

Real-world evidence on nirsevimab in pediatric populations: a systematic review

Real-world evidence on nirsevimab

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ABSTRACT

Respiratory syncytial virus (RSV) is the leading cause of acute lower respiratory tract infections in infants, with a substantial burden of hospitalizations, intensive care admissions, and healthcare costs worldwide. Nirsevimab, a long-acting monoclonal antibody targeting the RSV prefusion F protein,

demonstrated high efficacy and a favorable safety profile in randomized clinical trials and has since been incorporated into national RSV prevention programs in several countries. This systematic review synthesizes the available real-world evidence on the effectiveness and safety of nirsevimab in pediatric populations. The review was conducted according to PRISMA 2020 guidelines, searching PubMed/MEDLINE, Embase, Web of Science, and Scopus, supplemented by grey literature. Observational real-world studies enrolling infants and children aged ≤ 24 months who received nirsevimab were included. Risk of bias was appraised with the Newcastle–Ottawa Scale and certainty of evidence with GRADE; findings were synthesized narratively. Fifty-four studies from nine countries were included. Nirsevimab was consistently associated with substantial reductions in RSV-related hospitalizations, emergency department visits, and ICU admissions, with protection observed in both general and high-risk infant populations. Although less frequently reported, adverse events were uncommon, mostly mild and transient, with no unexpected safety signals. Certainty of evidence was moderate for RSV-related hospitalization and ICU admission, and low or very low for other outcomes. Current real-world evidence shows that nirsevimab is an effective and well-tolerated strategy for preventing RSV disease in infants and young children, consistent with the pivotal trials and supporting its role in immunization programs. Continued surveillance is needed to monitor long-term effectiveness and safety.

IMPACT STATEMENT

Real-world evidence from nine countries shows that nirsevimab substantially lowers infant hospitalizations and intensive care admissions for respiratory syncytial virus, supporting its role in national immunization programs and routine practice.

Key words

Nirsevimab; respiratory syncytial virus; real-world evidence; infant; immunization.

INTRODUCTION

Respiratory syncytial virus (RSV) is among the most common viral pathogens of childhood and the leading cause of acute lower respiratory tract infections (LRTIs) in infancy. Nearly all children are infected by two years of age, and disease is most severe in the first six months. RSV typically manifests as bronchiolitis, which in severe cases may progress to pneumonia, respiratory failure, apnea and, rarely, death; moreover, 30–40% of infants hospitalized for RSV bronchiolitis subsequently develop recurrent wheezing (1).

Each year, RSV is estimated to cause approximately 33.3 million LRTIs managed in outpatient care, 3.6 million hospitalizations, and more than 100,000 deaths, with roughly 5% of hospitalized infants requiring intensive care (1). Severity is strongly modulated by prematurity and by underlying conditions such as congenital heart disease, chronic lung disease, neurological disorders, and immunodeficiency (2). The mean cost of a hospitalization ranges from €4,000 to €6,000, excluding indirect costs (3).

Until recently, prevention relied on palivizumab, licensed in 1998, whose monthly dosing and cost have confined its use to selected high-risk infants, only 4–6% of the at-risk pediatric population, even though 70–90% of infants hospitalized for RSV are otherwise healthy, full-term newborns (2, 4). Nirsevimab (Beyfortus), a long-acting human IgG1 monoclonal antibody directed against the conserved antigenic site Ø of the RSV prefusion F protein, was developed to close this gap and was authorized between 2022 and 2023 (5). A single intramuscular dose confers protection for at least five months, sufficient to span an entire RSV season, and is recommended for all infants entering their first RSV season, as well as for selected children who remain at risk during their second (6).

Regulatory approval was supported by randomized controlled trials, including the phase 3 MELODY trial (74.5% efficacy against medically attended RSV LRTI), the palivizumab-controlled MEDLEY trial in high-risk infants, and the open-label phase 3b HARMONIE trial (82.7% efficacy against RSV-related hospitalization) (7, 8, 9). Such trials, however, are underpowered to detect rare or long-term

adverse events and tend to exclude infants with comorbidities (10, 11, 12). Real-world evidence (RWE), derived from electronic health records, registries, and other routinely collected data, addresses these gaps by capturing effectiveness and safety under everyday conditions and in broader, more heterogeneous populations (13, 14).

Since its approval, nirsevimab has been adopted by national RSV prevention programs across Europe, North America, and beyond (4, 6), and a rapidly growing body of observational and population-level studies has evaluated its real-world performance (15). Consolidating this evidence is now needed to complement the trial data (16).

Accordingly, this systematic review aims to synthesize the available real-world evidence on the effectiveness and safety of nirsevimab in pediatric populations, to characterize the study designs, healthcare settings, and patient populations represented in the current literature, and to identify evidence gaps and their implications for clinical practice and immunization policy.

METHODS

This systematic review was designed to identify, select, and critically appraise eligible studies and to extract and synthesize their data in response to a clearly formulated research question (17). The eligibility criteria and search strategy (Supplementary Table S1) were defined before screening began; no review protocol was registered or published. Its conduct and reporting followed the PRISMA 2020 guidelines (checklist in Supplementary Table S2) (18, 19).

Eligibility criteria

Eligibility was defined a priori using a PICO framework:

- Population: infants and children aged ≤ 24 months, including term and preterm infants and those at heightened risk of severe RSV disease (e.g. chronic lung disease, congenital heart disease, cystic fibrosis, Down syndrome, congenital diaphragmatic hernia, neuromuscular disorders, or immunodeficiency).

- Intervention: receipt of nirsevimab, irrespective of dose, formulation, or regimen.
- Comparators: no RSV prophylaxis, historical control cohorts, or alternative approaches such as palivizumab.
- Outcomes: effectiveness (RSV-related hospitalization, medically attended RSV infection, ICU admission, or all-cause LRTI) and/or safety (adverse events, serious adverse events, adverse events of special interest, or mortality).
- Study design: observational real-world studies (prospective or retrospective cohort, case-control, or database-, registry-, or surveillance-based).
- Other criteria: English-language studies published from the first regulatory approval of nirsevimab (2022) onward. We excluded randomized controlled trials, narrative and systematic reviews, purely theoretical modelling studies not informed by real-world data, editorials, and case series of fewer than 10 patients.

For the purposes of this review, real-world evidence was defined as evidence on the effectiveness or safety of nirsevimab derived from data collected in routine clinical practice or public-health activity, electronic health records, administrative and registry databases, surveillance systems, and prospective or retrospective observational studies conducted outside the controlled conditions of a randomized trial (13). The definition was deliberately inclusive, because the designs that meet it answer complementary questions: cohort and registry studies estimate effectiveness in whole populations and allow adjustment for measured confounders; test-negative designs limit confounding by healthcare-seeking behavior and are the standard approach for estimating immunization effectiveness against laboratory-confirmed infection; and surveillance and ecological analyses describe population-level impact but cannot attribute it to individual immunization. Because these designs differ in their susceptibility to bias and in the quantity they estimate, they were not treated as interchangeable. The design of every study is reported (Supplementary Table S3); each study providing an individual-level comparison was appraised with the version of the Newcastle–Ottawa Scale that matches its analysis;

studies providing no individual-level estimate were excluded from the synthesis of effectiveness estimates; and all estimates are interpreted as design-specific quantities. Although grey literature was searched to limit publication bias, no grey-literature source contributed a study to the review.

Information sources and search strategy

We systematically searched four major bibliographic databases, PubMed/MEDLINE, Embase, Web of Science, and Scopus. To limit publication bias, the search was extended to grey literature, including preprint servers (medRxiv, bioRxiv), conference proceedings, and regulatory reports from the EMA, FDA, and AIFA. For each database, the strategy combined controlled vocabulary with free-text terms covering RSV, nirsevimab, and real-world evidence; the complete search strings are provided in Supplementary Table S1. All sources were last searched in March 2026.

Study selection

Records were screened independently by two reviewers in two sequential stages: titles and abstracts were first assessed for potential eligibility, and the full texts of retained reports were then evaluated against the predefined criteria. Disagreements were resolved by consensus. The selection process is summarized in a PRISMA flow diagram (Figure 1).

Data extraction

Using a standardized form, one reviewer extracted citation details (first author, year, country); study design and data source; population characteristics (sample size, sex, age, gestational age, risk factors); intervention characteristics (timing and coverage of nirsevimab administration); comparator type; and effectiveness and safety outcomes. A second reviewer independently verified all extracted data against the source reports, and disagreements were resolved by discussion.

Risk of bias assessment

The methodological quality of the included studies was appraised with the Newcastle–Ottawa Scale (NOS) (20), using the cohort version for cohort studies and the case–control version for case–control studies, including test-negative designs. Two reviewers (AB, CMC) independently assessed each full

text, neither having access to the other's ratings before completion; disagreements were resolved by discussion, with a third reviewer (PP) adjudicating where consensus was not reached. Initial agreement between the two assessors was 95%.

Because the NOS does not specify item-level decision rules for several of the designs represented in this literature, anchoring statements were agreed a priori and are reported in full in Supplementary Text S1. Three of them are material to the interpretation of the scores. First, for the comparability item a study was awarded a star only if age was controlled at a granularity of month of birth or finer, since both the probability of receiving nirsevimab and the risk of RSV-related hospitalization vary steeply with age within the first year of life. Second, in the case-control version, test-negative designs were treated as equivalent to community-based controls for the item on selection of controls, whereas traditional case-control studies recruiting hospital controls were not; total scores are therefore not comparable across case-control design subtypes, and the subtype is reported alongside the score for every study. Third, each study was assigned to the version of the scale that matches the analysis from which its effectiveness estimate derives, rather than the design label used by its authors, so that the number of studies appraised with each version does not correspond to the descriptive design categories in Table 1.

The NOS does not define official thresholds for converting total scores into quality categories. We therefore applied the domain-based convention commonly attributed to the Agency for Healthcare Research and Quality (21), in which a study is rated good when it obtains 3–4 stars for selection, 1–2 for comparability and 2–3 for outcome or exposure; fair when it obtains 2 stars for selection with the same comparability and outcome requirements; and poor when it obtains 0–1 stars for selection, 0 stars for comparability, or 0–1 stars for outcome or exposure.

Eight of the 54 included studies could not be appraised with either version of the scale, because they report no individual-level comparison between recipients and non-recipients of nirsevimab. Seven of these provide no estimate of effectiveness and were excluded both from the appraisal and from the

synthesis of effectiveness estimates; the remaining study provides a legitimate estimate obtained with the screening method (22), for which the comparator is an aggregate coverage figure rather than a group of individuals, and was excluded from the appraisal but retained in the synthesis. All eight are listed, with the reason, in Supplementary Table S4. Risk-of-bias ratings were not used to weight, exclude or rank studies, and no summary quality score entered any synthesis.

Data synthesis

A quantitative meta-analysis was considered but not performed. The heterogeneity of the included studies in design, population and reported outcomes was one reason, but not the decisive one: the effectiveness estimates reported by these studies are not estimates of the same quantity. They differ in outcome definition, in the interval between immunization and observation (over which protection wanes), and in the estimator applied (crude or adjusted; cohort, test-negative, case-control or screening method; intention-to-treat or per-protocol), and several studies report materially different estimates for the same comparison depending on the estimator alone. Restricting pooling to RSV-related hospitalization, the most consistently reported endpoint, would not remove these differences, which are present within that outcome (Figure 2). Pooling such quantities would yield a summary estimate without a defined target, and a random-effects model would describe their dispersion without explaining it. Findings were therefore synthesized narratively, with structured comparison across key domains: country, study design, clinical setting, population characteristics, number of centers, study period, diagnostic method, and reported outcomes.

Certainty of the evidence

The certainty of the evidence was rated for each outcome with the GRADE approach (23) and is summarized in Supplementary Table S5. Because all included studies are non-randomized, rating began at low certainty for every outcome. We did not rate down further for risk of bias: although the appraisal identified limitations in individual studies, most often incomplete control for age, none was judged to bias the body of evidence beyond the confounding already reflected in the starting level.

For the two outcomes with a consistent definition across studies we did not rate down for inconsistency, because the dispersion of the estimates is accounted for by outcome definition, by the interval between immunization and observation, and by the estimator applied, and because the largest studies rated good quality converge on a narrow interval; for the outcomes whose definition varies materially between studies we rated down one level for indirectness. We rated up one level for magnitude of effect where the relative risks were consistently below 0.5 (24). We did not rate up by two levels for a very large effect, although several relative risks were below 0.2, because those estimates derive from smaller studies, broader outcome definitions or shorter intervals between immunization and observation, whereas the largest studies converge on relative risks of 0.23–0.35. We did not upgrade for plausible residual confounding, because the confounding most likely in this literature, a healthy-vaccinee effect, would inflate rather than reduce the observed effect. Certainty ratings were not used to weight or to exclude studies.

RESULTS

Search results

The database search yielded 1,217 records (PubMed, $n = 242$; Embase, $n = 339$; Scopus, $n = 322$; Web of Science, $n = 314$; registries, $n = 0$). After 708 duplicates were removed, 509 records underwent title and abstract screening, of which 431 were excluded. The remaining 78 reports were retrieved and assessed in full against the predefined criteria; 24 were subsequently excluded for the following reasons: a study period beginning before the first regulatory approval of nirsevimab in 2022 ($n = 11$), enrolment of infants older than 24 months ($n = 4$), an ineligible study design ($n = 7$), and outcomes that were irrelevant or unreported ($n = 2$). Fifty-four studies ultimately met all eligibility criteria and were included in the review (Figure 1) (2, 5, 14, 25–75). A further 15 records were identified through grey literature; all were assessed in full and excluded as duplicates of subsequently published peer-reviewed reports, so that every included study is a peer-reviewed publication (Figure 1).

Study characteristics

The 54 included studies spanned nine countries, Spain (n = 23), France (n = 10), Italy and the United States (n = 8 each), Chile (n = 2), and Germany, Australia, Canada, and Andorra (n = 1 each) (Supplementary Figure S1). One study was conducted in both Spain and Andorra (40) and is counted under both countries. Most were multicenter (n = 44). Inpatient care was the predominant setting (n = 27), followed by studies covering multiple settings (n = 21), emergency care (n = 4), and outpatient care (n = 2). Sex was reported in 42 studies, with a slight male predominance in 40, and RSV diagnosis relied chiefly on laboratory confirmation, most often PCR or rapid antigen testing, although the diagnostic method went unreported in 14 studies.

