.(13)

Regarding RSV-related ARI, Curran (2024) showed 79.0% efficacy (95% CI 54.3–91.5) against RSV-confirmed ARI with medically attended visits.(20) Ison (2024) showed 52.7% efficacy (95% CI 40.0–63.0) for one dose over 2 RSV seasons.(13)

1.2.2 RSVpreF vaccine (ABRYSVO™)

The RSVpreF (ABRYSVO™) vaccine by Pfizer demonstrated efficacy in older adults across several trials. For RSV-related LRTI/LRTD with ≥2 signs or symptoms, Walsh (2024) reported pooled data across two seasons showing 58.8% efficacy (95% CI 43.0–70.6). For RSV-related LRTI/LRTD with ≥3 signs or symptoms, Walsh (2024) reported 85.7% efficacy (96.66% CI 32.0–98.7) across two seasons combined.(14) For RSV-associated ARI, Walsh (2024) reported 62.1% efficacy (95% CI 37.1–77.9) across two seasons combined.(14)

1.2.3 mRESVIA™

Wilson (2023) evaluated the mRNA-1345 vaccine (mRESVIA™) in the ConquerRSV trial, a randomized, double-blind, placebo-controlled phase 2–3 trial that included 35,541 participants aged 60 years and older. For RSV-related LRTI/LRTD ≥2 signs or symptoms, the study found 83.7% efficacy (95.88% CI 66.0–92.2, one-sided P<0.001). For RSV-related LRTI/LRTD with ≥3 signs or symptoms, the efficacy was 82.4% (96.36% CI 34.8–95.3, one-sided P = 0.008). For RSV-related ARI, the study showed 68.4% efficacy (95% CI 50.9–79.7).(21)

1.3 Adults aged 18–50 years

In a challenge study, Schmoele-Thoma (2022) evaluated a bivalent prefusion F RSV vaccine (RSVpreF) in 70 healthy adults aged 18–50 years with low baseline RSV-neutralizing antibody titers and showed 86.7% efficacy (95% CI 53.8–96.5) against symptomatic RSV infection confirmed by any detectable viral RNA, and 100.0% efficacy (95% CI 72.8–100.0) against symptomatic RSV infection confirmed by quantifiable RT-qPCR or culture in a phase 2a, randomized, double-blind study.(11)

2. Effectiveness of RSV immunization products

2.1 Infants and children aged <2 years

2.1.1 Nirsevimab monoclonal antibody (BEYFORTUS™)

RSV-related LRTD/LRTI outcomes

López-Lacort (2025) reported nirsevimab effectiveness of 75.8% (95% CI 40.0–92.7) against medically attended RSV-related LRTD/LRTI in primary-care settings.(22) Six studies evaluated the effectiveness of nirsevimab against RSV-related LRTD/LRTI **hospitalizations.** Ezpeleta (2024) (23) demonstrated the highest effectiveness at 88.7% (95% CI 69.6–85.8) in Navarre, Spain, followed closely by López-Lacort (2024), who found effectiveness of 84.4% (95% CI 76.8–90.0) using screening method and 70.2% (95% CI 38.3–88.5) using a test-negative design in a multicentre active surveillance study conducted across nine hospitals in three regions of Spain.(24) Ares-Gómez (2024) (25) and Agüera (2024) (26) reported effectiveness of 82.0% (95% CI 65.6–90.2) in the NIRSE-GAL study conducted in Galicia, Spain and 81.0% (95% CI 60.9–90.7), respectively. Chauvel (2024) reported slightly lower effectiveness at 78.3% (95% CI 55.9–89.5).(27) Jimeno Ruiz (2024) provided valuable age-specific insights, showing a 79.3% reduction in RSV-related LRTD/LRTI hospitalizations (IRR: 0.21, 95% CI 0.12–0.34) among **infants under 3 months of age and** 66.9% reduction (IRR: 0.33, 95% CI 0.15–0.64) among **infants aged 3–6 months.(28)**

Two studies evaluated the effectiveness of nirsevimab against severe RSV-related LRTD/LRTI**.** Ares-Gómez (2024) reported effectiveness of 86.9% (95% CI 69.1–94.2) against severe RSV-related LRTD/LRTI **requiring oxygen support**.(25) Jimeno Ruiz (2024) provided comprehensive age-stratified analyses, showing a 77.3% reduction in RSV-related LRTD/LRTI with oxygen support (IRR: 0.23, 95% CI 0.11–0.42) and a 68.7% reduction (IRR: 0.32, 95% CI 0.16–0.56) in RSV-related LRTD/LRTI **hospitalizations involving ICU admission** among infants under 3 months of age. For infants aged 3-6 months,

the reduction was higher, with a 91.7% reduction (IRR: 0.08, 95% CI 0.01–0.39) in cases requiring oxygen support and a 67.9% reduction (IRR: 0.32, 95% CI 0.04–1.20) in ICU admissions.(28) **Additionally,** Jimeno Ruiz (2024) evaluated more intensive respiratory support interventions, demonstrating a 78.0% reduction (IRR: 0.22, 95% CI 0.11–0.41) in RSV-related LRTD/LRTI requiring non-invasive mechanical ventilation (NIMV) and/or high-flow nasal oxygen (HFNO) among infants under 3 months of age, and a 91.4% reduction (IRR: 0.09, 95% CI 0.01–0.41) among infants aged 3–6 months.(28)

*RSV-related **ARI outcomes***

Two studies evaluated the effectiveness of nirsevimab against RSV-related ARI**.** Moline (2025) reported nirsevimab effectiveness of **89% (95% CI 79–94)** in a multi-center US study,(29) while Lefferts (2024) reported effectiveness of 82% (95% CI 62–91) in the Yukon-Kuskokwim Delta region of Alaska.(30) Both studies demonstrate consistently high effectiveness of nirsevimab against RSV-related ARI, with overlapping confidence intervals suggesting reliable protection.

