Health Information and Quality Authority

An tÚdarás Um Fhaisnéis agus Cáilíocht Sláinte

Draft health technology assessment of immunisation against respiratory syncytial virus (RSV) in Ireland

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Foreword

Respiratory syncytial virus (RSV) is a highly contagious seasonal respiratory virus with outbreaks typically occurring during the winter months. In healthy individuals, infection with RSV is usually self-limiting. However, RSV can also cause more severe complications, especially in infants aged under six months, children aged under two years with risk factors for severe disease, and in older adults, particularly those with comorbidities or who are immunocompromised and those residing in long-term care facilities.

Since October 2022, a number of new interventions have been authorised or have received a positive recommendation for authorisation in Europe for the protection of infants and older adults in the general population. For infants, these include two extended half-life monoclonal antibody preparations, nirsevimab (Beyfortus®) and clesrovimab (Enflonsia®), and a maternal vaccine, RSVpreF (Abrysvo®). For adults aged 65 years and older, three vaccines have been authorised: RSVpreF (Abrysvo®), RSVPreF3 (Arexvy®) and RSV mRNA vaccine (mRESVIA®).

In Ireland, as a temporary measure for the 2024/25 and 2025/26 RSV seasons, the HSE implemented a publicly-funded Pathfinder Programme. For the 2025/26 RSV season, the programme offered immunisation with nirsevimab to all infants born between September 2024 and February 2025, and a catch-up programme for infants aged less than six months entering their first RSV season. The aim of this health technology assessment (HTA) is to provide advice to the Minister for Health and Health Service Executive to inform a long-term policy decision regarding an RSV immunisation strategy for infants and older adults in Ireland.

Work on the HTA was undertaken by an Evaluation Team from the HTA Directorate in HIQA. A multidisciplinary Expert Advisory Group was convened to advise the Evaluation Team during the course of the HTA. HIQA would like to thank the Evaluation Team, the members of the Expert Advisory Group and all who contributed to the preparation of this report.

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Healthcare Pricing Office, HSE

National Immunisation Office, HSE

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National Critical Care Programme, HSE

Acute Operations, HSE.

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Conflicts of Interest

It is noted that the Irish Pharmacy Union receives advertising revenue from the pharmaceutical industry through its publication, the IPU review. The Irish Pharmacy Union has also received funding for educational activities from the pharmaceutical industry.

Dr Daniel Hare reported receipt of a speaker's fee associated with his participation in the Irish RSV Network Forum — a non-promotional scientific educational meeting organised and sponsored by Sanofi.

General practices and pharmacies derive a small portion of their income from administration of vaccines.

There were no reported potential conflicts of interest for members of the Evaluation Team.

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Executive Summary

A health technology assessment (HTA) is intended to support evidence-based decision-making in regard to the optimum use of resources in healthcare services. Measured investment and disinvestment decisions are essential to ensure that overall population health gain is maximised, particularly given finite healthcare budgets and increasing demands for services provided. The aim of this HTA is to provide advice to the Minister for Health and Health Service Executive (HSE), to inform a long-term policy decision regarding an RSV immunisation strategy for infants and older adults in Ireland. This HTA considered the following domains:

- description of technology and review of international practice
- epidemiology and burden of disease
- clinical effectiveness and safety
- cost effectiveness
- budget impact analysis
- organisational issues
- ethical, patient and social considerations.

Background

Respiratory syncytial virus (RSV) is a highly contagious respiratory virus that is transmitted through airborne respiratory droplets, such as by coughing, sneezing or breathing. In Ireland, where RSV has been a notifiable disease since 2012, the RSV season typically lasts about six months, running from approximately September/October through February/March. While primary infection with RSV can cause lower respiratory tract disease (LRTD), in healthy individuals, infection with RSV is usually self-limiting and can be managed without medical attendance. However, RSV can cause more severe infections, such as pneumonia and bronchiolitis, which may lead to hospitalisation and could be fatal. RSV may also exacerbate chronic health conditions, in particular respiratory and circulatory conditions. Children at highest risk of severe RSV-associated lower respiratory tract disease (LRTD) include infants aged under six months, premature infants (that is, infants born before 37 completed weeks of gestation), children aged under two years with congenital heart or chronic lung disease, children who are immunocompromised and children with respiratory or neuromuscular disorders. Adults at highest risk of severe RSV include older adults (that is, those aged 65 years and older), particularly those who are immunocompromised, and those with certain chronic underlying medical conditions, such as chronic obstructive pulmonary disease (COPD), congestive heart failure (CHF), diabetes and asthma, and those residing in long-term care facilities (LTCFs).