A summary of the study characteristics is presented in Table 1, with full per-study detail in Supplementary Table S3. The evidence base encompassed a broad spectrum of observational designs (prospective and retrospective cohorts, test-negative and traditional case-control studies, and surveillance-, registry-, or population-based analyses) of which observational cohort and case-control/test-negative designs were the most frequent. Study populations were predominantly mixed, combining general-population and high-risk infants (33/54), whereas 17 studies were restricted to the general population and four to high-risk infants alone. Half of the studies were set exclusively in inpatient wards (27/54), typically drawing on hospital records to capture severe disease endpoints, while 21 spanned several care settings and thereby offered a more complete view of real-world effectiveness.

Real-world effectiveness

RSV-related hospitalization was the most frequently reported outcome (42 studies), followed by medically attended RSV infection (21 studies), RSV-related ICU admission (17 studies), and all-cause LRTI hospitalization (8 studies). Across this evidence base, nirsevimab was consistently associated with substantial reductions in RSV-related clinical outcomes in both general and high-risk infants younger than 24 months. Most studies documented a marked decline in RSV-related hospitalizations,

with effectiveness estimates against RSV-related hospitalization ranging from 63.8% (30) to 98% (5, 67) (Figure 2). These figures are not equivalent quantities: they differ in outcome definition, in the interval between immunization and observation, and in the estimator used, and the range should therefore be read as a set of design-specific estimates rather than as a confidence interval around a single effect (see Discussion). One further estimate (59) was not included in this range, because most of its non-immunized comparators had been admitted in the season before nirsevimab became available (Supplementary Table S3). Emergency department visits fell by 54% (35) to 87.9% (45), although one population-based cohort reported a decline from 66.7% at 30 days after immunization to 16.7% at 150 days (38), and ICU admissions by 51.1% (48) to 94.4% (38); the highest estimate against ICU admission was measured 30 days after immunization and fell to 92.1% at 90 days within the same study.

In outpatient and primary care settings, nirsevimab likewise reduced medically attended RSV infection and bronchiolitis, with effectiveness of 48.1% (41) to 79.7% (54), evidence of protection against milder presentations as well as severe disease requiring hospitalization, although these estimates were consistently lower than those against hospitalization; in infants followed into their second year of life, one population-based cohort reported relative risks of 0.56 against primary-care bronchiolitis and 0.81 against RSV infection diagnosed in primary care (25). In pediatric emergency departments, effectiveness against RSV bronchiolitis was 83.2% and 89.3% in two consecutive seasons, with no significant difference between them (47). Overall, effectiveness was lower against medically attended infection in ambulatory care than against hospitalization or intensive care admission, whereas differences between countries and healthcare systems were comparatively small. Protection also held in the youngest and highest-risk infants: ten studies enrolled infants younger than six months without detecting meaningful differences from older age groups, and mixed-population studies reported effectiveness comparable to that seen in the general infant population. Firm subgroup conclusions nonetheless remain constrained, as only four studies focused exclusively on preterm

infants or those with significant comorbidities. Likewise, the influence of administration timing and immunization coverage could not be established, given heterogeneous findings drawn from a limited subset of studies (33, 37, 38).

Real-world safety

Safety proved difficult to appraise: 14 studies reported some safety information, often limited to deaths, and only five reported adverse events after immunization (44, 60, 63, 73, 74). Where adverse events were described (63, 73), they were generally uncommon, mild, and transient, most commonly fever, injection-site reactions, and irritability or inconsolable crying, alongside occasional systemic events such as apnea or bradycardia, typically arising within 48 hours and resolving spontaneously within one to two days. Adverse events of special interest, including anaphylaxis and seizures, were not observed. A single serious adverse event requiring intubation was reported but deemed unrelated to nirsevimab. These observations mirror the safety data from the MELODY and HARMONIE trials. In the two immunization programs that reported pharmacovigilance data, none of the notified adverse events (5 after 9,408 doses in Galicia and 18 in Chile) was attributed to nirsevimab, further supporting a favorable safety profile while underscoring the value of continued pharmacovigilance (44, 74).

Risk of bias in the included studies

Forty-six of the 54 included studies were appraised with the Newcastle–Ottawa Scale: 23 with the cohort version and 23 with the case–control version. Item-level results are presented in Figure 3, and per-study ratings in Supplementary Table S4 and Supplementary Figure S2. Four of the nine items of the case–control version, and two of the cohort version, were satisfied by 96–100% of studies, whereas the two items that discriminated between studies were comparability and, in case–control studies, ascertainment of exposure. Control for age was not achieved by 43% of cohort studies (10/23) and 35% of case–control studies (8/23), and the source of immunization status was not documented in 43% of case–control studies (10/23).

Under the domain-based classification, 36 studies were rated good, 2 fair and 8 poor. Seven of the eight studies rated poor satisfied no comparability item at all, reporting no adjusted analysis of any kind, and the eighth met only one of the three exposure items. Item-level performance was, however, poorly reflected in the total score: of the 36 studies rated good, 11 did not adequately control for age and 7 did not document the source of immunization status.

Certainty of the evidence

Certainty was rated moderate for RSV-related hospitalization and for RSV-related intensive care admission, low for all-cause lower respiratory tract infection hospitalization, and very low for medically attended RSV infection and for safety outcomes (Supplementary Table S5). Moderate certainty was reached for the two outcomes in which the definition is consistent across studies, the estimates of the largest studies converge, and the magnitude of effect is large. A two-level upgrade for a very large effect was not applied, because the relative risks below 0.2 derive from smaller studies, broader outcomes or shorter intervals from immunization. For medically attended RSV infection, the criterion for a large effect was not met (the lowest estimate corresponds to a relative risk of 0.52), and certainty was therefore very low. The gradation corresponds to the distinctions drawn above: the evidence on hospitalization is the most secure, that on medically attended infection is weakened by heterogeneity in outcome definition and by smaller effects, and that on safety remains the most fragile, since only 14 of the 54 included studies reported any safety information, and only five reported adverse events after immunization.

DISCUSSION

This systematic review brings together the available real-world evidence on the effectiveness and safety of nirsevimab for preventing RSV-related disease in infants and young children. Taken together, the findings show that nirsevimab affords substantial protection against RSV-associated outcomes across diverse healthcare settings, populations, and national immunization strategies,

thereby confirming and extending the efficacy first demonstrated in randomized controlled trials (7–9).

Protection was consistent in direction and clinically meaningful across RSV-related hospitalizations, ICU admissions, and medically attended RSV infections (5, 41, 49, 53), although effectiveness was lower against the milder presentations managed in outpatient care than against hospitalization. Differences between countries and healthcare systems were comparatively small, whereas differences between study designs were larger and are examined below. The magnitude of protection against hospitalization is consistent with the pivotal MELODY and HARMONIE trials (7, 9), supporting the external validity of their findings in populations that include many infants underrepresented in randomized studies.

Whether protection is fully preserved in the highest-risk infants, and how far administration timing and immunization coverage modify it, cannot yet be established: only four studies were restricted to high-risk infants, and the data on timing and coverage are few and heterogeneous. Likewise, the favorable safety profile, consistent with the clinical trials (7, 9) and with the pharmacovigilance data reported by two immunization programs (44, 74), still rests on the few studies that collected adverse events, so continued pharmacovigilance remains necessary as population-level use expands.

The width of the reported range nonetheless warrants caution, and the risk-of-bias appraisal helps to explain it. The three largest studies rated good quality, which together include more than 640,000 infants in three countries on two continents, converge on a narrow interval of 65% to 77% against RSV-related hospitalization (49, 66, 74), and the fourth largest, conducted in infants in their second year of life, falls within the same interval (25); the higher estimates derive from smaller populations and, in several cases, from a broader outcome definition, a shorter interval between immunization and observation, or an unadjusted analysis. Two studies illustrate the point internally. One yields 62.9% from the crude proportions it reports, and 71% and 77% from Cox models with time-varying exposure, without and with adjustment for covariates (66); another obtains 87.5%, 80.3% and 71.0%

for the same effectiveness according to the estimator applied (33). The range should therefore be interpreted as a set of design-specific quantities rather than as uncertainty around a common effect. Nor does the summary score of the scale order these estimates: two Italian studies conducted in the same season and both rated good report 65.5% and 89.5% against RSV-related hospitalization (14, 61).

Strengths and limitations

A key strength of this review lies in the breadth of evidence synthesized, encompassing a wide range of observational designs, healthcare settings, and geographic regions; the inclusion of population-based and surveillance studies, in particular, allows effectiveness to be appraised at a broader public health level. Adherence to PRISMA guidelines, predefined eligibility criteria, and a transparent methodology further enhance reproducibility. Several limitations should nonetheless be acknowledged. Differences between studies in design, outcome definition and estimator precluded a quantitative meta-analysis and limited direct comparison. Safety data were variable in both availability and quality, as many studies addressed effectiveness alone. Most studies were also conducted during the early phase of implementation, frequently within a single RSV season, which restricts inferences about long-term effectiveness, durability of protection, and rare adverse events. Few studies focused exclusively on high-risk infants, limiting subgroup-specific conclusions, and publication and reporting biases cannot be ruled out given the rapid emergence of observational data. Finally, although every eligible study was appraised with the Newcastle–Ottawa Scale, the scale does not capture several design features that materially affect the estimates synthesized here, immortal time, the interval between immunization and the epidemic peak, the handling of time-varying exposure, and the breadth of the outcome definition. The appraisal is therefore reported at item level and interpreted alongside a narrative assessment of these features rather than as a summary quality score. The review was not prospectively registered and no protocol was published; moreover, the risk-of-bias appraisal and the certainty-of-evidence assessment were introduced at revision, in response to

peer review, and were therefore not pre-specified. Future syntheses in this field should be registered prospectively.

CONCLUSIONS

This systematic review supports nirsevimab as an effective and well-tolerated strategy for preventing RSV-related disease in infants and young children under routine clinical conditions. Evidence drawn from diverse healthcare settings and populations consistently points to substantial reductions in RSV-related hospitalizations, ICU admissions, and medically attended infections, confirming and extending the efficacy observed in randomized controlled trials. The close alignment between real-world effectiveness and trial efficacy reinforces the generalizability of these findings across healthcare systems and infant populations, although evidence in the highest-risk infants remains limited. Although safety data from everyday practice remain limited, the available evidence, together with the pharmacovigilance data reported by immunization programs, indicates a favorable profile, with no unexpected signals identified to date. As nirsevimab becomes further embedded in national immunization programs, its population-level impact holds considerable promise for easing the clinical and economic burden of RSV. Realizing that potential will depend on continued surveillance and on studies that follow immunized cohorts across several consecutive RSV seasons, so as to establish the durability of protection, its effect in the second season and beyond, and any shift in the age distribution of RSV disease. The expanding use of maternal RSV vaccination will also shape the future role of nirsevimab: studies comparing the two strategies, and evaluations of how they are best combined within national programs, including for infants of vaccinated mothers who remain at high risk, will be needed to consolidate its place within comprehensive RSV prevention frameworks.

COMPLIANCE WITH ETHICAL STANDARDS

Conflict of Interest Statement

The authors declare no conflicts of interest.

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Author contributions

AB, PP and AL conceived the systematic review, coordinated the working group, and drafted the initial version of the manuscript. CMC, GF and EL contributed to the literature review, methodology definition, and manuscript writing. AP and AL critically revised the manuscript for important intellectual content and supervised the overall work. All authors contributed to the study design, reviewed the manuscript critically, and approved the final version. They all agree to be accountable for the integrity and accuracy of the work. AB and PP contributed equally as co-first authors.

Ethical approval

Human studies and subjects

N/A.

Publication ethics

Plagiarism

The manuscript is free from plagiarism, and all sources and contributions have been appropriately acknowledged.

Data falsification and fabrication

The authors affirm that the work complies with the highest standards of research integrity. No data have been fabricated, manipulated, or falsified.

The authors confirm adherence to ethical principles regarding authorship, data transparency, and responsible communication of scientific results.

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Table 1. Summary characteristics of the 54 included studies.

Characteristic	Studies, n (%)
Country of conduct	
Spain	23 (43)
France	10 (19)
Italy	8 (15)
United States	8 (15)
Other (Chile, Germany, Australia, Canada, Andorra)	6 (11)
Study design	
Observational cohort	20 (37)
Case-control / test-negative	21 (39)
Surveillance / registry / population-based	12 (22)
Modelling	1 (2)
Healthcare setting	
Inpatient only	27 (50)
Multiple settings	21 (39)
Emergency department only	4 (7)
Outpatient only	2 (4)
Study population	
Mixed (general + high-risk)	33 (61)
General population	17 (31)
High-risk only	4 (7)
Number of centres	
Multicentre	44 (81)
Single-centre	10 (19)
Comparator	
No prophylaxis	41 (76)
No prophylaxis + historical controls	7 (13)
Historical controls only	5 (9)
No comparator group	1 (2)
Safety outcomes	
Reported	14 (26)
Not reported	40 (74)

Values are n (%). Percentages are calculated over the 54 included studies and may not total 100 owing to rounding. One study was conducted in both Spain and Andorra (40) and is counted under both countries, so that country counts

sum to 55. Study-design categories are mutually exclusive; studies combining multiple healthcare settings are grouped as “Multiple settings”. Full per-study characteristics are provided in Supplementary Table S3.

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Figure 1. PRISMA flowchart.