RSV-related bronchiolitis outcomes

Multiple studies evaluated nirsevimab effectiveness against RSV-bronchiolitis across different severity levels. For less severe outpatient cases, Coma (2024) reported effectiveness of 48.1% (95% CI 42.4–53.3) for primary-care attended bronchiolitis, while Lassoued (2024) found higher effectiveness of 79.7% (95% CI 67.7–87.3) against RSV-bronchiolitis in outpatients.(31) For emergency department visits, Coma (2024) demonstrated effectiveness of 55.4% (95% CI 48.4–61.5) (8) and Carbajal (2024) reported 83% (95% CI 71.0–90.0) against paediatric emergency department visits for RSV-associated bronchiolitis.(32)

For hospitalizations, effectiveness was consistently higher. Rodríguez-Fernández (2024) reported 85% (95% CI 32.0–97.0) effectiveness against hospital admission for RSV bronchiolitis in infants under 6 months of age.(33) Similarly, Carbajal (2024) (32) found 83% (95% CI 72.0–90.0) effectiveness against hospitalizations for RSV-associated bronchiolitis, and Coma (2024) reported 87.6% (95% CI 82.1–91.4) against hospital admission due to RSV bronchiolitis.(8)

For severe cases requiring additional interventions during hospitalization, Carbajal (2024) reported effectiveness of 88% (95% CI 74.0–95.0) against RSV-associated bronchiolitis requiring feeding by nasogastric tube and 91.0% (95% CI 78.0–96.0) against cases requiring supplemental oxygen.(32)

For the most severe cases requiring intensive care, Coma (2024) reported higher effectiveness of 90.1% (95% CI 76.3–95.9) against ICU admission due to RSV bronchiolitis,(8) while Paireau (2024) found effectiveness of 75.9% (95% CI 48.5–88.7) against severe RSV-bronchiolitis cases requiring pediatric ICU admission.(34) Assad (2024) demonstrated effectiveness of 69.6% (95% CI 42.9–83.8) against RSV-associated bronchiolitis leading to pediatric ICU admission and 67.2% (95% CI 38.6–82.5) against cases requiring ventilatory support.(35) Carbajal (2024) found similar effectiveness of 67.0% (95% CI –100.0–95.0) against hospitalizations requiring pediatric ICU admission.(32)

RSV-associated outcomes

Five studies evaluated RSV-associated outcomes without specifically classifying them as LRTI/LRTD, ARI or bronchiolitis outcomes. Ezpeleta (2024) reported the highest effectiveness at 87.9% (95% CI 70.3–95.1) **against RSV infection attended in the emergency room**.(23) Xu (2024) demonstrated varying effectiveness based on healthcare setting: 79% (95% CI 63–91) against medically attended RSV infection within two weeks post-immunization and to 87.6% (95% CI 67.7–95.3) at 16 weeks, 68.4% (95% CI 50.3–80.8) against medically attended RSV infection overall, and 61.6% (95% CI 35.6–78.6) specifically for outpatient visits.(36)

Estrella-Porter (2024) found effectiveness of 73.7% against RSV infection,(37) while Coma 2024 reported similar results with effectiveness of 68.9% (95% CI 51.7–80.0) against RSV infection.(8) These findings collectively demonstrate substantial protection against RSV infection across different healthcare settings and populations.

For the effectiveness of nirsevimab against RSV-related hospitalization, multiple studies reported consistently high protection rates. Lefferts (2024) (30) and Moline (2024) (38) both reported effectiveness of 93%, with confidence intervals of 64–99% and 82–97%, respectively. Similarly, Barbas Del Buey (2024) found effectiveness of 93.6% (95% CI 89.7–96.1) at 30 days to 87.6% (95% CI 67.7–95.3) at 150 days against hospitalization due to RSV infection, representing the highest point estimate with the narrowest confidence interval.(39) Xu (2024) reported slightly lower effectiveness at 80.5% (95% CI 52.0–93.5) for RSV-associated hospitalizations.(36) These consistently high effectiveness estimates across multiple studies demonstrate nirsevimab's robust protection against severe RSV disease requiring hospitalization.

Three studies evaluated nirsevimab effectiveness against severe RSV disease requiring intensive interventions. Barbas Del Buey (2024) reported the highest **effectiveness of** 94.4% (95% CI 87.3–97.5) at 30 days and 89.0% (95% CI –207.3-99.6) at 150 days against intensive care unit admission.(39) Agüera (2024) reported **effectiveness of** 85.6% (95% CI 41.7–96.4) **against RSV severe disease** (defined as need for non-invasive ventilation [NIV] or conventional mechanical ventilation [CMV]).(26) For the most severe cases requiring invasive mechanical ventilation (IMV), Jimeno Ruiz (2024) reported a 87.2% reduction (IRR: 0.13, 95% CI 0.01–0.68) among infants under 3 months of age. (28)

2.1.2 Maternal RSVpreF vaccine (ABRYSVO™)

None of the included studies examined the effectiveness of maternal RSVpreF vaccine against RSV-related outcomes among children under 2 years of age.