Description of technology and international practice

As of October 2025, three pharmaceutical interventions are authorised or have a positive recommendation for authorisation in Europe for the passive immunisation of the general population of infants against RSV-related LRTD. These include two extended half-life monoclonal antibody preparations, nirsevimab and clesrovimab, both of which are administered by intramuscular injection to the infant, with a single dose sufficient to confer protection against RSV for that season. A recombinant bivalent maternal vaccine, RSVpreF (Abrysvo®), is administered to pregnant women between 24 and 36 weeks' gestation to provide passive protection of infants from birth to six months of age through transplacental antibody transfer.

Considering the target adult population in this HTA, that is adults aged 65 years and older, as of October 2025, there are three vaccines authorised in Europe for their active immunisation against RSV-related LRTD; the recombinant bivalent vaccine RSVpreF (Abrysvo®), the recombinant adjuvanted vaccine RSVPreF3 (Arexvy®) and the RSV mRNA vaccine (mRESVIA®).

The National Immunisation Advisory Committee (NIAC) has issued recommendations with respect to the immunisation of infants and older adults against RSV. These recommendations have been updated over time as new interventions have been authorised and as additional evidence of the safety and effectiveness of the available interventions has emerged.

As of December 2025, NIAC recommends the passive immunisation with nirsevimab of:

- all infants born during the RSV season, preferably prior to discharge home from a maternity hospital
- all infants aged six months or younger at the start of the RSV season
- high-risk infants (eligible for palivizumab) aged 12 months or younger at the start of their first RSV season
- all ex-preterm infants under 24 months of age with chronic lung disease in their second RSV season.

For adults, NIAC recommends vaccination with either RSVPreF3, RSVpreF, or the RSV mRNA vaccine of:

- adults aged 75 years or older
- adults aged 60 to 74 years with any additional risk factors for severe RSV disease
- adults aged 60 years and older living in long-term care facilities.

For these older adults, NIAC advises that a single dose is recommended as the need for booster doses has not yet been established.

In Ireland, as a temporary measure for the 2024/25 RSV season, the HSE implemented a publicly-funded Pathfinder Programme, which offered immunisation with nirsevimab to all infants born between September 2024 and February 2025. Nirsevimab was also offered to all infants at high-risk of severe RSV disease and previously eligible for palivizumab, including those born prior to the start of the RSV season, as well as all children at high risk of RSV disease entering their second RSV season. The programme has continued during the 2025/26 RSV season with an expansion of the eligible cohort to include a catch-up programme for infants aged less than six months entering their first RSV season. As of November 2025, no RSV maternal vaccine or older adult immunisation programme is in place.

A review of nationally-funded immunisation programmes against RSV among countries of the EU/EEA and the UK was carried out and updated on 19 November 2025. Twenty-two countries, including Ireland, have publicly-funded immunisation programmes against RSV for the general infant population, with differences noted between the programmes. As with Ireland, some of these programmes have been implemented as a temporary measure. Seventeen countries, including Ireland, fund nirsevimab for those born during the RSV season, of which 15 also provide a catch-up for infants born outside the RSV season. Countries differ with regard to the eligibility criteria for the catch-up cohort. Twelve countries fund the maternal vaccine either as an alternative to nirsevimab or as their only option, with eight countries restricting eligibility based on the expected due date. The countries differ with respect to the range of gestational weeks within which the maternal vaccine is administered.

Eight countries, and the Italian region of Sicily, were identified as funding RSV vaccination for older adults. The programmes differed in terms of the RSV vaccine(s) offered and the population eligible for vaccination. Two programmes have age-based criteria only, with one funding vaccination for all those aged 65 years and older, and the second funding vaccination for those turning 75 years (with an additional one-year catch-up for those aged 75 to 79 years in 2024). Five programmes have adopted risk-based funding criteria for different older adult population groups in addition to funding vaccination for those aged 75 years or 75 years and older. Differences were noted in the criteria for which individuals were considered at higher risk of severe disease (for example, aged 60 or 65 years with different chronic diseases and or residing in a long-term care facility). Two of the eight programmes fund immunisation only for older adults with specified conditions.

It is likely that there will continue to be updates to national practices for the 2025/26 RSV season and subsequent seasons, as further evidence becomes available for the authorised interventions, and given the number of products in development.

Epidemiology

RSV has been a notifiable disease in Ireland since 2012. RSV incidence data (for children aged 0 to 2 years and adults aged 65 years and older) were sourced from the Health Protection Surveillance Centre (HPSC) in Ireland for RSV seasons 2018/19 to 2024/25. Hospital utilisation data were also sourced from the Hospital In-Patient Enquiry (HIPE) system (for 2018 to 2024 and 2025 Q1) for both cohorts.