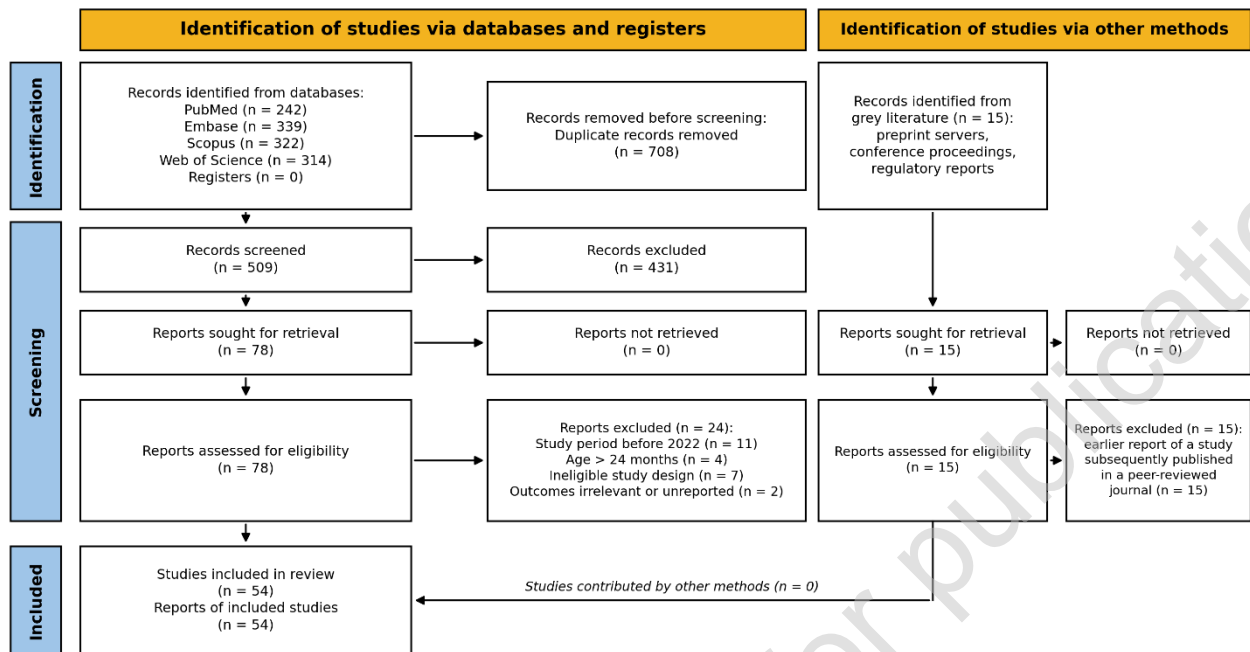


Figure 2. Effectiveness of nirsevimab against RSV-related hospitalization in the included studies.

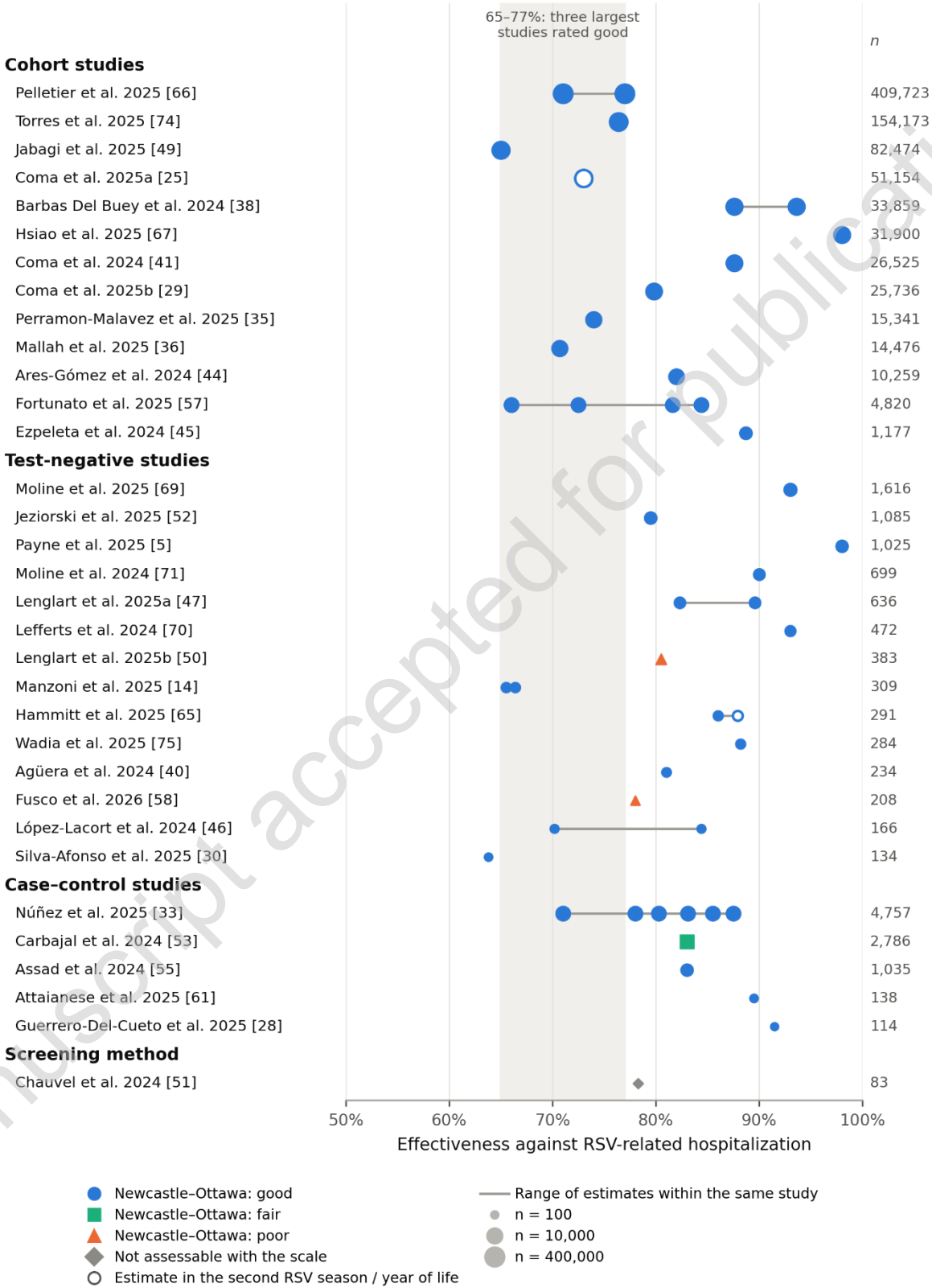


Figure 3. Risk of bias of the included studies assessed with the Newcastle–Ottawa Scale.

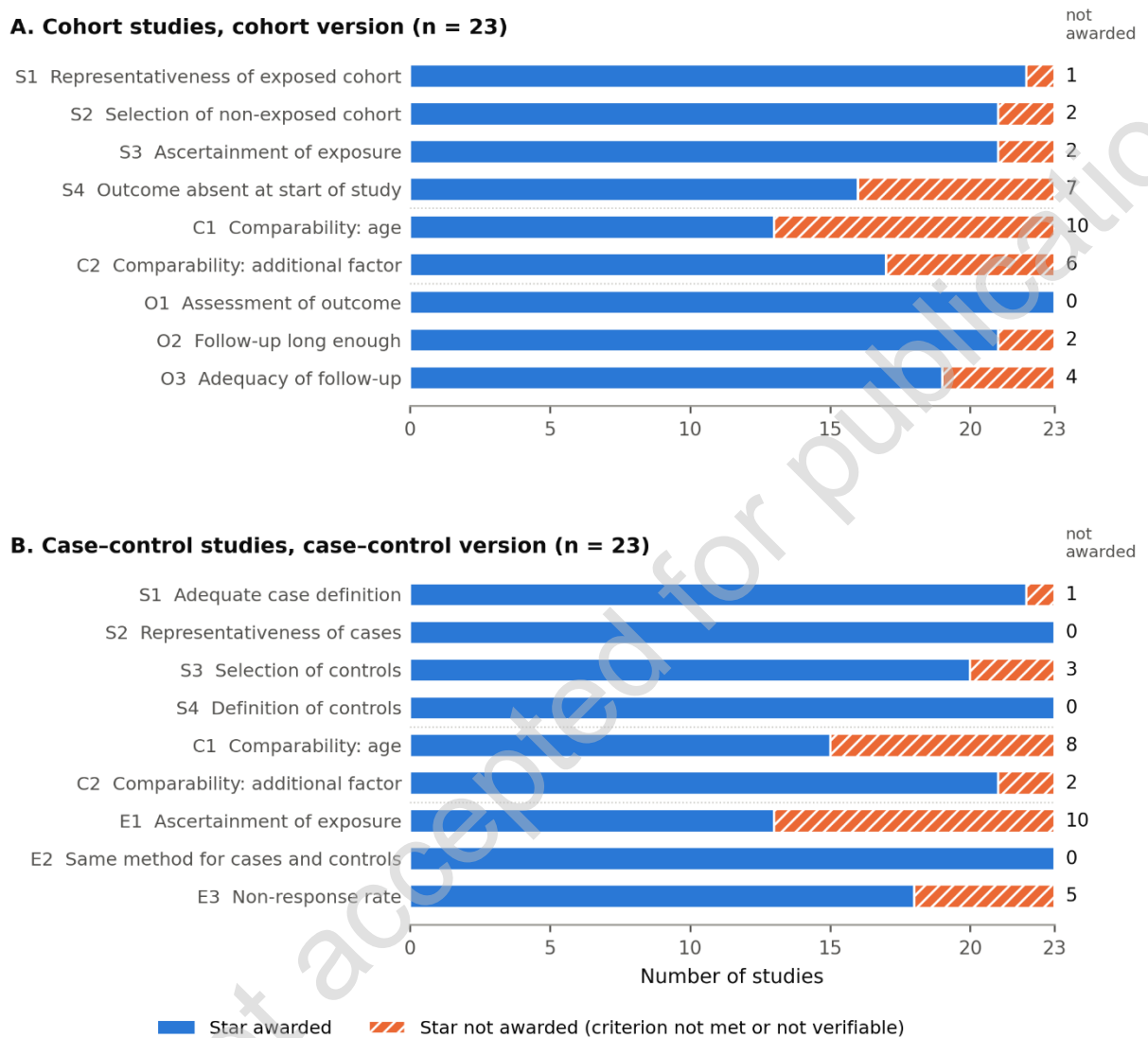
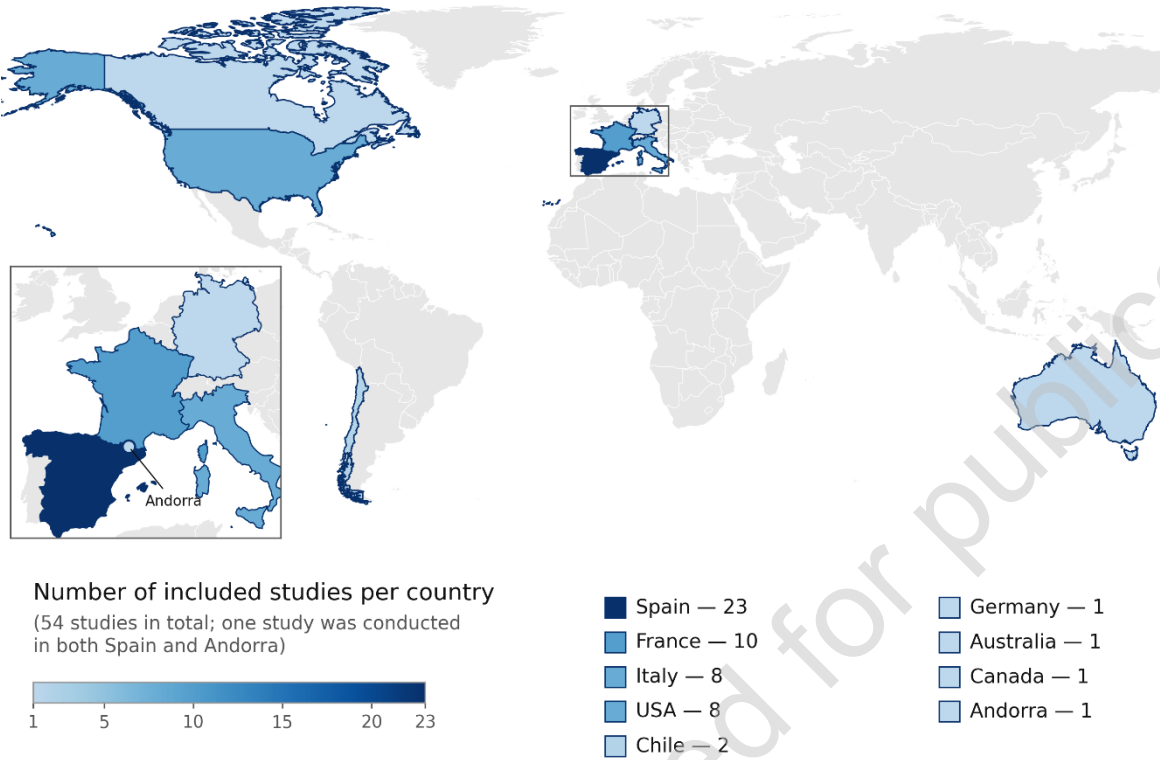


Figure S1. Geographic distribution of the 54 included real-world studies.



Countries are shaded according to the number of included studies conducted in each (Spain, $n = 23$; France, $n = 10$; Italy, $n = 8$; United States, $n = 8$; Chile, $n = 2$; Germany, $n = 1$; Australia, $n = 1$; Canada, $n = 1$; Andorra, $n = 1$). The inset enlarges western Europe, where Andorra is marked with a circle; one study was conducted in both Spain and Andorra and is counted under both countries. Country boundaries are from Natural Earth (public domain). The figure is supplied as a separate high-resolution file (FigureS1_geographic_distribution).