2.2 Older adults aged ≥60 years

2.2.1 RSVPreF3 vaccine (AREXVY™) and RSVpreF vaccine (ABRYSVO™)

RSV vaccines demonstrated substantial effectiveness against RSV-associated respiratory illness in adults aged 60 years and older. Surie (2024) evaluated both GSK's RSVPreF3 (Arexvy) and Pfizer's RSVpreF (Abrysvo) vaccines, finding overall vaccine effectiveness of 75.0% (95% CI 50.0–87.0) against RSV-associated hospitalization, with similar effectiveness between vaccine types.(40) Payne (2024) also assessed both vaccines, reporting vaccine effectiveness of 80.0% (95% CI 71.0–85.0) against RSV-associated hospitalization among immunocompetent adults, with GSK's Arexvy showing 83.0% (95% CI 73.0–89.0) and Pfizer's Abrysvo showing 73.0% (95% CI 52.0–85.0) effectiveness.(41) Additionally, Payne found 81.0% effectiveness (95% CI 52.0–92.0) against RSV-associated critical illness (ICU admission or death) and 77.0% effectiveness (95% CI 70.0–83.0) against emergency department encounters. The study further demonstrated effectiveness by time since vaccination, with higher protection (90.0%, 95% CI 79.0–95.0) at 14–59 days post-vaccination compared to ≥60 days post-vaccination (73.0%, 95% CI 60.0–82.0).(41) Tartof (2024) specifically evaluated Pfizer's RSVpreF (Abrysvo) vaccine in a case-control study, finding effectiveness of 87.0% (95% CI –8.0–98.0) against RSV-related LRTD hospitalizations and 93.0% (95% CI 45.0–99.0) against RSV-related LRTD/LRTI emergency department visits.(42)

2.2.2 mRESVIA™

None of the included studies examined the effectiveness of mRESVIA vaccine against RSV-related outcomes in adults aged 60 years and older.

Next steps based on the identified evidence

The following recommended actions, synthesized from comprehensive review of the evidence, address critical knowledge gaps in RSV vaccine effectiveness. They provide a structured framework to enhance research and public health responses to seasonal RSV outbreaks. These recommendations aim to strengthen our understanding of vaccine performance across different populations while improving outbreak management strategies.

- Research Recommendations

- **Address evidence gaps** in maternal RSVpreF vaccine effectiveness by conducting real-world studies focused on infant outcomes (0–6 months) and evaluating mRESVIA's effectiveness in older adults (≥60 years) to provide a complete picture of all available RSV prevention options.
- **Investigate duration of protection** through extended follow-up studies to better understand the waning effectiveness observed across products, particularly focusing on protection beyond 150 days for nirsevimab in infants and beyond 60 days for adult RSV vaccines.

- Policy Implications
  - **Design and implement vaccination strategies** for nirsevimab programs focusing on protecting young infants under 6 months of age, where the evidence shows strongest protection against severe RSV disease requiring hospitalization and respiratory support.
  - **Establish surveillance systems** to monitor real-world effectiveness across different populations and geographic regions, particularly as products like maternal RSVpreF vaccine and mRESVIA lack effectiveness data but may be incorporated into immunization programs.
  - **Consider seasonal timing of immunization** for older adults receiving RSV vaccines, given the evidence of waning protection after 60 days, to ensure optimal coverage during peak RSV seasons in different geographic regions.

Table 1: Characteristics of all included studies reporting on the efficacy of RSV immunization products

Reference (author year) with URL	Research question addressed	Geographical location	Design and Study Period	Population	Analysis	Type of immunization product	Risk of Bias
Curran 2024	• Vaccine efficacy (VE) against medically attended acute respiratory infection and lower respiratory tract disease (LRTD)	Not reported	Design: Observer blind multi-country randomized trial Study period: N/A	24,960 adults (over the age of 60) were included	VE was estimated using the conditional exact binomial method based on the Poisson model	• AREXVY™ (RSVPreF3 OA)	Low
Walsh 2023	• VE against RSV-associated lower respiratory tract illness (LRTI) based on signs and symptoms and overall among older adults (60 years and older)	**Multinational (**Argentina, Canada, Finland, Japan, the Netherlands, South Africa, United States)	Design: Phase three, multinational, double-blinded, randomized, placebo-controlled trial Study period: 31 August 2021–14 July 2022	34,284 participants (aged ≥60 years) received one intramuscular 120-ug dose of RSVpreF or placebo	Used a risk ratio-based approach to calculate VE, comparing the incidence of RSV-associated LRTI and acute respiratory illness between the vaccine and placebo groups, with confidence intervals calculated using a conditional exact test adjusted for interim analysis using Pocock error spending	• RSVpreF	Low
Kampmann 2023	• VE against RSV-associated both severe LRTI, hospitalization, and all-cause LRTI	18 countries (Argentina, Australia, Brazil, Canada, Chile, Denmark, Finland, Gambia, Japan, Mexico, the Netherlands, New Zealand, Philippines, Republic of Korea, South Africa, Spain, Taiwan, United States)	Design: Phase three, multinational, randomized, placebo-controlled trial Study period: 17 June 2020–24 November 2023	7,358 women were randomly assigned one dose of 120 ug of RSVPreF vaccine or placebo; 3,570 infants (0 to 2 years old) whose mothers received RSVpreF and 3,558 infants whose mothers received placebo were included The two endpoints were either medically attended severe RSV-associated LRTI and medically attended RSV-associated LRTI in infants at 90, 120, 150, and 180 days after birth	Binominal distribution of the number of cases of disease in the RSV vaccine group and given the total number of cases in both groups	• Maternal RSVpreF	Some concerns
Papi 2023	• VE against RSV-associated LRTD, severe LRTD, and acute respiratory infection (ARI)	Multinational including 17 countries in Africa, Asia, Australia, Europe and North America	Design: Phase three, multinational, randomized, placebo-controlled trial	A total of 24,966 participants (aged ≥60 years)	One minus the relative risk with the use of the conditional exact binomial method based on the Poisson model	• RSVpreF3-OA	Low