The RSV burden was consistently and substantially higher among those aged less than two years compared with all other age bands examined as part of this assessment including adults aged 65 years and older. Among those aged 0 to 2 years, infants aged less than one year accounted for 41% to 69% of all notified cases each year. In the 2024/25 season, there were substantial reductions in the RSV burden in those aged less than six months. The largest difference was seen in those aged less than three months after the implementation of the HSE's Pathfinder Programme, which offered immunisation with nirsevimab to all infants born in the six-month period between 1 September 2024 and 28 February 2025, and infants and children up to two years of age at high risk of severe disease (palivizumab eligible population). In those aged less than two years, infants aged less than six months accounted for 23% of the total notified cases, 24% of RSV ED visits and 26% of RSV hospitalisations in the 2024/25 RSV season. This compared with 55%, 53% and 57%, respectively of all such cases between the 2018/19 and 2023/24 RSV seasons in the same cohort. Among older adults, burden typically increased with age. In adults aged 65 years and older, those aged 80 years and older accounted for 47% of notified cases, 46% of RSV-related ED visits and 48% of RSV-related hospital admissions.

HIPE data also highlight the substantial burden associated with RSV in those aged 0 to 2 years. From 2018 to 2024 (excluding 2020), in those with a primary diagnosis of RSV, on average, there were 1,633 (range 1,342 to 2,195) discharges that did not include an ICU stay per annum (infants aged less than one year accounted for 86% of these discharges). The mean annual length of stay (LOS) was 3.3 days, and the mean total bed days associated with these discharges was 5,359 (range: 2,946 to 7,059) per annum. Additionally, on average, there were 133 (range 67 to 191) discharges that included an ICU stay (infants aged less than one year accounted for 91% of these discharges). The mean annual LOS was 8.3 days, and the mean total bed days associated with these discharges was 1,099 (range: 462 to 1,450) per

annum. The majority of hospital discharges occurred in quarter four (Q4), that is, October to December each year. For example, among infants aged less than one year, 69% to 88% of discharges without an ICU stay occurred in Q4 each year. There was a substantial reduction in discharges in those aged less than one year in Q4 of 2024 (n= 533) compared with 2018 to 2023 (range: 785 to 1,601).

HIPE data indicate that in adults aged 65 years and older, the number of discharges is relatively low. From 2018 to 2024, the total number of discharges without an ICU stay ranged from 8 to 130 per annum, the mean annual hospital LOS ranged from 8.4 to 16.3 days, and the total bed days associated with these discharges ranged from 130 to 1,825 per annum. Discharges that included an ICU stay were uncommon, and cannot be reported due to data suppression of quarterly data by age band over this time period.

Annual RSV-related mortality rates have been consistently low. In children aged less than two years, the estimated mortality rate was 0.6 per 100,000 in 2023/24, with no recorded RSV-related deaths during the 2024/25 season. In those aged 65 years and older, the estimated mortality rate was 4.9 per 100,000 and 6.9 per 100,000 during the 2023/24 and 2024/25 seasons, respectively. In total, 67% of notified RSV deaths in older adults were in those aged 80 years and older. However, as such data is contingent on RSV being listed as a cause of death on a death certificate, it is likely underestimated.

For the period 2018 to 2024 (excluding 2020), the total cost of inpatient stays for all age groups with a primary diagnosis of RSV ranged from €2.2 to €6.2 million per annum for cases that included an ICU stay, and €9.9 to €20.4 million per annum for cases that did not include an ICU stay.

These data are likely an underestimate of the total burden of RSV particularly in primary care, as not all RSV cases are laboratory confirmed and some discharges may not be coded. While there is an apparent trend of increasing incidence over time, this may reflect changing testing practices (increased laboratory capacity in hospital settings and updated HSE guidance relating to use of multiplex tests that include RSV in surveillance testing, and when testing patients that present with acute respiratory tract infection).

Clinical efficacy, effectiveness and safety

Systematic review evidence was used to address four research questions relating to the efficacy, effectiveness and safety of authorised interventions and approaches for the prevention of RSV and associated complications. These approaches comprised: the active immunisation of adults aged 65 years and older through vaccination; the

passive immunisation of infants through maternal vaccination; and the passive immunisation of infants and young children through the use of extended half-life monoclonal antibody preparations (EHL-mAbs).