Figure S2. Newcastle–Ottawa Scale ratings of each included study

A. Cohort version of the Newcastle–Ottawa Scale (n = 23)

	Selection				Comparability		Outcome			Total	Rating
	S1	S2	S3	S4	C1	C2	O1	O2	O3		
Coma et al., 2025a	+	+	+	+	+	+	+	+	+	9	Good
Barbas Del Buey et al., 2024	+	+	+	+	+	+	+	+	+	9	Good
Perramon-Malavez et al., 2025	+	+	+	+	+	+	+	+	+	9	Good
Coma et al., 2024	+	+	+	+	+	+	+	+	+	9	Good
Espeleta et al., 2024	+	+	+	+	+	+	+	+	+	9	Good
Jabagi et al., 2025	+	+	+	+	+	+	+	+	+	9	Good
Hsiao et al., 2025	+	+	+	+	+	+	+	+	+	9	Good
Pelletier et al., 2025	+	+	+	+	+	+	+	+	+	9	Good
Torres et al., 2025	+	+	+	+	+	+	+	+	+	9	Good
Coma et al., 2025b	+	+	+	+	+	+	+	+	+	8	Good
Moreno-Pérez et al., 2025	+	+	+	-	+	+	+	+	+	8	Good
Ares-Gomez et al., 2024	+	+	+	+	-	+	+	+	+	8	Good
Fortunato et al., 2025	+	+	+	+	-	+	+	+	+	8	Good
Mallah et al., 2025	+	+	+	+	-	+	+	+	-	7	Good
Estrella-Porter et al., 2024	+	+	+	-	-	+	+	+	+	7	Good
Marouk et al., 2025	+	+	-	-	+	+	+	+	+	7	Fair
Ma et al., 2025	-	+	+	+	+	+	+	+	-	7	Good
Consolati et al., 2024	+	+	+	+	-	-	+	-	+	6	Poor
García-García et al., 2025	+	+	+	-	-	-	+	+	+	6	Poor
Andina Martínez et al., 2025	+	+	+	-	-	-	+	+	+	6	Poor
Manzanares et al., 2025	+	-	+	-	-	-	+	+	+	5	Poor
Costantino et al., 2025	+	+	+	+	-	-	+	-	-	5	Poor
González-Bertolín et al., 2025	+	-	-	-	-	-	+	+	+	4	Poor

B. Case-control version of the Newcastle–Ottawa Scale (n = 23)

	Selection				Comparability		Exposure			Total	Rating	Design
	S1	S2	S3	S4	C1	C2	E1	E2	E3			
Payne et al., 2025	+	+	+	+	+	+	+	+	+	9	Good	TN
Lassoued et al., 2024	+	+	+	+	+	+	+	+	+	9	Good	TN
Moline et al., 2025	+	+	+	+	+	+	+	+	+	9	Good	TN
Lefferts et al., 2024	+	+	+	+	+	+	+	+	+	9	Good	TN
Moline et al., 2024	+	+	+	+	+	+	+	+	+	9	Good	TN
Wadia et al., 2025	+	+	+	+	+	+	+	+	+	9	Good	TN
Manzoni et al., 2025	+	+	+	+	+	+	-	+	+	8	Good	TN
Silva-Afonso et al., 2025	+	+	+	+	-	+	+	+	+	8	Good	TN
Agüera et al., 2024	+	+	+	+	+	+	-	+	+	8	Good	TN
Lenglar et al., 2025a	+	+	+	+	+	+	-	+	+	8	Good	TN
Hammit et al., 2025	+	+	+	+	-	+	+	+	+	8	Good	TN
Lopez-Lacort et al., 2025	+	+	+	+	-	+	+	+	-	7	Good	TN
Lopez-Lacort et al., 2024	+	+	+	+	-	+	+	+	-	7	Good	TN
Lenglar et al., 2025b	+	+	+	+	+	+	-	+	-	7	Poor	TN
Jeziorski et al., 2025	+	+	+	+	-	+	-	+	+	7	Good	TN
Paireau et al., 2024	+	+	+	+	-	+	+	+	-	7	Good	TN
Arico et al., 2025	+	+	+	+	-	+	-	+	+	7	Good	TN
Fusco et al., 2026	+	+	+	+	-	-	-	+	+	6	Poor	TN
Assad et al., 2024	+	+	-	+	+	+	-	+	+	7	Good	HCC
Attaianesi et al., 2025	+	+	-	+	+	+	-	+	+	7	Good	HCC
Carbaljal et al., 2024	-	+	-	+	+	+	-	+	+	6	Fair	HCC
Nunez et al., 2025	+	+	+	+	+	+	+	+	+	9	Good	PCC
Guerrero-del-Cueto et al., 2025	+	+	+	+	+	-	+	+	-	7	Good	PCC

TN, test-negative; HCC, case-control with hospital controls; PCC, case-control with population controls. Scores are not comparable between the two versions of the scale or between case-control design subtypes.

● + Star awarded ● - Star not awarded (criterion not met or not verifiable)

Each row is one of the 46 studies appraised with the scale and each column one item: (A) the 23 studies appraised with the cohort version (S1–S4, selection; C1–C2, comparability; O1–O3, outcome); (B) the 23 studies appraised with the case-control version (S1–S4, selection; C1–C2, comparability; E1–E3, exposure), with the design subtype (TN, test-negative; HCC, case-control with hospital controls; PCC, case-control with population controls). Blue circles with a plus sign indicate that the star was awarded; orange circles with a minus sign indicate that it was not, either because the criterion was not met or because it could not be verified from the published report. Totals and ratings follow the domain-based convention described in Supplementary Text S1 and correspond to Supplementary Table S4; scores are not comparable between the two versions of the scale or between case-control design subtypes. The eight studies that could not be appraised are listed in Supplementary Table S4c. The figure is supplied as a separate high-resolution file (FigureS2_risk_of_bias_per_study).

Table S1. Full search strategies.

PubMed/MEDLINE

("Respiratory Syncytial Virus"[Mesh] OR "respiratory syncytial virus"[tiab] OR RSV[tiab]) AND (nirsevimab[tiab] OR Beyfortus[tiab]) AND ("Real-World Data"[tiab] OR "Real World"[tiab] OR real-world[tiab] OR observational[tiab] OR "post-marketing"[tiab] OR registry[tiab] OR registries[tiab] OR cohort[tiab] OR cohorts[tiab] OR surveillance[tiab] OR database[tiab] OR claims[tiab] OR effectiveness[tiab]) AND ("Infant"[Mesh] OR "Child"[Mesh] OR infant*[tiab] OR newborn*[tiab] OR neonat*[tiab] OR child*[tiab] OR pediatric*[tiab] OR paediatric*[tiab])

Scopus

TITLE-ABS-KEY(("respiratory syncytial virus" OR RSV) AND (nirsevimab OR Beyfortus) AND ("real-world" OR "real world" OR observational OR "post-marketing" OR registry OR registries OR cohort OR cohorts OR surveillance OR database OR claims OR effectiveness) AND (infant* OR newborn* OR neonat* OR child* OR pediatric* OR paediatric*))

Embase

((('respiratory syncytial virus'/exp OR 'respiratory syncytial virus':ti,ab,kw OR RSV:ti,ab,kw)) AND ('nirsevimab':ti,ab,kw OR 'beyfortus':ti,ab,kw) AND ('real world data':ti,ab,kw OR 'real world evidence':ti,ab,kw OR 'real world':ti,ab,kw OR 'observational study'/exp OR observational:ti,ab,kw OR 'post marketing surveillance'/exp OR 'post marketing':ti,ab,kw OR registry:ti,ab,kw OR registries:ti,ab,kw OR cohort:ti,ab,kw OR cohorts:ti,ab,kw OR surveillance:ti,ab,kw OR database:ti,ab,kw OR claims:ti,ab,kw OR effectiveness:ti,ab,kw) AND ('infant'/exp OR 'child'/exp OR infant*:ti,ab,kw OR newborn*:ti,ab,kw OR neonat*:ti,ab,kw OR child*:ti,ab,kw OR pediatric*:ti,ab,kw OR paediatric*:ti,ab,kw))

Web of Science Core Collection (TS field)

TS=(("respiratory syncytial virus" OR RSV) AND (nirsevimab OR Beyfortus) AND ("real-world" OR "real world" OR observational OR "post-marketing" OR registry OR registries OR cohort OR cohorts OR surveillance OR database OR claims OR effectiveness) AND (infant* OR newborn* OR neonat* OR child* OR pediatric* OR paediatric*))

Grey literature sources

Preprint servers (medRxiv, bioRxiv)

The shared medRxiv/bioRxiv search interface does not support controlled vocabulary or nested Boolean operators; a simplified free-text string was therefore applied to all fields, and the retrieved records were screened manually for relevance to RSV and to the pediatric age range.

nirsevimab OR Beyfortus

Conference proceedings

Abstract archives of the main international and national meetings in pediatric infectious diseases and pediatric respiratory medicine held from 2022 onwards were searched by free-text term, as these repositories do not support structured queries.

nirsevimab; Beyfortus; respiratory syncytial virus

Regulatory reports (EMA, FDA, AIFA)

The public document repositories of the European Medicines Agency, the US Food and Drug Administration, and the Italian Medicines Agency were searched by product name, and the retrieved assessment, post-authorisation, and pharmacovigilance documents were screened for real-world effectiveness or safety data.

nirsevimab; Beyfortus

All grey literature sources were last searched in March 2026, in parallel with the bibliographic databases. Records retrieved from these sources were screened separately from the database records against the same predefined eligibility criteria (see Figure 1).

Table S2. PRISMA 2020 Checklist

Section	Item	Sub	Name	Description of checklist item	Location in manuscript
TITLE					
TITLE	1		Title	Identify the report as a systematic review.	Title page — 'Real-world evidence on nirsevimab in pediatric populations: a systematic review'
ABSTRACT					
ABSTRACT	2		Abstract	See the PRISMA 2020 for Abstracts checklist.	Abstract (unstructured, 250 words)
INTRODUCTION					
INTRODUCTION	3		Rationale	Describe the rationale for the review in the context of existing knowledge.	§1 Introduction — burden of RSV, limitations of prior strategies, rationale for RWE synthesis
INTRODUCTION	4		Objectives	Provide an explicit statement of the objective(s) or question(s) the review addresses.	§1 Introduction, final paragraph
METHODS					
METHODS	5		Eligibility criteria	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	§2.1 Eligibility criteria (PICO table: population, intervention, comparators, outcomes, study design, other criteria)
METHODS	6		Information sources	Specify all databases, registers, websites, organisations, reference lists, and other sources searched or consulted. Specify the date when each source was last searched or consulted.	§2.2 Information sources — PubMed/MEDLINE, Embase, Web of Science, and Scopus, supplemented by grey literature (medRxiv, bioRxiv, EMA, FDA, AIFA). All sources were last searched in March 2026.
METHODS	7		Search strategy	Present the full search strategies for all databases and registers, including any filters and limits used.	Supplementary Table S1 — complete search strings for all 4 databases and the grey-literature sources; record counts per source in §3.1 and Figure 1
METHODS	8		Selection process	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved for eligibility, whether they worked independently, and if applicable, details of automation tools used.	§2.3 Study selection — two-stage screening (titles/abstracts, then full texts). Records were screened independently by two reviewers; disagreements were resolved by consensus. No automation tools were used.
METHODS	9		Data collection process	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used.	§2.4 Data extraction — data extracted by one reviewer and independently verified against the source reports by a second reviewer, using a standardised extraction form. No automation tools were used.
METHODS	10	a	Data items	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought, and if not, the methods used to decide which results to collect.	§2.4 — effectiveness outcomes (RSV-H, ICU-A, ED visits, medically attended RSV, all-cause LRTI-H) and safety outcomes (AE, SAE, AESI, mortality)
METHODS	10	b	Data items	List and define all other variables for which data were sought (e.g., participant and intervention characteristics, funding sources).	§2.4 — citation details, study design, data source, population (n, sex, age, GA, risk factors), intervention (timing, coverage), comparator

Section	Item	Sub	Name	Description of checklist item	Location in manuscript
METHODS	11		Study risk of bias assessment	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study, and whether they worked independently.	§2.5 Risk of bias assessment — every eligible study appraised with the Newcastle–Ottawa Scale (cohort or case–control version) by two independent reviewers, with a third adjudicating; a priori anchoring statements in Supplementary Text S1. Design features not captured by the scale are discussed in §4.1.
METHODS	12		Effect measures	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	§3.3 — effectiveness reported as VE %, RR, OR, HR, aOR as reported by original authors; no pooled effect measure (narrative synthesis)
METHODS	13	a	Synthesis methods	Describe the processes used to decide which studies were eligible for each synthesis.	§2.6 — all 54 studies eligible for narrative synthesis; the seven studies providing no effectiveness estimate were excluded from the synthesis of effectiveness estimates (§2.5; Supplementary Table S4c); meta-analysis not performed (rationale in §2.6, §3.3 and §4)
METHODS	13	b	Synthesis methods	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	§2.6 — qualitative synthesis; no data transformation performed
METHODS	13	c	Synthesis methods	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	Table 1 (summary characteristics); Supplementary Table S3 (per-study detail); Figure 2 (effectiveness estimates by study); Supplementary Figure S1 (geographic distribution); Figure 3 and Supplementary Table S4 (risk of bias); Supplementary Table S5 (certainty of the evidence)
METHODS	13	d	Synthesis methods	Describe any methods used to synthesize results and provide a rationale for the choice(s).	§2.6 — narrative synthesis chosen given substantial heterogeneity in design, population, and outcomes; estimates differ in outcome definition, interval from immunisation and estimator (§3.3, §4)
METHODS	13	e	Synthesis methods	Describe any methods used to explore possible causes of heterogeneity among study results.	Discussed narratively (§3.3, §4) — country, design, setting, population, timeframe identified as heterogeneity sources; formal heterogeneity statistics not applicable (no meta-analysis)
METHODS	13	f	Synthesis methods	Describe any methods used to assess risk of bias that could affect the cumulative evidence.	§2.7 — risk of bias across the body of evidence considered within the GRADE assessment (Supplementary Table S5); potential for selective reporting and publication bias acknowledged in §4.1; no formal sensitivity analysis performed.
METHODS	14		Reporting bias assessment	Describe any methods used to assess risk of reporting biases (such as publication bias) across studies.	§4.1 Limitations — publication and reporting bias acknowledged; no formal test (e.g. funnel plot) performed
METHODS	15		Certainty assessment	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	§2.7 Certainty of the evidence — GRADE applied per outcome; rating began at low for all outcomes as all studies are non-randomised; domain-by-domain reasoning in Supplementary Table S5.
RESULTS					
RESULTS	16	a	Study selection	Describe the results of the search and selection process, including the number of records identified in searches and assessed for eligibility, and the number of studies included in the review, preferably using a flow diagram.	§3.1 — 1,217 records identified; 708 duplicates removed; 509 screened; 431 excluded; 78 full-texts; 24 excluded; 54 included. PRISMA flow diagram: Figure 1
RESULTS	16	b	Study selection	Cite reasons for excluding studies assessed as eligible.	§3.1 — wrong timeframe (n=11), wrong age (n=4), wrong study design (n=7), irrelevant/unreported outcomes (n=2)
RESULTS	17		Study characteristics	Cite each included study and present its characteristics.	§3.1–3.2; Table 1; Supplementary Table S3; references [2, 5, 14, 25–75]