Reference (author year) with URL	Research question addressed	Geographical location	Design and Study Period	Population	Analysis	Type of immunization product	Risk of Bias
			Study period: 25 May 2021–31 January 2022				
Simoes 2023	• Efficacy of nirsevimab against RSV-related LRTI and hospital admissions in infants	Multinational • Phase 2b trial: 164 sites across 23 countries in Europe, North America, South America, and Australasia • MELODY primary cohort: 160 sites across 21 countries in Europe, North America, Asia, and South Africa • MEDLEY: 126 sites across 25 countries in Europe, North America, Asia, and South Africa	Design: Double-blind, randomized, controlled trials Study period: 7 July 2019–30 September 2021	2,350 infants: 860 infants born preterm (≥29 to <35 weeks gestational age) who weighed less than 5 kg in the phase 2b trial, and 1,490 infants born at term or late preterm (≥35 weeks' gestational age) in the primary cohort of the MELODY trial	Intention-to-treat population using Poisson regression model with robust variance adjusted for age and location and multiple imputation; a prespecified subgroup analysis assessed data by hemisphere, age at randomization, sex, ancestry or ethnic group, weight at baseline, country, and geographical region Post hoc exploratory endpoints of health resource use, outpatient visits, and antibiotic use were also assessed	• Monoclonal antibody (nirsevimab)	Low
Drysdale 2023	• Efficacy of nirsevimab compared to standard care, on hospitalization, ICU admission, and LRTI	France, Germany, United Kingdom	Design: Phase 3b, open-label, two-group, randomized trial Study period: 8 August 2022–28 February 2023	A total of 8,058 infants (12 months or younger) participated in this study (4,037 vaccinated, 4,021 standard care)	A time-to-first event analysis and Cox proportional-hazard regression model was used adjusted for age group and country; P values and Bonferroni corrections were calculated for primary and secondary endpoints	• Monoclonal antibody BEYFORTUS™ (nirsevimab) by Sanofi	Moderate
Dieussaert 2024	• VE, compared to placebo, on infection and severe RSV	24 countries	Design: Double-blind, randomized, placebo-controlled trial Study period: 4 October 2022–5 October 2023	5,328 pregnant women were given the vaccine or placebo; a total of 3,426 infants (0 to 6 months) were included in the vaccinated group and 1,711 in the placebo	VE was calculated using a Bayesian model and the equation: 1-relative risk; in interim safety analysis was also performed	• Maternal AREXVY™ (RSVPreF3)	Some concerns

Reference (author year) with URL	Research question addressed	Geographical location	Design and Study Period	Population	Analysis	Type of immunization product	Risk of Bias
Ison 2024	• VE over two seasons of one dose of RSVPreF3 OA or two doses administered in consecutive RSV seasons in adults aged ≥60 years against RSV-associated LRTD, medically attended RSV-LRTD, severe RSV-LRTD, and acute respiratory infection	Belgium, Canada, Estonia, Finland, Germany, Italy, Japan, Mexico, Poland, South Korea, Russian Federation, Spain, United Kingdom, United States, Australia, New Zealand, South Africa	Design: Randomized, placebo-controlled trial Study period: 25 May 2021–31 January 2022	24,973 participants (aged ≥60 years), in season one 12,470 received RSVPreF3 OA and 12,503 received placebo In season two 19,990 of the original participants were included; 4,966 were revaccinated, 4,991 received a placebo as their second dose (but had previously received the first vaccine dose), and 10,033 received their second placebo dose	This study uses the conditional exact binomial method based on a Poisson model to estimate over the course of two seasons the efficacy of one RSVPreF3 OA dose followed by revaccination a year later against RSV-associated LRTD, severe RSV-LRTD, and RSV-associated ARI in adults ≥60 years old Season, age, and region were covariates in the model Secondary analyses were performed for efficacy based on RSV subtype, season, year, age, comorbidities, and frailty	• RSVPreF3 OA	Low
Griffin 2020	• Evaluation of nirsevimab efficacy against medically attended RSV-associated LRTI and hospitalization due to RSV-LRTI	Argentina, Australia, Belgium, Brazil, Bulgaria, Canada, Chile, Czech Republic, Estonia, Finland, France, Hungary, Italy, Latvia, Lithuania, New Zealand, Poland, South Africa, Spain, Sweden, Turkey, United Kingdom, United States	Design: Randomized, placebo-controlled trail Study period: 3 November 2016–1 December 2017	1,453 preterm infants (born at gestational age 29 weeks 0 days to 34 weeks 6 days ≤1 year old) included, 969 (66.7%) received nirsevimab and 484 (33%) received placebo	This study uses a Poisson regression model to evaluate nirsevimab against RSV-associated medically attended LRTI and RSV-associated hospitalization in preterm infants) ≤1 year old A Cochran-Mantel-Haenszel test and Kaplan-Meier curves were used for secondary analyses Subgroup analyses were performed for efficacy based on hemisphere, age, sex, race, gestational age, and siblings (twins/triplets)	• Monoclonal antibody BEYFORTUS™ (nirsevimab) by Sanofi	Low
Otsuki 2024	• VE of maternal RSVpreF against medically attended RSV-LRTI (RSV-MA-LRTI), severe	Japan	Design: Randomized controlled trial	462 maternal participants (≤49 years old at 24–36 weeks' gestation) were vaccinated with RSVpreF (230) or placebo (232); 434 infants were followed after birth (218 were born to	Calculated using the equation 1-(hP/[1-P])	• ABRYSVO™ (RSVpreF) by Pfizer	Low