The evidence for the vaccination of older adults against RSV was updated to 25 April 2025 and included three RCTs (n=97,547) and three observational studies (two test-negative case control studies (n=81,595) and one target trial emulation (n=146,852 vaccinated matched to 582,936 unvaccinated controls)). The evidence identified relates to adults aged 60 years and older and included three authorised RSV vaccines: RSVPreF3 (Arexvy®); RSVpreF (Abrysvo®); and the mRNA vaccine mRESVIA®. Based on pooled data from three RCTs, vaccine efficacy against RSV-related lower respiratory tract disease was 78% over one RSV season, with high certainty of evidence. There was evidence of waning immunity based on two RCTs reporting cumulative and per season data for two seasons (RSVPreF3 and RSVpreF) and three seasons (RSVPreF3). Cumulative vaccine efficacy against RSV-related LRTD was estimated at 67% over two seasons and 69% over three seasons, based on two RCTs and one RCT, respectively. Based on pooled data from two test-negative case control studies, vaccine effectiveness against RSV-related hospitalisation was 77%, with moderate certainty of evidence. A similar estimate (80%) was reported by the trial emulation study. The RCTs were underpowered to detect differences in RSV-related hospitalisation, and there were insufficient data to determine the impact of RSV vaccination on RSV-related ICU admissions or RSV-related mortality.

In terms of safety data for older adults, solicited local reactions (for example, injection site pain or redness) and systemic reactions (such as fever or fatigue) were common but mostly mild-to-moderate in severity; severe solicited adverse events (that is, reactions considered medically significant) were less common. Serious adverse events (SAEs) related to the intervention were rare; there was no statistically significant difference in risk between vaccine and placebo groups in the pooled analysis of three RCTs, with low certainty of evidence. Post-marketing surveillance data generally support the safety of RSV vaccination among older adults. While there is some uncertainty over potential SAEs such as Guillain-Barré syndrome (GBS) (a rare disorder where the body's immune system causes nerve damage) the evidence suggests these events are rare. The estimated number of excess cases (that is, those above what would be expected in the population) ranged from 16 to 25 and from 3 to 10 per million doses for RSVpreF and RSVPreF3, respectively.

The evidence for the passive immunisation of infants against RSV through maternal vaccination was updated to 25 April 2025 and included one RCT (n=7,420) and one

observational study (test-negative case control study (n=505)). The evidence identified included RSVpreF (Abrysvo®), the only RSV vaccine authorised in Europe for the passive immunisation of infants through maternal vaccination. Based on estimates from one RCT, vaccine efficacy against medically attended (MA) RSV-related LRTD and RSV-related hospitalisation at 180 days' follow-up after birth was 49% and 55%, respectively, with moderate certainty of evidence. Based on data from one test-negative case control study, vaccine effectiveness against RSV-related hospitalisation at 180 days' follow-up after birth was 73%, with low certainty of evidence. Based on one event in one RCT, there was no statistically significant effect of maternal vaccination on RSV-related mortality, with low certainty of evidence.

In terms of safety data for maternal vaccination, most reactions reported in the period up to one month after vaccination were mild-to-moderate in severity. SAEs related to the intervention were rare; there was no statistically significant difference in risk between vaccine and placebo groups in one RCT, with low certainty of evidence. While countries continue to closely monitor recipients due to some concerns regarding a potential safety signal relating to risk of preterm birth, post-marketing surveillance data support the safety of maternal RSV vaccination.

The evidence for the passive immunisation of infants against RSV through the use of EHL-mAbs was updated to 23 April 2025 and included four RCTs (n=16,121) and fifteen observational studies (n=96,392). The RCT data relate to both nirsevimab (Beyfortus®) and clesrovimab (Enflonsia®) (clesrovimab data from the CLEVER RCT were included as a post-hoc update), whereas the observational data relate exclusively to nirsevimab. Based on estimates from three RCTs, efficacy against medically attended RSV-related lower respiratory tract infection (LRTI) over one season was 69%, with high certainty of evidence. Based on pooled data from two observational studies, nirsevimab effectiveness against RSV-related LRTI incidence over one season was 87%, with moderate certainty of evidence. Based on pooled estimates from four RCTs, efficacy against RSV-related LRTI with hospitalisation over one season was 83%, with moderate certainty of evidence. Based on pooled data from nine observational studies, effectiveness of nirsevimab against RSV-related hospitalisation over one season was 87%, with low certainty of evidence. RCT evidence indicated that EHL-mAbs probably do not reduce MA RSV-related LRTI over two seasons, while nirsevimab probably does not reduce RSV-related LRTI with hospitalisation over two seasons. Based on pooled estimates from four observational studies, there was evidence that nirsevimab probably reduces RSV-related ICU admissions over one season, with moderate certainty of evidence. There were insufficient data to determine efficacy against RSV-related ICU admissions, or efficacy and or effectiveness against RSV-related mortality.

In terms of safety data for EHL-mAbs, adverse events were common but typically mild-to-moderate in severity. SAEs related to the intervention were rare, with only two participants (out of 8,380) reported to have had an SAE that was related to an EHL-mAb, while one participant (out of 6,190) had an SAE related to a placebo. While rare, due to the low certainty of evidence, it is unclear if EHL-mAbs are associated with SAEs related to the study intervention. However, to date, post-marketing surveillance supports the overall safety of nirsevimab administration in infants.