Section	Item	Sub	Name	Description of checklist item	Location in manuscript
RESULTS	18		Risk of bias in studies	Present assessments of risk of bias for each included study.	§3.5 Risk of bias in the included studies; Figure 3 (item-level); Supplementary Table S4 and Supplementary Figure S2 (per-study ratings). Study-level methodological limitations (design heterogeneity, variable outcome definitions, immunisation coverage data availability) are discussed narratively in §4.1.
RESULTS	19		Results of individual studies	For all outcomes, present for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision.	§3.3 Real-world effectiveness; §3.4 Real-world safety; per-study detail in Supplementary Table S3
RESULTS	20	a	Results of syntheses	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	§3.2 Study characteristics; §3.5 and Figure 3 (risk of bias); §4.1 Strengths and limitations
RESULTS	20	b	Results of syntheses	Present results of all statistical syntheses conducted.	Narrative synthesis only — range of effectiveness estimates reported in §3.3
RESULTS	20	c	Results of syntheses	Present results of any investigations of possible causes of heterogeneity among study results.	§3.3, §4 — country, design, setting, and population discussed as sources of heterogeneity
RESULTS	20	d	Results of syntheses	Present results of any sensitivity analyses conducted to assess robustness of the synthesized results.	Not applicable (narrative synthesis; no quantitative pooling)
RESULTS	21		Reporting biases	Present assessments of risk of reporting biases (such as publication bias) across studies.	§4.1 Limitations — acknowledged qualitatively
RESULTS	22		Certainty of evidence	Present assessments of certainty (or confidence) in the body of evidence for each outcome.	§3.6 Certainty of the evidence; Supplementary Table S5 — moderate for RSV-related hospitalisation and intensive care admission, low for all-cause LRTI hospitalisation, very low for medically attended RSV infection and for safety (see Methods, item 15).
DISCUSSION					
DISCUSSION	23	a	Discussion	Provide a general interpretation of the results in the context of other evidence.	§4 Discussion — effectiveness aligned with MELODY/HARMONIE trials [7–9]; comparison across countries and settings
DISCUSSION	23	b	Discussion	Discuss any limitations of the evidence included in the review.	§4.1 Strengths and limitations — heterogeneity, safety data scarcity, single-season studies, high-risk subgroup paucity, publication bias
DISCUSSION	23	c	Discussion	Discuss any limitations of the review processes used.	§4.1 — data extracted by one reviewer and independently verified by a second; design features not captured by the Newcastle–Ottawa Scale; the review was not prospectively registered; risk-of-bias and GRADE assessments added at revision and not pre-specified.
DISCUSSION	23	d	Discussion	Discuss implications of the results for practice, policy, and future research.	§4 Discussion; §5 Conclusions — support for immunization programs, need for surveillance, timing/coverage optimization
OTHER					
OTHER	24		Registration and protocol	Provide registration information for the review, including the register name and registration number, or state that the review was not registered. Provide where the protocol can be accessed, or state that a protocol was not prepared.	This systematic review was not prospectively registered in PROSPERO or any other register, and no a priori protocol was prepared or published. This is acknowledged as a limitation of the review (§4.1). The eligibility criteria and search strategy were defined before screening began; the risk-of-bias and GRADE assessments were introduced at revision and were not pre-specified (§2, §4.1).

Section	Item	Sub	Name	Description of checklist item	Location in manuscript
OTHER	25		Support	Describe sources of financial or other support for the review, and the role of the funders or sponsors in the review.	This work was conducted within the framework of the NICE-RSV project (Ricerca corrente cod. 08069025), funded by Fondazione IRCCS Policlinico San Matteo, Pavia, Italy. No specific funding was allocated for the conduct of this systematic review, and the funder had no role in its design, conduct, or reporting. See Conflicts of Interest & Funding section.
OTHER	26		Competing interests	Declare any competing interests of review authors.	The authors declare no competing interests. See Conflicts of Interest & Funding section.
OTHER	27		Availability of data, code, and other materials	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	All data extracted from the included studies are available in Supplementary Table S3. No additional data, analytic code, or other materials were generated. The full search strings are provided in Supplementary Table S1.

Source: Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ*. 2021;372:n71. doi:10.1136/bmj.n71

Table S3. Characteristics of the 54 included real-world studies on nirsevimab.

Study	Country	Study design	Setting	Population	Sample size (n)	Sex (M/F)	Age	Centers	Timeframe	Dx	Outcomes assessed	Effectiveness outcomes	Safety
Coma et al., 2025a [25]	Spain	Retrospective population-based cohort study	OP, IP, EC	G	51,154	51.6 % M 48.4 % F	<22 months	Multiple	Oct 2023-Feb 2025	RAT	• RSV-H • RSV-ICU-A • ED visit • Primary care attended RSV bronchiolitis • Positive RSV RAT in primary care	• H-A: RR 0.27 • ICU-A: RR 0.21 • ED visits: RR 0.35 • Primary care bronchiolitis: RR 0.56 • Primary care RSV infections: RR 0.81	NR
González-Bertolín et al., 2025 [26]	Spain	Prospective observational study	IP	G	230	61% M 39% F	6-24 months	Multiple	S1: Oct 2022-Mar 2023 S2: Oct 2023-Mar 2024 S3: Oct 2024-Feb 2025	RT-PCR	• RSV-LRTI-H • O2 requirement • NIV requirement • ICU-A • LOS • Concurrent infections • Antibiotics	• Difference between immunized and non-immunized group: • O2 requirement: 97% vs 92% • NIV: 0% vs 9% • ICU-A: 3% vs 9% • Length of hospital stay: 4 vs 4 days	NR
Andina Martínez et al., 2025 [27]	Spain	Retrospective observational study (before–after comparison)	EC, IP	Mixed	947	57.8% M 42.2% F	<1 year	Multiple	Nov 2023-Jan 2024	RAT or PCR	• RSV-H • ICU-A • LOS • Maximum respiratory	RSV positivity: Immunized: 42.1% Non-I: 86.5%	Mortality: 0 death among hospit

Study	Country	Study design	Setting	Population	Sample size (n)	Sex (M/F)	Age	Centers	Timeframe	Dx	Outcomes assessed	Effectiveness outcomes	Safety
											support required • Mortality		alized bronchiolitis cohort
Guerrero-Del-Cueto et al., 2025 [28]	Spain	Retrospective population-based matched case-control study (two controls per case, born on the same day in the province)	IP	Mixed	• 114 • Cases: 38 • Controls: 76	Cases: 68.4% M, 31.6% F Controls: 56.6% M, 43.4% F	< 2 years	Single	Sep 2023-Mar 2024	PCR	• RSV-H • ICU-A • LOS • O2 requirement • Co-infections • Readmission	E against RSV-H: 91.5%	NR
Coma et al., 2025b [29]	Spain	Retrospective cohort study	OP, IP, EC	G	• 25,736 • Immunized: 24,115 • Non-I: 1,621	NR	<1 years	Multiple	Oct 2024-Feb 2025	NR	• Primary care RSV infections • Primary care RSV bronchiolitis • ED visits due to RSV bronchiolitis • H due to RSV bronchiolitis • ICU-A due to RSV bronchiolitis	• E against primary care RSV infections: 76.1% • E against primary care RSV bronchiolitis: 67.4% • E against emergency visits due to RSV bronchiolitis: 80.9% • E against RSV-H: 79.8% • E against RSV-ICU-A: not estimable	NR

Study	Country	Study design	Setting	Population	Sample size (n)	Sex (M/F)	Age	Centers	Timeframe	Dx	Outcomes assessed	Effectiveness outcomes	Safety
Silva-Afonso et al., 2025 [30]	Spain	Retrospective test-negative case-control study	IP	Mixed	134	53 % M 47 % F	<1 years	Single	Oct 2023-May 2024	- RAT for SARS-CoV-2 and Influenza A/B - RT-PCR	- SARI hospitalization - RSV SARI-H	- aE against RSV SARI H: 63.8% - aE against Influenza SARI H: 28.2% - aE against COVID-19 SARI-H: 29.2%	NR
Manzanares et al., 2025 [31]	Spain	Prospective population-based cohort study	IP	Mixed	69	56.5% M 43.5% F	<1 year	Multiple	Sep 2023-Apr 2024	PCR	- RSV-LRTI-H - O2 requirement - RSV-ICU-A - NIVM and IMV - LOS - RSV-associated pneumonia - Co-infections - Death	Reduction in RSV-LRTI-H in 2023-2024: 89%	NR
García-García et al., 2025 [2]	Spain	Prospective observational study	IP	Mixed	669 S1: 480 S2: 189	64% M 36% F	<12 months	Multiple	S1: Oct 2022-Mar 2023 S2:	RT-nested PCR	- Primary: - RSV-H	Reduction in all-cause LRTI-H: 62.5%	NR

Study	Country	Study design	Setting	Population	Sample size (n)	Sex (M/F)	Age	Centers	Timeframe	Dx	Outcomes assessed	Effectiveness outcomes	Safety
									Oct 2023-Mar 2024	R assay, RT-PCR for SARS-CoV-2	• All-cause LRTI-H - Secondary: • RSV-ICU • LOS • O2 requirement • MV • Coinfections • Antibiotic use • Fever frequency and duration	• Reduction of RSV-H: 78% • Reduction of ICU-A: 74.5% • Reduction in length of hospital stay • Reduction in O2 requirement • Reduction in hospitalization due to: HMPV: 36.6% - Adenovirus: 69.5%	
Moreno-Pérez et al., 2025 [32]	Spain	Retrospective observational cohort study	IP	Mixed	222	59.9% M 40.1% F	<6 months	Multiple	Oct 2023-Feb 2024	PCR	• O2 requirement • MV • NG tube • IV access • Antibiotic use • CXR • Co-infections • ICU-A • LOS • Duration of outcomes	Reduction of: Use of nasal cannula: 64% Mechanical ventilation: 48% ICU-A: 54% Length of hospital stay: 31%	Higher frequency of co-infections in the nirsevimab group
Núñez et al., 2025 [33]	Spain	Population-based matched	IP	Mixed	4,757: 952 cases,	• Catch-up I: 57.6%	<1 year	Multiple	RSV season 2023-2024	PCR	• RSV-H • ICU-A	• E against RSV-H of • Catch-up immunization	NR

Study	Country	Study design	Setting	Population	Sample size (n)	Sex (M/F)	Age	Centers	Timeframe	Dx	Outcomes assessed	Effectiveness outcomes	Safety
		case control study			3,805 controls	M/42.4% F (cases), 52.6% M/47.4% (controls) • At-birth I: 62.1% M/37.9% F (cases), 52.1% M/47.9% F (controls)					• Need for mechanical ventilation • Co-infections	Pragmatic: 87.5% Intention to treat: 71% Per protocol: 80.3% • At birth immunization: Pragmatic: 85.5% Intention to treat: 78% Per protocol: 83.1%	
Vazquez-Lopez et al., 2025 [34]	Spain	Retrospective ecological before–after study	EC	G	NR	NR	NR	Multiple	1 Dec -26 Dec in S1 2022-2023 and S2 2023-2024	NR	• Pediatric emergency visits/day • Bronchiolitis /day • Admission/days • Bronchiolitis admissions/day • RSV-H/day	• Reduction in: • PED visits: 41.6% • Bronchiolitis admissions: 55.4% • RSV-H: 60.3% • ICU-A: 81.3% • Bronchiolitis transfer: 73.4% • O2 requirement: 60.9	NR

Study	Country	Study design	Setting	Population	Sample size (n)	Sex (M/F)	Age	Centers	Timeframe	Dx	Outcomes assessed	Effectiveness outcomes	Safety
											• ICU-A/day • Bronchiolitis transfer/day • O2 requirement		
Perramon-Malavez et al., 2025 [35]	Spain	Retrospective cohort study	EC, IP	G	15,341	• Immunized 51.4% M 48.6% F • Non-I 53.7% M 46.3% F	• <4 months Mean age: • Non-I: 60.5 days • I: 69 days	Multiple	Oct 2023-Jan 2024	NR	• ED visits for all-cause LRTI • ED visits for RSV-LRTI • All-cause LRTI-H • RSV-H • RSV ICU-A • All-cause LRTI ICU-A	• E against RSV ICU-A: 85% • E against RSV-H: 74% • E against RSV-ED visits: 54% • E against all-cause LRTI ICU-A: 77% • E against all-cause LRTI-H: 55% • E against all-cause LRTI ED visits: 51%	1 death in the non-I group and not related to RSV infection
Mallah et al., 2025 [36]	Spain	Prospective population-based cohort study	IP	Mixed	• Eligible infants: 14,476 • I: 13,320 • Catch-up cohort: 7,061	NR	<2 years	Multiple	Sep 2023-Apr 2024	NR	• Primary outcome: • RSV-LRTI-H - Secondary outcome: • RSV-H with O2 requirement • All-cause bronchiolitis or bronchitis H	• E against RSV-LRTI-H: 70.7% • E against RSV-LRTI-H with O2 requirement: 80.3% • E against all-cause bronchiolitis or bronchitis: 46%	NR

Study	Country	Study design	Setting	Population	Sample size (n)	Sex (M/F)	Age	Centers	Timeframe	Dx	Outcomes assessed	Effectiveness outcomes	Safety
											• All-cause pneumonia H • All-cause LRTI-H • All-cause H		
López-Lacort et al., 2025 [37]	Spain	Test-negative study	OP	Mixed	160	63.75% M 36.25% F	<10 months	Multiple	Nov 2023-Feb 2024	RT-PCR	• Medically attended RSV-LRTI • RSV-H	• E against medically attended RSV-LRTI: 75.8% • E against medically attended RSV-LRTI in catch-up group: 80.2%	NR
Barbas Del Buey et al., 2024 [38]	Spain	Prospective and dynamic population-based cohort study	OP, IP, EC	Mixed	33,859	51.57% M 48.38% F	<1 year	Multiple	Oct 2023-Feb 2024	RAT and PCR	• RSV-H • RSV-ICU-A • ED visits • Primary care episodes	• E against RSV-H: At 30 days: 93.6% At 150 days: 87.6% • E against ICU-A At 30 days: 94.4% At 90 days: 92.1% • E against ED visits At 30 days: 66.7% At 150 days: 16.7%	During the follow-up 30 deaths, non due to RSV infection, 12 immunized and 5 extremely premature