Reference (author year) with URL	Research question addressed	Geographical location	Design and Study Period	Population	Analysis	Type of immunization product	Risk of Bias
	RSV-MA-LRTI, RSV-associated hospitalization, and all-cause medically attended LRTI (MA-LRTI) in infants		Study period: 12 November 2020–2 September 2022	mothers who received RSVpreF, 216 were born to mothers who received placebo) until 12–24 months old			
Schmoele-Thoma 2022	• VE of RSVpreF against symptomatic RSV infection confirmed by viral detection on two consecutive days, symptomatic RSV infection confirmed by two quantifiable RT-qPCR results on ≥2 consecutive days, culture-confirmed symptomatic RSV infection, and RSV infection regardless of symptom confirmed with RT-qPCR results on ≥2 consecutive days or a quantifiable culture-confirmed infection	Not reported	Design: Phase 2a, single-centre, randomized, double-blind, exploratory study Study period: N/A	70 healthy adults (age 18-50 years old) were randomized to receive the RSVpreF vaccine (n = 35) or placebo (n = 35); 62 participants (31 in each group) were challenged with the RSV A Memphis 37b preparation; 60 participants completed the full 12-day observation	VE against RSV infection was estimated using the equation (1 – incidence rate ratio) x 100% using the intention to treat population	• ABRYSVO™ (RSVpreF) by Pfizer	Low
Walsh 2024	• VE over two seasons of one dose of RSVpreF3 against RSV-associated LRTD in adults aged ≥60 years with at least three symptoms	Argentina, Canada, Finland, Japan, the Netherlands, South Africa, United States	Design: International phase 3, double-blind, randomized, placebo-controlled trial	18,050 participants (aged ≥60 years) were at risk in the RSVpreF group at the end of season 1; 16,164 participants were at risk in the RSVpreF group at the end of season 2; across both seasons, 18,050 participants in the RSVpreF group were at risk at some point	VE was calculated using case count ratio, calculated as 1 – (P/[1–P]), where P is the number of RSVpreF cases divided by the total number of cases; cases in season 1 and season 2 were pooled to	• ABRYSVO™ (RSVpreF) by Pfizer	Some concerns

Reference (author year) with URL	Research question addressed	Geographical location	Design and Study Period	Population	Analysis	Type of immunization product	Risk of Bias
			Study Period: 12 July 2022–6 November 2023	18,074 participants (aged ≥60 years) were at risk in the placebo group at the end of season 1; 16,059 participants in the placebo group remained at risk at the end of season 2; across both seasons, 18,074 participants in the placebo group were at risk at some point	estimate the VE across both seasons		
Wilson 2023	• VE against RSV-associated LRTD (with at least two signs or symptoms and with at least three signs or symptoms) and RSV-associated acute respiratory disease	Multiple – 22 countries (not reported in detail)	Design: Randomized, double-blind, placebo-controlled study Study period: 17 November 2021–31 October 2022	35,541 participants were randomized, where 17,793 participants were assigned to the mRNA-1345 group and 17,748 were assigned to the placebo group. The mean age of the participants at enrollment was 68.1 years, 49.0% were women, 36.1% were non-White, and 34.5% were Hispanic or Latino One or more coexisting conditions were reported by 29.3% of the participants, with 1.1% reporting a history of congestive heart failure and 5.5% reporting a history of chronic obstructive pulmonary disease (COPD) A total of 21.9% of the participants were assessed as vulnerable or frail, as defined according to the Edmonton Frailty score All participants who had undergone randomization completed at least one visit or surveillance contact 14 days after injection	Vaccine efficacy was calculated as 1 – hazard ratio (mRNA – 1,345 vs. placebo) x 100% The confidence interval for VE was based on a stratified Cox proportional-hazards models in the per-protocol efficacy population	• mRNA-based RSV PreF (mRNA-1345)	Low

Table 2: Characteristics of all included studies reporting on the effectiveness of RSV immunization products