Overall, there is consistent evidence that all currently authorised RSV immunisation products are safe and effective for the prevention of RSV and associated complications, over one season. For older adults, there is evidence of continued effectiveness for up to three RSV seasons, but that immunity wanes over time. While local and systemic events are common, these are mostly mild-to-moderate in severity; SAEs are rare. Continued monitoring and vigilance will be required given that these are new interventions. The potential harms that are associated with immunisation must be considered in the context of the potential clinical benefit within the given population.

Review of economic modelling studies

The most recent systematic review of economic modelling studies of RSV immunisation strategies with a focus on modelling inputs was published in 2021, based on a literature search conducted up to 2020. However, it did not include studies relating to the newly authorised forms of RSV vaccination or EHL-mAb preparations. To establish and assess the most up-to-date international evidence on the approaches taken to the economic modelling of immunisation strategies, a rapid review of studies published since 2020 was undertaken.

Sixteen studies were identified in the rapid review. Ten of the included studies were conducted using non-industry funding sources such as government agencies, research bodies and or charitable foundations, three received EU funding, two of which also received funding from industry. The remaining three studies were solely industry-funded.

Thirteen of the 16 included studies employed a static modelling approach, while two used dynamic transmission models. One study presented a model comparison of three static models and two dynamic transmission models. The time horizon varied across the studies ranging from one RSV season to 10 years with some studies including longer time horizons for long-term outcomes or in secondary analyses.

Seven studies conducted their analysis from a healthcare perspective; a further two studies adopted a societal perspective, while the remaining seven studies adopted a dual perspective (considering both the healthcare and societal perspective) in the base-case analysis.

A critical appraisal of included studies was undertaken. There were some concerns with regard to the inconsistency in the inclusion of the health states, the transparency on structural assumptions, the transparency of data identification, and the description of model validation in a minority of studies.

This rapid review identified several notable modelling features for consideration when developing an economic model of immunisation of young children and adults, all of which were considered in the development of a de novo economic model for Ireland.

While included studies found immunisation of infants and adults to be cost effective, this was typically sensitive to the assumed unit price (or price per dose delivered) of the interventions, and were frequently at significant reductions relative to their list price. Moreover, for infants, the optimal strategy (maternal vaccination or EHL-mAb) was sensitive to relative prices.

Economic evaluation

A Markov model was developed to characterise the incidence of medically attended cases of RSV in Ireland and to estimate the cost effectiveness and budget impact of both an infant- and adult-based RSV immunisation programme. The budget impact of RSV immunisation for a cohort of adults aged 60 years and older with additional risk factors for severe disease was also estimated. Model parameters including disease incidence, hospitalisation and mortality rates, EHL-mAb and vaccine efficacy, transition probabilities, costs and utility values were estimated from a variety of published sources and national datasets for Ireland.

Five alternative infant-based RSV immunisation strategies were assessed:

- an extended half-life monoclonal antibody (EHL-mAb) offered seasonally at birth to infants born during the RSV season – strategy 1 (S1)
- an EHL-mAb offered both seasonally at birth to infants born during the RSV season and as catch-up in the first month of the season to infants born prior to their first RSV season - strategy 2 (S2)

- a maternal vaccine offered seasonally to pregnant women between 24 and 36 weeks' gestation where the estimated due date falls during the RSV season - strategy 3 (S3)
- a combination of a maternal vaccine offered seasonally to pregnant women between 24 and 36 weeks' gestation where the estimated due date falls during the RSV season, and an EHL-mAb offered seasonally at birth to infants born during the RSV season who are not protected by maternal vaccination - strategy 4 (S4)
- a combination of a maternal vaccine offered seasonally to pregnant women between 24 and 36 weeks' gestation where the estimated due date falls during the RSV season, and an EHL-mAb offered seasonally at birth to infants born during the RSV season who are not protected by maternal vaccination, and an EHL-mAb offered as catch-up in the first month of the season to infants born prior to their first RSV season - strategy 5 (S5).

Four alternative adult-based RSV immunisation strategies were assessed, which offered a once-off RSV vaccine to those aged:

- 65 to 69 years in year one of the programme and those aged 65 years only in subsequent years – strategy 6 (S6)
- 70 to 74 years in year one of the programme and those aged 70 years only in subsequent years – strategy 7 (S7)
- 75 to 79 years in year one of the programme and those aged 75 years only in subsequent years – strategy 8 (S8)
- 80 years and older in year one of the programme and those aged 80 years only in subsequent years – strategy 9 (S9).