Study	Country	Study design	Setting	Population	Sample size (n)	Sex (M/F)	Age	Centers	Timeframe	Dx	Outcomes assessed	Effectiveness outcomes	Safety
Molina Gutiérrez et al., 2024 [39]	Spain	Ambispective observational study (between-season comparison)	EC, IP	Mixed	264	59.1% M 40.9% F	Infants born between April and December (<8 months)	Single	Oct-Dec of 2022 and 2023	RT-PCR	- Number of PED visits - Severity - O2 requirement - H-A - PICU-A	PED attendance in 2022 was 80.3% compared to 19.7% in 2023	NR
Agüera et al., 2024 [40]	Spain and Andorra	Prospective observational test negative case-control study	IP	Mixed	234	59% M 41% F	<12 months	Multiple	Nov 2023-Feb 2024	PCR	- Primary: - RSV-H - Severe RSV disease (need for ventilation) - Secondary - BROSJOD score at admission - O2 requirement - LOS	- E against RSV-LRTI-H: 81% - E against severe disease: 85.6% Subgroup: <3 months: 78.2% 3-6 months: 85.3% - No comorbidities: 82.4% - Preterm < 36 wga: 98.9%	NR, no increase in viral coinfections, and in clinical severity among immunized infants once hospitalized
Coma et al., 2024 [41]	Spain	Retrospective cohort study Population-based	OP, IP, EC	Mixed	26,525	Case: 51.5% M, 48.5% F Control: 51.2% M,	<6 months	Multiple	Oct 2023-Jan 2024	Primary care: RAT Inpatient:	- RSV-infection - Primary care attended bronchiolitis - Viral pneumonia	- E against RSV-H: 87.6% - E against RSV-ICU-A: 90.1% - E against ED visits for bronchiolitis: 55.4%	2 deaths observed, both non-immunized

Study	Country	Study design	Setting	Population	Sample size (n)	Sex (M/F)	Age	Centers	Timeframe	Dx	Outcomes assessed	Effectiveness outcomes	Safety
						48.7% F				RSV testing	(primary care) • ED visits for bronchiolitis • RSV-H • RSV-ICU-A • All-cause mortality	• E against viral pneumonia: 60.7% • E against primary-care attended bronchiolitis: 48.1% • E against RSV infection: 68.9%	
Estrella-Porter et al., 2024 [42]	Spain	Retrospective observational study Population-based	OP, IP	Mixed	27,362	51.1% M 48.9% F	• 0-6 months in catch-up group • Newborns <5 months • high-risk children <24 months	Multiple	Oct 2023-Mar 2024	NR	• RSV-infection • ARI-H • ICU-A • LOS	E against RSV infection: 73.7%	NR
Mazagatos et al., 2024 [43]	Spain	Observational surveillance study (aggregate, observed vs expected)	IP	Mixed	• Observed RSV-H in infants <1 years: • Weeks 40/2022-8/2023: 13,120	NR	<1 years	Multiple	40/2023-8/2024 (Oct 2023-Feb 2024)	PCR	• Averted RSV-H • Reduction in RSV-H incidence	• Reduction in RSV-H: 74-75% • Estimated averted RSV-H: 9,364-9,875	NR

Study	Country	Study design	Setting	Population	Sample size (n)	Sex (M/F)	Age	Centers	Timeframe	Dx	Outcomes assessed	Effectiveness outcomes	Safety
					• Weeks 40/2023-8/2024: 3,357								
Ares-Gómez et al., 2024 [44]	Spain	Prospective population-based longitudinal study	IP	Mixed	10,259	50.7% M 49.3% F	<9 months	Multiple	Sep 2023-Dec 2023	NR	• RSV-LRTI-H • Severe RSV-LRTI requiring O2 support • Mechanical ventilation ICU-A • All-cause LRTI-H • All-cause H • Averted RSV-LRTI-H	• E against RSV-LRTI-H: 82% • E against severe RSV-LRTI requiring O2 support: 86.9% • E against all-cause LRTI-H: 69.2% • E against all-cause H: 66.2%	5 reported after 9,408 doses; 3 categorized as severe, none considered related to nirsevimab
Ezpeleta et al., 2024 [45]	Spain	Prospective population-based cohort study	EC, IP	G	1,177	53.7% M 46.3% F	<4 months	Multiple	Oct 2023-Feb 2024	PCR	• RSV-H • Emergency room attendance • RSV-ICU-A	• E against RSV-LRTI-H: 88.7% • E against emergency room attendance: 87.9% • E against RSV-ICU-A: 85.9%	NR
López-Lacort et al., 2024 [46]	Spain	Test-negative case-control study; screening method in Murcia and Valladolid	IP	G	166	NR	<9 months	Multiple	Oct 2023-Dec 2023 or Jan 2024	PCR	RSV-LRTI-H	• Screening method: E against RSV-LRTI-H • Valencia: 69.3%	NR

Study	Country	Study design	Setting	Population	Sample size (n)	Sex (M/F)	Age	Centers	Timeframe	Dx	Outcomes assessed	Effectiveness outcomes	Safety
												• Murcia: 86.9% • Valladolid: 97% Pooled E against RSV-LRTI-H: 84.4% TND: pooled E of Valencia and Murcia: 70.2%	
Lenglart et al., 2025a [47]	France	Prospective test negative case control study	EC	Mixed	636	52.4% M 47.6% F	< 1y	Multiple	S1: Oct 2023-Feb 2024 S2: Oct 2024-Jan 2025	RAT or PCR	• RSV-bronchiolitis vs RSV-negative bronchiolitis • RSV-H • O2 requirement • Need for respiratory support	• E against RSV-bronchiolitis: • S1: 83.2% • S2: 89.3% No significant difference between seasons (P = 0.97) • E against RSV-H: • S1: 82.3% • S2: 89.6%	NR
Marouk et al., 2025 [48]	France	Retrospective observational study with nested test-negative analysis	EC	Mixed	739	NR	< 3 months	Multiple	Oct-Dec 2023	RAT and PCR	• H for bronchiolitis after ED visit • ICU-A • RSV positivity	• aE against H after ED visit: 53.5% • E against ICU-A: 51.1% • Reduction of RSV positivity: 79.6%	NR
Jabagi et al., 2025 [49]	France	Population-based observational study	OP, IP	Mixed	82,474	52.5% M 47.5% F	<12 months Mean age: 4.4-4.5 months	Multiple	Sep 2023-Jan 2024	NR	• RSV-LRTI-H • RSV-ICU-A • RSV-HDU (high dependency unit)-A	• E against RSV-LRTI-H: 65% • E against RSV-ICU-A: 74% • E against RSV-HDU-A: 64%	NR

Study	Country	Study design	Setting	Population	Sample size (n)	Sex (M/F)	Age	Centers	Timeframe	Dx	Outcomes assessed	Effectiveness outcomes	Safety
											• RSV requiring ventilation • RSV requiring O2	• E against RSV requiring ventilation: 66% • E against RSV requiring O2: 67%	
Lenglart et al., 2025b [50]	France	Test-negative design study	EC, IP	Mixed	383	NR	<1 year	Multiple	Oct 2023-Feb 2024	PCR or RAT	RSV positive bronchiolitis	• Adjusted effectiveness in preventing RSV-bronchiolitis at PEDs: 82.5% • E against H after PEDs visits: 80.5%	NR
Chauvel et al., 2024 [51]	France	Retrospective observational study; screening method	IP	Mixed	83	46% M 54% F	<6 months	Single	Oct 2023-Mar 2024	RT-PCR	• Primary outcome: • RSV-LRTI-H - Secondary outcome: • Age at admission • Preterm birth • O2 requirement • Need for feeding support • ICU-A	E against RSV-LRTI-H: 78.3%	NR
Jeziorski et al., 2025 [52]	France	• Prospective observational study • Test-negative	IP	Mixed	1,085	RSV(+): 56.1% M, 43.9% F RSV(-)	<1 year	Multiple	Oct 2023-Feb 2024	PCR or RAT	• Primary outcomes: • RSV-H • All-cause LRTI-H	• E against RSV-H: 79.5% • Reduced O2 requirement: 20.2%	NR

Study	Country	Study design	Setting	Population	Sample size (n)	Sex (M/F)	Age	Centers	Timeframe	Dx	Outcomes assessed	Effectiveness outcomes	Safety
		case-control study for effectiveness analysis				): 61.6% M, 38.4% F					Secondary outcomes: • LOS • O2 requirement • Ventilatory support • ICU-A	(immunized) vs 30.6% (non-immunized) • Reduced length of hospital stay: 4.1 (immunized) vs 5.2 days (non-I)	
Carbajal et al., 2024 [53]	France	Retrospective case-control study	EC, IP	G	2,786	• Case • <3 months : 60% M, 40% F • 3-6 months : 57% M, 43% F • 6-12 months : 60% M, 40% F - Control s • <3 months : 54% M, 46% F • 3-6 months	<12 months	Single	Oct 2023-Feb 2024	RT-PCR	• ED visits for all-cause bronchiolitis • ED visits for RSV-bronchiolitis • All-cause bronchiolitis -H • RSV-bronchiolitis -H • O2 requirement • NG tube requirement • RSV-ICU-A	• E against ED visits (All-cause bronchiolitis): 47% • E against ED visits (RSV-bronchiolitis): 83% • E against all-cause bronchiolitis-H: 59% • E against RSV-H: 83% • E against O2 requirement: 91% • E against NG tube requirement: 88% • E against ICU-A: 67%	NR

Study	Country	Study design	Setting	Population	Sample size (n)	Sex (M/F)	Age	Centers	Timeframe	Dx	Outcomes assessed	Effectiveness outcomes	Safety
						: 57% M, 43% F • 6-12 months : 55% M, 45% F							
Lassoued et al., 2024 [54]	France	National-based test negative case-control study	OP	G	883	• Case: 59.4% M, 40.6% F • Control : 64.9% M, 35.1% F	<12 months	Multiple	Sep 2023-Feb 2024	RAT	RSV-bronchiolitis	Adjusted E against RSV-bronchiolitis: 79.7% <3 months: 65.5% 3-6 months: 87.8% > 6 months: 82%	NR
Assad et al., 2024 [55]	France	Prospective matched case-control study	IP	Mixed	1,035	Case: 52% M, 48% F Control : 57.1% M, 42.9% F	<12 months	Multiple	Oct-Dec 2023	PCR	• RSV-H • RSV-ICU-A • Ventilatory support	• Adjusted E against RSV-H: 83% • E against RSV-ICU-A: 69.6% • E against need for ventilatory support: 67.2%	NR
Paireau et al., 2024 [56]	France	Test negative case control study	IP	Mixed	288	55% M 45% F	< 1 month at study start <5 months in case	Multiple	Sept 2023-Jan 2024	PCR	• RSV-ICU-A • Need for ventilation • Death during PICU stay	• AE against RSV-ICU-A: 75.9% (main analysis) • Sensitivity analysis: 80.6% 80.4%	0 deaths were reported

Study	Country	Study design	Setting	Population	Sample size (n)	Sex (M/F)	Age	Centers	Timeframe	Dx	Outcomes assessed	Effectiveness outcomes	Safety
							of comorbidities						
Fortunato et al., 2025 [57]	Italy	- Prospective hospital-based active surveillance - E estimated using: - Screening method - TND - Cohort study approach	IP	Mixed	4,820 (256 hospitalized, 82 RSV-positive)	- Immunized: 52.6% M, 47.4% F - Non-I: 50.7% M, 49.3% F	<1 year	Multiple	Oct 2024-Apr 2025	RT-PCR	- RSV-H - ICU-A - LOS - Co-infections	- E against RSV-H - Screening method: 84.4% - TND: Crude E: 66% Adjusted E: 72.5% - Cohort study: - Crude effectiveness: 84.4% - Adjusted effectiveness: 81.6%	NR
Fusco et al., 2026 [58]	Italy	Retrospective test-negative case-control study	EC	G	208	NR	<1y	Single	Nov 2024-Mar 2025	RAT or PCR	- RSV infection - RSV-H - ICU-A	- E against RSV infection: 82% - E against RSV-H: 78% - E against ICU-A: 84%	NR
Manzoni et al., 2025 [14]	Italy	Retrospective observational test-negative case-control study	IP	G	309 140 RSV(+) cases 169 RSV(-) controls	- RSV(+): 60% M, 40% F - RSV(-): 57.4% M, 42.6% F	≤ 7 months	Multiple	Nov 2024-Apr 2025	PCR	- RSV(+) vs RSV(-) hospitalizations - O2 requirement - ICU-A - LOS	- E against RSV-H - Crude effectiveness: 66.4% - Adjusted effectiveness: 65.5%	NR

Study	Country	Study design	Setting	Population	Sample size (n)	Sex (M/F)	Age	Centers	Timeframe	Dx	Outcomes assessed	Effectiveness outcomes	Safety
Aricò et al., 2025 [59]	Italy	Retrospective : observational study	IP	Mixed	471	S1 (2023-2024): 59% M, 41% F S2 (2024-2025): 51% M, 49% F	<12 months	Multiple	Nov-Mar: S1 (2023-2024), S2 (2024-2025)	RAT or PCR	• RSV-H • Need for respiratory support • ICU-A • Days of O2 therapy • LOS	• Reduction of RSV-H in 24/25 season: • Center 1: 85% • Center 2: 51% • Center 3: 68% • Center 4: failed, increase of 9% • IPTW-weighted OR for RSV positivity, immunized vs non-immunized infants hospitalized for bronchiolitis: 0.57 (95% CI 0.43–0.76); 303 of the non-immunized comparators were admitted in 2023–2024, before nirsevimab was available	NR
Costantino et al., 2025 [60]	Italy	Retrospective observational real-world study	IP	Mixed (preterm)	2,035	53% M 47% F	• Mean age at admission (days): • 2024-2025: 21 ± 3.6	Single	S1: 2022-2023 S2: 2023-2024 S3: 2024-2025	NR	• RSV cases • Short-term safety • Need for ventilatory support • ICU-A • Concurrent infections	• RSV cases: 2024-2025: 0.52% 2023-2024: 1.61% 2022-2023: 0.71% • Relative risk vs 2023-2024: RR 0.31	AE 0% within 30 days