Reference (author year) with URL	Research question addressed	Geographical location	Design and Study Period	Population	Analysis	Type of immunization product	Risk of Bias
Ares-Gomez 2024	• Effectiveness of nirsevimab against RSV-related lower respiratory tract infection (LRTI) hospitalizations and severe RSV-related LRTI requiring oxygen support in infants	Galicia, Spain	Design: Longitudinal study Study period: 25 September 2023–31 March 2024	Participants included 10,259 infants (0 to 2 years old) eligible for nirsevimab, with 9,408 (91.7%) receiving the immunization and 851 (8.3%) not receiving nirsevimab	Nirsevimab effectiveness was estimated using Poisson regression models with robust variance, adjusted for enrollment group (seasonal or catch-up), sex, and residential area, with Cox proportional hazards models used as a secondary analysis for confirmation	• Monoclonal antibody BEYFORTUS ™ (nirsevimab) by Sanofi	Moderate
Estrella-Porter 2024	• Effectiveness of nirsevimab against hospitalizations for cases with RSV	Spain	Design: Observational retrospective study Study period: 1 October 2023–31 March 2024	Participants included 27,362 children (0–2 years old) eligible for the nirsevimab, with 24,223 vaccinated	Nirsevimab effectiveness was calculated using multivariate logistic regression, controlling for factors such as breastfeeding intention, mother's country of origin, gestational weeks, and campaign group, to derive an adjusted odds ratio comparing RSV infection rates between immunized and non-immunized infants	• Monoclonal antibody BEYFORTUS ™ (nirsevimab) by Sanofi	Moderate
Ezpeleta 2024	• Effectiveness of nirsevimab against hospitalizations for cases with RSV, RSV-related emergency department (ED) consultations, and RSV-related ICU admissions	Spain	Design: Population based study, prospective cohort design Study period: July 2023–January 2024	Participants included 1,177 infants (0–2 years old), 1,083 had received a vaccine receiving the vaccine seven days after birth	Epidemiological surveillance, assessing nirsevimab effectiveness and relative risk Hospitalization rates were confirmed using Cox regression adjusted for sex and week of birth, with nirsevimab immunization as a time-dependent variable, estimating effectiveness as (1 – hazard ratio) x 100 for various RSV-related outcomes	• Monoclonal antibody BEYFORTUS ™ (nirsevimab) by Sanofi	Moderate
Moline 2024	• Nirsevimab Effecti veness against infection and hospitalization	United States	Design: Test-negative case-control design	A total of 699 infants (0–2 years old) were included in the study	Pearson's chi-square was used to compare demographic questionnaire by vaccine status. Multivariate logistic	• Monoclonal antibody BEYFORTUS ™	Moderate

Reference (author year) with URL	Research question addressed	Geographical location	Design and Study Period	Population	Analysis	Type of immunization product	Risk of Bias
			Study period: 1 October 2023–29 February 2024		regression was used to estimate vaccine effectiveness	(nirsevimab) by Sanofi	
Lopez-Lacort 2024	• Effectiveness of nirsevimab on infection and lower respiratory tract infection	Spain	Design: Test-negative design Study period: October 2023 to January 2024	A total of 15,676 infants (0–2 years old) were eligible for this study	Bayesian logistic regression was used and supported by a sensitivity analysis to estimate vaccine effectiveness	• Monoclonal antibody BEYFORTUS ™ (nirsevimab) by Sanofi	Moderate
Lassoued 2024	• Effectiveness of nirsevimab against RSV-positive bronchiolitis	France	Design: Test-negative case-control study Study period: 15 September 2023–1 February 2024	A total of 883 infants (0–12 months) were included in the study	Multivariate logistic regression estimated nirsevimab effectiveness; subgroup analyses were performed based on infant's age and gestational age at birth	• Monoclonal antibody BEYFORTUS ™ (nirsevimab) by Sanofi	Moderate
Assad 2024	• Effectiveness of nirsevimab against hospitalization for RSV-positive bronchiolitis	France	Design: Prospective matched case-control study Study period: 15 October 2023–10 December 2023	1,035 patients (690 cases, 345 controls; aged <12 months); 157 (15.2%) were immunized with nirsevimab (60 case patients, 97controls)	A conditional logistic-regression model and a multivariate regression model estimate nirsevimab effectiveness; subgroup analyses were performed based on infant's age, pediatric intensive care unit (PICU) admission, ventilatory support, and at least one risk factor for severe bronchiolitis	• Monoclonal antibody BEYFORTUS ™ (nirsevimab) by Sanofi	Serious
Agüera 2024	• Nirsevimab effectiveness against hospitalization for RSV-associated bronchiolitis and severe RSV disease, Bronchiolitis Score of Sant Joan de Déu, need for oxygen support, and length of hospital stay in	Spain and Andorra	Design: Test-negative case-control Study period: November 2023–February 2024	234 children (up to 12 months old), 141 cases and 93 controls; 181 patients were eligible for nirsevimab; 109 (46.6%) patients had received nirsevimab, 72 (30.8%) were eligible but had not been immunized, and 53 (22.6%) were not eligible	Multivariate analysis using a logistic regression model adjusted for age, weight, and presence of one or more preexisting conditions was used to estimate nirsevimab effectiveness; subgroup analyses were performed by age and presence of comorbidities	• Monoclonal antibody BEYFORTUS ™ (nirsevimab) by Sanofi	Moderate