The epidemiological analysis indicated that based on coverage rates of 62.0%, 82.6% and 76.0% for the maternal vaccine, seasonal and catch-up EHL-mAb, respectively, infant-based immunisation strategies would result in reductions of 11.6% (S3) to 43.2% (S2) in the annual number of medically attended RSV cases in those aged up to one year compared with no immunisation. The highest reductions in medically attended RSV cases were reported in the 0- to 2-month-old age group, at 52.8% and 22.6% for S2 and S3, respectively. The estimated reduction in the annual number of hospitalised cases in those aged up to one year ranged from 52.1% for S2 to 12.2% for S3, with the highest reductions reported in the 0- to 2-month-old age group, at 62.5% and 23.3% for S2 and S3, respectively. For the adult-based strategies, immunisation would result in reductions of 28.2% for S6

(coverage rate of 60.1%) to 41.9 % for S8 (coverage rate of 88.4%) in the annual number of medically attended RSV cases compared with no immunisation.

From both the payer and societal perspectives, the base-case incremental cost-effectiveness ratios (ICERs) for all infant- and adult-based RSV immunisation strategies assessed, exceeded willingness-to-pay (WTP) thresholds of €20,000 and €45,000 per quality-adjusted life-year (QALY) gained. At assumed prices of €301 and €165 (ex VAT) for the EHL-mAb and maternal vaccine, respectively, the ICERs for the infant-based strategies were €210,000 per QALY for S5 compared with no immunisation, and €310,000 per QALY for S2 compared to S5. All other infant-based strategies were eliminated in the incremental analysis. Sensitivity analysis demonstrated that at a price of €166 or less (ex VAT) for the EHL-mAb and a price of at least €90 for the maternal vaccine, S2 would be cost effective compared with no immunisation at a WTP threshold of €45,000 per QALY. At a price of €47 or less (ex VAT) for the maternal vaccine and a price of at least €190 for the EHL-mAb, S3 would be cost effective compared with no immunisation at a WTP threshold of €45,000 per QALY. At a price of €165 (ex VAT) for the adult vaccine, S9 dominated (less costly and generated more QALYs) all other adult-based RSV immunisation strategies. The ICER for S9 was €232,576 per QALY compared with no immunisation. Sensitivity analysis demonstrated that at a vaccine price of €20 or less (ex VAT), that is an 88% reduction from base case, S9 would be cost effective compared with no immunisation at a WTP threshold of €45,000 per QALY.

The five-year incremental budget impact for the infant-based strategies, assuming a price of €301 plus VAT for an EHL-mAb (a seasonal coverage rate of 82.6% and catch-up coverage rate of 76%) and a price of €165 plus VAT for the maternal vaccine (coverage rate of 62%), ranged from €15.6 million for S3 to €58.5 million for S2. The five-year incremental budget impact for the adult-based immunisation strategies, assuming a price of €165 plus VAT for the adult vaccine and coverage rates ranging from 60.1% (S6) to 88.4% (S8 and S9), ranged from €70.6 million for S9 to €73.7 million for S6. Based on a coverage rate of 97.8%, the total budget impact over five years for the full cohort of adults aged 60 years and over with additional risk factors for severe disease due to comorbidity or who are resident in a LTCF (that is, including all individuals for whom NIAC recommends vaccination) was estimated at €93.4 million. Of this figure, €7.9 million related to vaccine procurement, administration and pick and pack for those resident in a LTCF.

All models are subject to limitations due to both the quantity and quality of data available to populate the models. The applicability of the findings is dependent on the underlying assumptions that underpin the model structure and the chosen parameter values. Despite these limitations, the infant-based model outputs broadly

align with those reported by the HSE for the 2024/25 Pathfinder RSV immunisation programme. Based on extensive scenario and sensitivity analyses, the findings of the economic evaluations presented are largely robust to data and structural assumptions with the exception of the uncertainty over the price of EHL-mAbs and vaccines.

Based on the analyses presented, RSV immunisation would be associated with potentially large reductions in medically attended cases and RSV hospitalisations. However, these benefits would come at a high financial cost. Substantial reductions in the estimated current vaccine and EHL-mAb prices would be required for either an infant- or adult-based RSV immunisation programme to represent an efficient use of healthcare resources in Ireland. As such, policy decision-making regarding the potential introduction of an RSV immunisation programme in Ireland should consider both the price and the relative prices of EHL-mAbs and RSV vaccines that can be achieved in the tendering process.

Organisational issues

The organisational implications of each of the immunisation strategies for infants and older adults included in the economic evaluation were considered.

In terms of passive immunisation of infants, approximately 27,500 infants would be eligible for immunisation per year with a seasonal programme, increasing to over 55,000 infants if a catch-up programme is also provided. For seasonal EHL-mAb strategies, hospital-based administration after birth in the maternity unit and or hospital would be consistent with the approach successfully adopted in the HSE Pathfinder Programme, which achieved high coverage rates.