Study	Country	Study design	Setting	Population	Sample size (n)	Sex (M/F)	Age	Centers	Timeframe	Dx	Outcomes assessed	Effectiveness outcomes	Safety
							• 2023-2024: 19.3 ± 5.3 • 2022-2023: 23.4 ± 5.8				• Radiological findings • LOS • Treatment duration		
Attaianese et al., 2025 [61]	Italy	Prospective matched case-control study	IP	G	138	52.9 % M 47.1 % F	Mean age at admission: 4 months	Multiple	Nov 2024-Mar 2025	PCR	• RSV-H • O2 requirement • Need for ventilatory support • ICU-A • Enteral feeding • Concurrent infections • LOS	Adjusted Immunization effectiveness: 89.5%	NR
Menegale et al., 2025 [62]	Italy	Catalytic model	OP, IP	Mixed	Lombardy population: 9,965,046	NR	All ages and infants < 1 years	Multiple (population-based)	Nov 2024-Apr 2025	NR	• Primary: • Medically attended RSV cases • RSV-H • Secondary: • Number of averted cases • Number of averted hospitalizations	• Nirsevimab administration (80% infant coverage) • Reduction of RSV-H in infants: 61% • Reduction of RSV-H in all population: 50.2% • Reduction in medically	NR

Study	Country	Study design	Setting	Population	Sample size (n)	Sex (M/F)	Age	Centers	Timeframe	Dx	Outcomes assessed	Effectiveness outcomes	Safety
												attended RSV cases: 5.75% Maternal RSVpreF vaccination (65% coverage) • Reduction of RSV-H in infants: 37.7% • Reduction of RSV-H in all population: 30.5% • Reduction in medically attended RSV cases: 3.48% Combined strategies: • Reduction of RSV-H in all population: 44.3-49.2% • Reduction of RSV-H in infants: 53.8-59.8%	
Consolati et al., 2024 [63]	Italy	Prospective observational cohort study	IP	G	556	NR	<9 months	Single	Dec 2023-Feb 2024	NR	• RSV-H • Short term adverse effects	• H risk in 2023-2024: 3.2% • H risk in 2022-2023: 7% After start of nirsevimab campaign:	• Reported short-term AEs (generally

Study	Country	Study design	Setting	Population	Sample size (n)	Sex (M/F)	Age	Centers	Timeframe	Dx	Outcomes assessed	Effectiveness outcomes	Safety
												• H risk in untreated infants: 8.3% • H risk in treated infants: 0%	mild/transient, typically within 48 hrs) • Fever: 6.5% • Local injection-site reactions: 4% • Barely consolable crying: 0.4% • Rash: 0%
Zhou et al., 2025 [64]	Germany	Retrospective observational surveillance study	OP, IP	G	833	NR	< 2y	Multiple	Nov 2024-Mar 2025	PCR	• Incidence RSV-LRTI • Age distribution of RSV-LRTI • LOS • ICU-A	• RSV-LRTI cases in infants < 6 months: • Hospitalized: 53% (S1), 56% (S2) → 28% (S3) • Outpatients: 19% (S1), 20% (S2) → 7% (S3)	NR

Study	Country	Study design	Setting	Population	Sample size (n)	Sex (M/F)	Age	Centers	Timeframe	Dx	Outcomes assessed	Effectiveness outcomes	Safety
												RSV-LRTI cases in infants < 1 year: • Hospitalized: 78% (S1), 80% (S2) → 42% (S3) • Outpatients: 44% (S1), 60% (S2) → 33% (S3)	
Hammitt et al., 2025 [65]	USA (Alaska and Southwest)	Prospective test-negative case-control study	IP	HR	• 291: 136 RSV(+) cases • 155 RSV(-) controls	NR	• S1: < 8 months • S2: 8-19 months	Multiple	Nov 2023-May 2024	PCR, NAAT, antigen, RT-PCR	RSV-H	• E against RSV-H: • S1: 86% • S2: 87.9%	NR
Payne et al., 2025 [5]	USA	Retrospective observational EHR-based test-negative case-control study	EC, IP	Mixed	• ED encounters: 5,039 • Hospitalizations: 1,025	• ED-encounters: 56% M, 44% F • RSV-H: 58% M, 42% F	< 8m	Multiple	Oct 2023-Mar 2024	Molecular or antigen test	• RSV-ED encounters • RSV-H	• E against RSV-ED encounters: 77% • E against RSV-H: 98%	NR
Pelletier et al., 2025 [66]	USA	Retrospective cohort study	IP	G	409,723	51.1% M 48.9% F	<5-10 months	Multiple	Feb 2024-Jan 2025	NR	• RSV-H • RSV-ICU-A • RSV-H requiring intubation	• RSV-H: • Treated patients: 0.4% • Untreated patients: 1.2% • RSV-ICU-A:	NR

Study	Country	Study design	Setting	Population	Sample size (n)	Sex (M/F)	Age	Centers	Timeframe	Dx	Outcomes assessed	Effectiveness outcomes	Safety
												• Treated patients: 0.2% • Untreated patients: 0.4% RSV-H requiring intubation: <0.1%. E against RSV-H: 77% (adjusted HR 0.23, 95% CI 0.21–0.26); 71% (unadjusted HR 0.29, 95% CI 0.26–0.32)	
Hsiao et al., 2025 [67]	USA	Retrospective cohort study	OP, IP, EC	G	31,900	50.8% M 49.2% F	<1 year	Multiple	Oct-2023-Apr 2024	PCR	• RSV-LRTI • RSV-H • RSV-ED visits • RSV-outpatient visits	• E against RSV-LRTI: 87.2% • E against hospitalized RSV-LRTD: 98% (post hoc analysis) • E against RSV infection: 71%	NR
Ma et al., 2025 [68]	USA	Retrospective population-based cohort study, database-based	OP, IP	Mixed	192,677	Nirsevimab group: 50.4% M, 49.6% F Non-recipient group: 52.8% M, 47.2% F	<12 months	Multiple	Oct 2023-Mar 2024	NR	• RSV-infection • Wheezing	• Immunized have decreased risk of RSV infection (HR: 0.24; 95% CI, 0.17-0.33) • Immunized have decreased risk of wheezing (HR: 0.73, 95% CI, 0.58-0.93)	NR
Moline et al., 2025 [69]	USA	• Prospective observational	OP,	Mixed	• 28,689 for	57% M 43 % F	• <5 years for burden	Multiple	Sep 2023-Apr 2024	RT-PCR	• Medically attended RSV-	• E against medically attended RSV-	1 death reported

Study	Country	Study design	Setting	Population	Sample size (n)	Sex (M/F)	Age	Centers	Timeframe	Dx	Outcomes assessed	Effectiveness outcomes	Safety
		surveillance study • Test-negative case-control study for effectiveness analysis	IP, EC		burden analysis • 1616 for E analysis		and incidence analysis • <8 months for effectiveness analysis	multiple			associated ARI • RSV-H	associated ARI: 89% • E against RSV-H: 93%	death among hospitalized RSV-ARI children
Lefferts et al., 2024 [70]	USA (Alaska)	Observational, test-negative case-control study	OP, IP, EC	HR	472	53% M 47% F	<20 months	Multiple	Oct 2023-Jun 2024	RSV RNA testing	• Medically attended RSV-associated ARI • RSV-H	• E against medically attended RSV-associated ARI: 82% • E against RSV-H: 93%	NR
Moline et al., 2024 [71]	USA	Prospective population-based test-negative case control study	IP	Mixed	699	58% M 42% F	<8 months	Multiple	Oct 2023-Feb 2024	RT-PCR	RSV-H	E against RSV-H: 90%	NR
Yan et al., 2025 [72]	Canada	Retrospective observational study	OP, IP, EC	HR	42	62% M 38% F	< 2 years	Single	Oct 2024-Apr 2025	NR	• ED visits • RSV-H • RSV-ICU-A • Death	• Effectiveness NR • RSV infection in 10% of infants • RSV in recipients: 8% • RSV in non-recipients: 13%	1 RSV-related death in a non-recipient led to ICU-A and death

Study	Country	Study design	Setting	Population	Sample size (n)	Sex (M/F)	Age	Centers	Timeframe	Dx	Outcomes assessed	Effectiveness outcomes	Safety
Izquierdo et al., 2025 [73]	Chile	Prospective observational, uncontrolled study	IP	HR	110	43.7% M 56.3% F	GA < 34 weeks	Single	Apr 2024-Sep 2024	NR	- Local AE - Systemic AE within 48 hrs post-immunization - Serious AE (SAEs) - Adverse events of special interest (AESIs)	NR	- Local AE: 0 - Systemic AE: 16.5% - Fever: 7.8% - Apnea: 8.7% - Bradycardia: 2 infants - SAEs: 1 infants required intubation, but it was unrelated to nirsevimab - AESIs: Anaphylaxis:

Study	Country	Study design	Setting	Population	Sample size (n)	Sex (M/F)	Age	Centers	Timeframe	Dx	Outcomes assessed	Effectiveness outcomes	Safety
													0 Seizures: 0 • Mortality: NR
Torres et al., 2025 [74]	Chile	Retrospective observational cohort study	IP	G	154,173	50.68% M 49.32% F	<1 years	Multiple	Apr 2024-Sep 2024	PCR	• RSV-LRTI • RSV-ICU-A • All-cause LRTI-H • All-cause H	• E against RSV-LRTI-H: 76.41% • E against RSV-ICU-A: 84.94% • E against all-cause LRTI-H: 66.50% • E against all-cause H: 47.90% • Reduction of RSV-LRTI-H compared to average of previous years (2019-2023): 77.46%	18 adverse events, none were directly attributed to nirsevimab
Wadia et al., 2025 [75]	Australia	Observational test-negative case-control study	IP	Mixed	284	53.9% M 46.1% F	• Median age: • RSV-positive cases: 0.37 years • RSV-negative controls:	Multiple	Apr 2024-Oct 2024	PCR	• RSV-ARI-H • ICU-A • O2 requirement • LOS	• E against RSV-ARI-H: 88.2% • E against O2 requirement: 61.8%	NR

Study	Country	Study design	Setting	Population	Sample size (n)	Sex (M/F)	Age	Centers	Timeframe	Dx	Outcomes assessed	Effectiveness outcomes	Safety
							0.28 years						

Note. Entries labelled “Reduction in...” are between-period or between-season comparisons and are not estimates of effectiveness; they are reported for completeness and are not included in the range given in §3.3. The weighted odds ratio reported by Aricò et al. [59] is likewise not included in the range or in Figure 2: 303 of the 471 infants analysed were admitted in 2023–2024, before nirsevimab was available, and the model does not account for season, so that the comparison is largely between seasons. E, effectiveness; H, hospitalization; ICU-A, intensive care unit admission; ED, emergency department; LRTI, lower respiratory tract infection; NR, not reported.

Text S1. A priori anchoring statements for the Newcastle–Ottawa Scale.

The Newcastle–Ottawa Scale specifies each item in general terms and leaves its application to the review team. Because several of the designs represented in this literature are not anticipated by the scale — test-negative designs, screening-method analyses, studies enrolling infants already admitted to hospital — the following anchoring statements were agreed before any study was assessed, and were applied unchanged by both reviewers. Four general decisions apply across both versions of the scale.

General decisions

D1. Month of birth as a control for age. Month of birth is accepted as control for age at the comparability item, because within a circumscribed birth window it determines age at the start of the RSV season more finely than a classification into age bands. Two conditions apply: the variable must be the month (not the year or the quarter), and the cohort must be defined by a circumscribed birth window. In studies recruiting from heterogeneous birth cohorts the star is not awarded. Where month of birth is used as a stratification variable rather than as a covariate, so that no comparison crosses months, the second condition does not apply.

D2. Methodological inheritance by citation. Letters and brief reports frequently refer to a previous publication for methods. The distinction is made by the nature of the item, not by the format of the publication. Items describing HOW a study was conducted — source of exposure data, database, outcome definitions — are inherited by explicit and cited cross-reference, and the star is awarded with a note. Items describing WHAT happened in that particular cohort — exclusions, participant flow, losses to follow-up — are not inherited; where they are not described, the star is not awarded.

D3. Studies enrolling infants already admitted to hospital. The item asking that the outcome be absent at the start of the study serves to exclude the possibility that the outcome precedes the exposure. Where enrolment coincides with the event that defines the cohort, that function is not served and the star is not awarded. Such studies are additionally flagged as severity or descriptive analyses, because they answer a different question — severity among breakthrough cases — and do not estimate effectiveness.

D4. Anchoring of the control-selection and control-definition items in the case–control version. The original anchors had been written around the test-negative design, in which the selection items are satisfied almost by construction; applied to traditional case–control studies they penalised them as a class, by difference of instrument rather than of conduct. Two distinct provisions follow. For the definition of controls, the original wording of the scale is used, which requires the absence of a history of the disease and not laboratory confirmation of negativity; this removes an addition of ours rather than modifying the scale, and no test-negative study changes score. For the selection of controls, the anchor is unchanged: the standard scale rewards community or population controls and not hospital controls, so a study recruiting hospital controls does not receive the star. This is declared in the Methods, together with the statement that the anchor treats test-negative controls as equivalent to community controls, and scores are reported stratified by design subtype. Comparisons between scores are made within a subtype and never across subtypes.