Reference (author year) with URL	Research question addressed	Geographical location	Design and Study Period	Population	Analysis	Type of immunization product	Risk of Bias
	children younger than 12 months						
Coma 2024	• Effectiveness of nirsevimab against primary care attended bronchiolitis, RSV infection, viral pneumonia diagnosed in primary care, ED visits due to bronchiolitis, RSV-related hospitalization, and RSV-related ICU admission in infants born between April and September 2023	Spain	Design: Retrospective cohort study Study period: 1 October 2023–31 January 2024	26,525 infants (0–6 months old) born between April and September 2023; 23,127 (87.2%) had received nirsevimab	The Kaplan-Meier estimator and Cox regression models were used to evaluate nirsevimab effectiveness; the analysis was adjusted for age at beginning of study, sex, area of residence, nationality, rurality, and socioeconomic status; a final Cox regression model stratified by months of birth was performed	• Monoclonal antibody BEYFORTUS ™ (nirsevimab) by Sanofi	Moderate
Paireau 2024	• Effectiveness of nirsevimab against PICU hospitalization for RSV-associated bronchiolitis in infants <5 months old (or <9 months old if they had comorbidities)	France	Design: Test-negative case-control Study period: 15 September 2023–31 January 2024	288 infants (0–9 months old, 238 cases and 50 controls), 58 (20%) had received nirsevimab prior to treatment in the paediatric intensive care unit (PICU)	A logistic regression model was used to estimate the nirsevimab effectiveness on hospitalization to PICU for RSV-bronchiolitis in infants, adjusting for age group, sex, presence of comorbidities, prematurity, and time period	• Monoclonal antibody BEYFORTUS ™ (nirsevimab) by Sanofi	Moderate
Barbas Del Buey 2024	• Effectiveness of nirsevimab against hospitalization, ICU admission, ED care, and medically attended bronchiolitis/bronchitis for infants aged 0–10 months old	Spain	Design: Prospective cohort study Study period: 1 October 2023–29 February 2024	37,067 (80.8% immunized) infants (0 to ten months old) born between April and December 2023 were included in the population eligible for immunization; 33,859 were included in the analysis of nirsevimab effectiveness	A multivariable Cox regression model was used to estimate the effectiveness of nirsevimab. The model was adjusted for the following variables: sex, age, gestational age at birth, type of gestation, presence of comorbidities, net income of household, cumulative incidence of RSV infection in children aged 0–5 years old in	• Monoclonal antibody BEYFORTUS ™ (nirsevimab) by Sanofi	Moderate

Reference (author year) with URL	Research question addressed	Geographical location	Design and Study Period	Population	Analysis	Type of immunization product	Risk of Bias
					the area of residence, and epidemiological week		
Xu 2024	• Effectiveness of nirsevimab against medically attended RSV infection, hospitalization, outpatient visits, severe RSV, all-cause LRTI, all-cause LRTI hospitalization, and RSV-associated LRTI	United States	Design: Test-negative case-control Study period: 1 October 2023–9 May 2024	3,090 infants (0–2 years old, 680 cases, 2,410 controls); 330 (10.7%) were immunized with nirsevimab	Nirsevimab effectiveness was estimated using a multivariable logistic regression model adjusted for age, calendar months, and presence of at least one risk factor; effectiveness was additionally estimated by time since immunization and dosage	• Monoclonal antibody BEYFORTUS ™ (nirsevimab) by Sanofi	Moderate
López-Lacort 2025	• Effectiveness of nirsevimab in preventing RSV-LRTI in overall and catch-up infants <10 months old	Spain	Design: Test-negative design (TND) Study period: November 1, 2023 [week 45], and February 29, 2024	160 infants (0 to <10 months old); 141 infants (88%) received nirsevimab; 29 infants (21%) was administered in hospital and 112 (79%) administered to catch-up group (targeted effort outside of hospital administration)	A Bayesian logistic regression model was used to analyze the effectiveness of nirsevimab in preventing RSV-LRTI in infants <20 months of age (both overall and for catch-up infants); effectiveness was calculated using (1 – Odds Ratio) x 100% and random effects was calculated to account for primary care center variability; non-informative priors were also set for model parameters to avoid bias on estimations	• Monoclonal antibody BEYFORTUS ™ (nirsevimab) by Sanofi	Moderate
Carbajal 2024	• Effectiveness of nirsevimab in reducing paediatric emergency department visits, ICU admissions, hospitalizations and severe RSV-bronchiolitis for all-cause bronchiolitis and RSV-associated bronchiolitis	France	Design: Case-control study Study period: 14 October 2023–29 February 2024	2,786 infants (0–12 months old, 864 case infants diagnosed with bronchiolitis, 1,922 control infants without bronchiolitis); 178 (21%) case infants had received nirsevimab, 686 (79%) had not received Of 864 infants diagnosed with bronchiolitis, 277 (32%) were RSV PCR tested; of the 67 infants tested for RSV who had received nirsevimab, 22 (33%) tested positive	The effectiveness of nirsevimab in reducing ED visits was calculated using odds ratio ((1–Odds Ratio) x 100%) adjusted for week of ED visit, sex, and age; sensitivity analyses were also conducted including logistic regression analysis with age as a continuous variable; a Bayesian logistic model was used to predict RSV status in infants who did not undergo PCR sampling	• Monoclonal antibody BEYFORTUS ™ (nirsevimab) by Sanofi	Serious