For the seasonal maternal vaccination strategy, the vaccine would be offered between 24 and 36 weeks' gestation and where the estimated due date falls during the RSV season. This would correspond with the maternal vaccine being offered between approximately May until late January. Administration in primary care would be consistent with the approach for other vaccines recommended in pregnancy. Timing of RSV immunisation to coincide with a scheduled antenatal visit may be possible in some instances and would reduce the burden on patients and providers. Co-administration with influenza vaccine and COVID-19 vaccine is possible, but a minimum interval of two weeks is recommended between administration of RSVpreF and (pertussis) Tdap vaccines. Consideration may be needed for maternity unit-based vaccination for individuals without a GP.

For a catch-up programme, provision in GP practice settings would be consistent with the approach for other vaccines on the Primary Childhood Immunisation

Schedule. Complexities include the large number of infants involved and the aim for them to be immunised as close to the start of the RSV season as possible. Timing of RSV immunisation to coincide with a scheduled visit (for example, post-natal examination at 2- or 6-weeks; or the 2-, 4- or 6-month vaccination visit) may be possible in some instances and would reduce the burden on parents and providers. While co-administration with scheduled vaccines is possible, there may be a preference to limit the number of vaccines and or injections to which consent is sought at a single visit, as the two-month visit currently includes three injections, while the four- and six-month visits currently include two injections each.

In terms of vaccination of older adults, providing vaccination for all cohorts identified in the 2025 NIAC recommendations within the first year of a programme would likely prove challenging given the large number of individuals (over 550,000) involved, the substantial budget impact, and commitments under existing immunisation programmes for these cohorts. Provision of RSV vaccination through GP practices and community pharmacies, supported by mobile vaccination teams for residents of long-term care facilities, would be consistent with the approach for other vaccines in the adult programme. Co-administration with other vaccines such as influenza, COVID-19 and pneumococcal would reduce the number of vaccine-related healthcare visits. However, this presents challenges, including the potential for increased side effects that may impact future uptake of seasonal vaccines, possible decreased immune responses to certain influenza strains when co-administered with the influenza vaccine (the clinical significance of which is unknown), and reluctance to administer three (or potentially four) vaccines at a single visit.

Each year, RSV has a substantial and predictable seasonal burden on the healthcare system, particularly on paediatric services due to the disproportionate burden in young children, especially those aged less than one year. This can impact the delivery of other scheduled and unscheduled care, increase pressure on staff, increase the risk of hospital-acquired infections, and challenge the ability to provide safe and effective care.

A decision to fund RSV immunisation could have considerable financial and logistical implications depending on the population group for whom the programme of immunisation is funded. The likely uptake of RSV immunisation is uncertain and may differ depending on the immunisation approach (for example, maternal vaccination or EHL-mAB) and or the population group to whom the programme is offered. As with other immunisation interventions, all RSV interventions have stringent storage and handling requirements. Given existing seasonal influenza and COVID-19 vaccination programmes, providers may need to manage large amounts of stock in the autumn period to meet demand.

If a decision were made to fund RSV immunisation, resource considerations would include the appropriate recruitment, provision and training of healthcare workers (including but not limited to nurses, midwives, doctors, pharmacists), and an information campaign and materials to clearly communicate benefits, risks and eligibility regarding RSV immunisation. This would include resources to engage with representatives of typically under-represented or hard-to-reach groups and to support uptake in these groups. Additionally, resources may be required for programme monitoring and evaluation, including monitoring uptake in target populations.

Ethical, patient and social considerations

The ethical, patient and social issues relevant to the evaluated RSV immunisation strategies for infants and older adults were considered. Parents of infants hospitalised with RSV report worry, guilt and anxiety and that RSV prophylaxis programmes provide peace of mind. Positive predictors of acceptance of infant or maternal RSV immunisation included perceived protection and the perceived severity of RSV. Concerns about the safety of an intervention are the primary reason for refusal or hesitation of an RSV immunisation to protect infants, along with a lack of RSV knowledge. For older adults, the emotional and physical impacts of RSV illness affect day-to-day tasks and social activities. Overall, the findings of studies conducted with older adults showed a limited knowledge and awareness of RSV, but generally positive attitudes towards prevention strategies. Acceptance of immunisations may be tied to cultural backgrounds. Tailoring interventions that increase trust in immunisation and address concerns can help improve uptake.