Item-level anchors — cohort version

Item	Anchor
S1 Representativeness of the exposed cohort	Star: representative, or reasonably representative, of the infants eligible for nirsevimab in the source population — population-based or registry studies, or consecutive admissions. No star: a selected group of users, or no description.
S2 Selection of the non-exposed cohort	Star: non-immunised infants drawn from the same population and the same season as the immunised. No star: historical controls from earlier seasons, or a different source. In mixed designs, the star is not awarded where only a minority of the unexposed are contemporaneous.
S3 Ascertainment of exposure	Star: immunisation status taken from a vaccination registry, an electronic health record, or other secure documentation. No star: parental report, or source not specified. D2 applies.
S4 Outcome not present at start of study	Star: explicit statement that infants were free of the outcome at entry — for example immunisation before the start of the season, or counting of incident events. No star: not stated. D3 applies.
C1 Comparability: control for age	Star: the design or the analysis controls for chronological age at the RSV season, by matching, stratification or adjustment. D1 applies.
C2 Comparability: any additional factor	Star: control for at least one further factor — gestational age, prematurity, comorbidity, sex, calendar time, or a deprivation index.
O1 Assessment of outcome	Star: RSV confirmed in the laboratory (PCR or antigen), or linkage to a validated discharge database. No star: self-reported, unspecified, or clinical diagnosis alone.

Item	Anchor
O2 Follow-up long enough for outcomes	Star: follow-up extending over the whole RSV season, or at least 150 days from immunisation. For in-hospital outcomes, follow-up coinciding with the admission.
O3 Adequacy of follow-up	Star: complete follow-up, or losses described and unlikely to introduce bias. No star: losses not described. D2 applies.

Item-level anchors — case-control version

Item	Anchor
S1 Adequate case definition	Star: RSV case confirmed by PCR or antigen test, with the method stated. No star: a clinical or administrative definition without laboratory confirmation.
S2 Representativeness of the cases	Star: a consecutive or clearly representative series of cases. No star: no description of selection.
S3 Selection of controls	Star: community or population controls — the design the scale rewards — or test-negative controls presenting to the same setting with the same syndrome. No star: hospital controls selected for other conditions, or no description. D4 applies.
S4 Definition of controls	Star: controls without a history of the disease, ascertained and described — test-negative controls tested with the same assay as the cases, or explicit selection for conditions that exclude the syndrome, with clinical history collected. No star: the disease status of the controls neither ascertained nor described. D4 applies.
C1 Comparability: control for age	Star: cases and controls matched or adjusted for chronological age. D1 applies.
C2 Comparability: any additional factor	Star: matching or adjustment for at least one further factor — gestational age, comorbidity, calendar time, centre, or sex.
E1 Ascertainment of exposure	Star: immunisation status taken from a registry or a medical record. No star: parental report, or not described. D2 applies.
E2 Same method of ascertainment	Star: the same method of ascertainment for cases and controls.
E3 Non-response rate	Star: the same rate in both groups, or non-response described and comparable. No star: not described. D2 applies.

Thresholds. The scale does not define official thresholds for converting total scores into quality categories. The domain-based convention commonly attributed to the Agency for Healthcare Research and Quality was applied: good — 3–4 stars for selection, 1–2 for comparability and 2–3 for outcome or exposure; fair — 2 stars for selection with the same comparability and outcome requirements; poor — 0–1 stars for selection, 0 stars for comparability, or 0–1 stars for outcome or exposure.

Table S4. Newcastle–Ottawa Scale ratings of the included studies.

S4a. Cohort studies assessed with the cohort version of the scale ($n = 23$). Items: S1–S4, selection; C1–C2, comparability; O1–O3, outcome. Each item scored 0 or 1; maximum 9.

Study	Country	S1	S2	S3	S4	C1	C2	O1	O2	O3	Total	Rating
Coma et al., 2025a	Spain	1	1	1	1	1	1	1	1	1	9	Good
Barbas Del Buey et al., 2024	Spain	1	1	1	1	1	1	1	1	1	9	Good
Perramon-Malavez et al., 2025	Spain	1	1	1	1	1	1	1	1	1	9	Good
Coma et al., 2024	Spain	1	1	1	1	1	1	1	1	1	9	Good
Ezpeleta et al., 2024	Spain	1	1	1	1	1	1	1	1	1	9	Good
Jabagi et al., 2025	France	1	1	1	1	1	1	1	1	1	9	Good
Hsiao et al., 2025	USA	1	1	1	1	1	1	1	1	1	9	Good
Pelletier et al., 2025	USA	1	1	1	1	1	1	1	1	1	9	Good
Torres et al., 2025	Chile	1	1	1	1	1	1	1	1	1	9	Good
Coma et al., 2025b	Spain	1	1	1	1	1	1	1	1	0	8	Good
Moreno-Pérez et al., 2025	Spain	1	1	1	0	1	1	1	1	1	8	Good
Ares-Gomez et al., 2024	Spain	1	1	1	1	0	1	1	1	1	8	Good
Fortunato et al., 2025	Italy	1	1	1	1	0	1	1	1	1	8	Good
Mallah et al., 2025	Spain	1	1	1	1	0	1	1	1	0	7	Good
Estrella-Porter et al., 2024	Spain	1	1	1	0	0	1	1	1	1	7	Good
Marouk et al., 2025	France	1	1	0	0	1	1	1	1	1	7	Fair

Study	Country	S1	S2	S3	S4	C1	C2	O1	O2	O3	Total	Rating
Ma et al., 2025	USA	0	1	1	1	1	1	1	1	0	7	Good
Consolati et al., 2024	Italy	1	1	1	1	0	0	1	0	1	6	Poor
García-García et al., 2025	Spain	1	1	1	0	0	0	1	1	1	6	Poor
Andina Martínez et al., 2025	Spain	1	1	1	0	0	0	1	1	1	6	Poor
Manzanares et al., 2025	Spain	1	0	1	0	0	0	1	1	1	5	Poor
Costantino et al., 2025	Italy	1	1	1	1	0	0	1	0	0	5	Poor
González-Bertolín et al., 2025	Spain	1	0	0	0	0	0	1	1	1	4	Poor

S4b. Case-control studies assessed with the case-control version of the scale (n = 23). Items: S1–S4, selection; C1–C2, comparability; E1–E3, exposure. Scores are not comparable between design subtypes (see Supplementary Text S1, decision D4).

Study	Country	Subtype	S1	S2	S3	S4	C1	C2	E1	E2	E3	Total	Rating
Payne et al., 2025	USA	Test-negative	1	1	1	1	1	1	1	1	1	9	Good
Lassoued et al., 2024	France	Test-negative	1	1	1	1	1	1	1	1	1	9	Good
Moline et al., 2025	USA	Test-negative	1	1	1	1	1	1	1	1	1	9	Good
Lefferts et al., 2024	USA (Alaska)	Test-negative	1	1	1	1	1	1	1	1	1	9	Good
Moline et al., 2024	USA	Test-negative	1	1	1	1	1	1	1	1	1	9	Good
Wadia et al., 2025	Australia	Test-negative	1	1	1	1	1	1	1	1	1	9	Good
Manzoni et al., 2025	Italy	Test-negative	1	1	1	1	1	1	0	1	1	8	Good
Silva-Afonso et al., 2025	Spain	Test-negative	1	1	1	1	0	1	1	1	1	8	Good
Aguera et al., 2024	Spain and Andorra	Test-negative	1	1	1	1	1	1	0	1	1	8	Good
Lenglart et al., 2025a	France	Test-negative	1	1	1	1	1	1	0	1	1	8	Good
Hammit et al., 2025	USA (Alaska and Southwest)	Test-negative	1	1	1	1	0	1	1	1	1	8	Good
Lopez-Lacort et al., 2025	Spain	Test-negative	1	1	1	1	0	1	1	1	0	7	Good
Lopez-Lacort et al., 2024	Spain	Test-negative	1	1	1	1	0	1	1	1	0	7	Good
Lenglart et al., 2025b	France	Test-negative	1	1	1	1	1	1	0	1	0	7	Poor
Jeziorski et al., 2025	France	Test-negative	1	1	1	1	0	1	0	1	1	7	Good
Paireau et al., 2024	France	Test-negative	1	1	1	1	0	1	1	1	0	7	Good
Arico et al., 2025	Italy	Test-negative	1	1	1	1	0	1	0	1	1	7	Good
Fusco et al., 2026	Italy	Test-negative	1	1	1	1	0	0	0	1	1	6	Poor
Assad et al., 2024	France	Hospital-based case-control	1	1	0	1	1	1	0	1	1	7	Good
Attaianese et al., 2025	Italy	Hospital-based case-control	1	1	0	1	1	1	0	1	1	7	Good
Carbajal et al., 2024	France	Hospital-based case-control	0	1	0	1	1	1	0	1	1	6	Fair
Nunez et al., 2025	Spain	Population-based case-control	1	1	1	1	1	1	1	1	1	9	Good
Guerrero-del-Cueto et al., 2025	Spain	Population-based case-control	1	1	1	1	1	0	1	1	0	7	Good

S4c. Studies that could not be appraised with either version of the scale (n = 8).

Study	Country	Design	Why the scale does not apply	Handling
Vazquez-Lopez et al., 2025 [34]	Spain	Retrospective ecological before–after study	Ecological comparison between two periods; no individual-level exposure data.	Excluded from appraisal and from the synthesis of effectiveness estimates.
Molina Gutiérrez et al., 2024 [39]	Spain	Ambispective observational study	Between-season comparison at a single centre; the recipient/non-recipient comparison is restricted to cases.	Excluded from appraisal and from the synthesis of effectiveness estimates.
Mazagatos et al., 2024 [43]	Spain	Observational surveillance study	Aggregate weekly surveillance data; no individual exposure variable; observed versus expected.	Excluded from appraisal and from the synthesis of effectiveness estimates.
Chauvel et al., 2024 [51]	France	Screening method	The comparator is the aggregate coverage of the birth cohort, not a group of individuals; neither version of the scale has an object.	Excluded from appraisal but retained in the synthesis: the estimate is obtained by a recognised method.
Menegale et al., 2025 [62]	Italy	Catalytic model	A transmission model fitted to population data; not a study of individuals.	Excluded from appraisal and from the synthesis of effectiveness estimates.
Zhou et al., 2025 [64]	Germany	Brief report on coverage and age distribution	Coverage, hospital cases and national notifications come from three unlinked sources; no case is classified as immunised or not. The authors state that the study was not designed to evaluate effectiveness.	Excluded from appraisal and from the synthesis of effectiveness estimates.
Yan et al., 2025 [72]	Canada	Retrospective observational study	A recipient/non-recipient comparison exists (2/26 versus 2/16) but yields no estimate of effect; RSV testing was not systematic and the authors state that the impact on RSV outcomes could not be analysed.	Excluded from appraisal and from the synthesis of effectiveness estimates.
Izquierdo et al., 2025 [73]	Chile	Prospective uncontrolled study	No comparison group; a study of safety.	Excluded from appraisal and from the synthesis of effectiveness estimates.

Ratings follow the domain-based convention set out in Supplementary Text S1. Total scores are not comparable between the two versions of the scale. The same ratings are displayed in Supplementary Figure S2.

Table S5. Certainty of the evidence (GRADE).

Certainty was rated for each outcome across the body of evidence. All included studies are non-randomised and therefore started at low certainty. RR values are derived from the reported effectiveness estimates ($RR = 1 - \text{effectiveness}$).

Outcome	Studies (n)	Effectiveness estimates reported	Certainty (GRADE)	Reasons for the rating
RSV-related hospitalization	42	63.8% to 98% ($RR \approx 0.02-0.36$); the three largest studies rated good quality, including more than 640,000 infants, converge on 65% to 77%	⊕⊕⊕○ MODERATE	Started at low (non-randomised studies). Not rated down for risk of bias: the starting level already reflects the confounding inherent to these designs, and 36 of the 46 appraised studies were rated good. Not rated down for inconsistency: the dispersion is accounted for by outcome definition, interval from immunisation and estimator, and the largest studies converge. Not rated down for indirectness or imprecision. Rated up one level for large magnitude of effect (RR consistently <0.5 , in several studies <0.2).
RSV-related intensive care admission	17	51.1% to 94.4% ($RR \approx 0.06-0.49$)	⊕⊕⊕○ MODERATE	As above. The highest estimate was measured 30 days after immunisation and fell to 92.1% at 90 days within the same study, a pattern consistent with waning of the antibody. Rated up one level for large magnitude of effect.
Medically attended RSV infection	21	48.1% to 89% ($RR \approx 0.11-0.52$)	⊕○○○ VERY LOW	Started at low. Rated down one level for indirectness: the outcome definition varies materially between studies, from bronchiolitis attended in primary care, through medically attended acute respiratory illness, to any diagnosis coded as due to RSV including otitis media and upper respiratory infection. Not rated up:

Outcome	Studies (n)	Effectiveness estimates reported	Certainty (GRADE)	Reasons for the rating
				the relative risks are not consistently below 0.5, the lowest estimate corresponding to a relative risk of 0.52.
All-cause lower respiratory tract infection hospitalization	8	46% to 69.2% (RR ≈ 0.31–0.54)	⊕⊕○○ LOW	Started at low. Not rated down further. Not rated up: the relative risks are not consistently below 0.5, as expected for an outcome that includes disease nirsevimab cannot prevent. One study reports 47.9% effectiveness against all-cause hospitalisation, a magnitude not attributable to the prevention of RSV alone and consistent with some residual confounding.
Safety (adverse events)	14	Adverse events uncommon, mild and transient; no adverse events of special interest observed	⊕○○○ VERY LOW	Started at low. Rated down one level for risk of bias, since adverse events were not collected systematically in most studies and the five studies that reported adverse events after immunisation described them in recipients only, without comparison with non-recipients, and one level for imprecision, the number of events being small. Not rated up.

⊕⊕⊕○ moderate certainty: we are moderately confident in the effect estimate; the true effect is likely to be close to the estimate, but there is a possibility that it is substantially different. ⊕⊕○○ low certainty: our confidence in the effect estimate is limited. ⊕○○○ very low certainty: we have very little confidence in the effect estimate. No outcome was rated up by two levels for a very large effect: relative risks below 0.2 derive from smaller studies, broader outcomes or shorter intervals from immunisation, whereas the largest studies converge on relative risks of 0.23–0.35. The upgrading criterion for plausible residual confounding was not applied, because the residual confounding plausible in this literature — a healthy-vaccine effect — would act to inflate rather than to reduce the observed effect.