Reference (author year) with URL	Research question addressed	Geographical location	Design and Study Period	Population	Analysis	Type of immunization product	Risk of Bias
Rodríguez-Fernández 2024	• Effectiveness of nirsevimab against hospitalization	Spain	Design: Case-control study Study period: 1 September 2015–31 December 2023	138 infants (<6 months old), 32 admitted for bronchiolitis (21 with RSV bronchiolitis); of the 21 admitted for RSV bronchiolitis 6 (28%) had received nirsevimab. Of the 11 admitted for bronchiolitis due to another cause 8 (72%) received nirsevimab	The effectiveness of nirsevimab in reducing hospitalization was calculated using (1– Odds Ratio) x 100%; Sensitivity Analyses were also performed to compare seasons with lower RSV and other factors	• Monoclonal antibody BEYFORTUS ™ (nirsevimab) by Sanofi	Serious
Tartof 2024	• Respiratory Synctial Virus Prefusion F effectiveness in older adults	California, United States	Design: Retrospective case-control study and test-negative design Study period: May–September 2024	A total of 10 566 patients, 60 years or older, who had LRTD hospitalizations or emergency department encounters; approximately 76.5% of participants had a nasal swab, 60.7% were tested for RSV, and 64.2% of participants were included in the final analysis	Vaccine effectiveness was assessed using 1 – Odds Ratio x 100%; the 95% confidence interval was reported; a multivariate logistic regression was used	• RSVpreF (Abrysvo)	Moderate
Chauvel 2024	• Effectiveness of Nirsevimab against RSV-LRTI in infants younger than 6 months	France	Design: Retrospective observational study Study period: 2023–2024 season	A total of 83 infants younger than 6 months, born in the Hospices Civils de Lyons, and hospitalized during the 2023 to 2024 RSV season were included in this study	Incidence rates of the RSV-associated hospitalizations, with 95% confidence intervals comparing two historical periods were calculated	• Nirsevimab	Moderate
Moline 2024	• Compare the epidemiology and disease burden of RSV-associated acute respiratory illness in children younger than 5 years	United States	Design: Case-control study Study period: RSV seasons (September to April), 2017–2020	A total of 28,689 children younger than 5 years, with medically attended acute respiratory illness participated in this study; medically attended was defined as a visit to urgent care, emergency department, or hospitalization	The effectiveness of nirsevimab was estimated using a test-negative design and multivariable logistic regression model; site, age, months of enrollment, and presence of a high-risk medical condition was accounted for in the model Effectiveness was calculated using (1 – adjusted odds ratio) x 100% Hospitalization incidence rates were calculated per 1,000 participants with a 95% bootstrap percentile confidence interval	• Nirsevimab	Moderate
Jimeno Ruiz 2024	• Evaluate effectiveness of nirsevimab in	Spain	Design: Retrospective	A total of 646 infants less than 6 months of age at the beginning of the study	Poisson regression models with robust variance and Cox proportional hazard were used	• Nirsevimab	Moderate

Reference (author year) with URL	Research question addressed	Geographical location	Design and Study Period	Population	Analysis	Type of immunization product	Risk of Bias
	reducing RSV disease burden in infants		multicentre observational study Study period: Pre-Covid: October 2018–March 2019, Covid: October 2019–March 2020, Post-Covid: March 2022–2023, Nirsevimab: March 2023–2024	period, from three hospitals in Spain, were included in this study	The efficacy of nirsevimab against RSV hospitalization was caclulcated as (1 – point estimate) x 100 and 95% confidence intervals were generated Hospitalization rates were calculated per 10,000 individuals in the same age group The incidence ratio was obtained by comparing (rate difference/ of Post-COVID to nirsevimab rate) x 100		
Lefferts 2024	• Effectiveness of nirsevimab against RSV-related medically attended acute respiratory illness and hospitalization in children in their first and second RSV seasons	United States	Design: Test-negative case-control Study period: October 2023–June 2024	472 children aged <20 months on 1 October 2023 or born after that date; 48% of included patients had received nirsevimab	Odds ratios of medically attended acute respiratory illness (ARI) associated with RSV was evaluated using multivariable logistic regression adjusted for age, sex, calendar month, residence community type, and presence of underlying conditions; effectiveness of nirsevimab was estimated as (1 – adjusted odds ratio) x 100%	• Monoclonal antibody BEYFORTUS ™ (nirsevimab) by Sanofi	Moderate
Payne 2024	• A test-negative study assessing the effectiveness of RSV vaccination against hospitalization and emergency department encounters for adults ≥60 years.	United States	Design: Test-negative study Study period: 1 October 2023 to 31 March 2024	36,706 hospitalizations of patients ≥60 years old with RSV-like illness and RSV testing during the study period were identified, with 34,780 (95%) being linked to RSV-negative tests and 1,926 (5%) being linked to RSV-positive tests 37,842 emergency department patients ≥60 years old with RSV-like illness and RSV testing during the study period were identified, with 35,082 (93%) being linked to RSV negative tests and 2,760 (7%) being linked to RSV positive tests	Vaccine effectiveness (VE) against hospitalizations and emergency department encounters was measured by comparing the odds of vaccination among RSV-positive case patients and RSV-negative control patients	• RSVPreF3 (Arexvy, GSK) • RSVPreF (Abrysvo, Pfizer)	Moderate

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