When weighing up the benefits of RSV immunisation it should be noted that infants are a vulnerable population, especially in the first few months of life. While, the evidence supports protection for a single RSV season only, this covers the period for when they are likely at most risk. When weighing up the benefits for older adults, it should be considered that those in long-term care facilities may not have the ability to control their exposure to infection and outbreaks of RSV can spread quickly in such environments. Older adults with significant comorbidities may also be particularly vulnerable. There is a need to temper expectations of long-term immunity for older adults; while there is evidence of waning immunity over time, the need for booster doses has not been demonstrated. Recent data indicate an association between older adult RSV vaccination and an increased number of cases of GBS, although the absolute risk remains small. Overall, serious adverse events with RSV immunisations are rare.

Wider societal benefits of a successful RSV immunisation programme may include an easing of the workflow for healthcare providers in primary and secondary care. Before the introduction of the Pathfinder RSV immunisation programme, paediatric hospitals in particular had winter surges in RSV admissions which have led to greater than 100% paediatric ICU bed occupancy, with implications for patient safety and the provision of other necessary care including elective surgeries. With regard to possible societal harms, the decision on which time of year an older adult funded RSV vaccine would be administered could be crucial in order to minimise any reduction in uptake of existing vaccination programmes.

A decision between the maternal RSV vaccine and the EHL-mAb (within strategies where both are funded) may be perceived as having moral implications for some parents, with some studies indicating a preference among parents for the maternal vaccine if efficacy were equal.

This is a rapidly changing area of research and new types of RSV immunisation, extensions to indications and longer-term efficacy and safety data are likely to become available in the near future. Recently implemented RSV immunisation programmes have demonstrated substantial benefits of immunisation. While it could be considered unethical to unnecessarily delay access to authorised RSV interventions given the strong evidence base to support their safety and effectiveness in the populations under consideration. Conversely, access must be balanced with the fact that none of the included strategies were found to be cost effective at typical willingness-to-pay thresholds. Funding of interventions that are not cost effective creates issues of justice and equity with respect to a fair distribution of healthcare resources. However, it may also be viewed as unjust if infants are not provided with the same level of protection in future seasons as those currently eligible for the Pathfinder programme.

Conclusion

The findings of this HTA highlight the substantial and predictable seasonal impact that RSV has on the healthcare system in Ireland. This is most acutely evident in secondary paediatric healthcare services due to the disproportionate burden in young children, particularly in those aged less than one year. This can affect the delivery of other scheduled and unscheduled care, increase pressure on staff, increase the risk of hospital-acquired infections, and challenge the ability to provide safe and effective care.

There is clear and consistent evidence that all currently authorised RSV immunisation products are safe and effective for the prevention of RSV and associated complications over one season. While local and systemic events are

common, these are mostly mild-to-moderate in severity; serious adverse events are rare. For older adults, there is evidence of longer-term effectiveness, with data limited to a maximum of three years' follow-up; however, immunity wanes over time.

Based on the analyses presented, RSV immunisation would be associated with significant reductions in medically attended cases and RSV hospitalisations, with the greatest impact seen in the paediatric setting due to the higher burden of disease in this cohort. However, these benefits would come at a high financial cost. Considerable reductions in the estimated current vaccine and EHL-mAb prices would be required for either an infant- or adult-based RSV immunisation programme to represent an efficient use of healthcare resources in Ireland. As such, policy decision-making regarding the potential introduction of an RSV immunisation programme in Ireland should consider both the price and the relative prices of EHL-mAbs and RSV vaccines that can be achieved in the tendering process.

Plain language summary

What is RSV?

Respiratory syncytial virus, or RSV, is an infection that is caused by a virus. RSV affects the lungs and upper airways. The RSV season in Ireland usually runs from from October to March, with outbreaks every winter.

In healthy people, RSV infection can usually be managed without needing to see a doctor. However, RSV can cause more severe infections in some people, and hospital care may be needed.

People at increased risk of severe disease include infants aged less than six months, premature babies, and children aged less than two years with certain medical conditions. Older adults are also at increased risk of severe disease, particularly those with chronic heart or lung disease or who live in long-term care facilities.

What did we look at?

We looked at the impact of immunising infants and older adults against RSV infection.

There are two ways to protect infants. One way is a vaccine injection given to the mother, during pregnancy. The other is an antibody injection given to babies after they are born. There are three vaccines available for older adults.

As a temporary measure, the Health Service Executive (HSE) implemented a programme called Pathfinder that offered the antibody injection, nirsevimab (Beyfortus®), to babies born between September 2024 and February 2025. This programme has been offered again for the 2025/26 RSV season, this time including babies aged less than six months on the 1 September.

This assessment will inform a decision by the Department of Health for the 2026/27 RSV season and onwards.

Do similar immunisation programmes exist in other countries?

Twenty-two countries in Europe have recently introduced RSV immunisation programmes for infants. Some, including Ireland, only introduced these programmes as a temporary measure. The programmes differ in what they offer and to whom. Eight countries have recently introduced programmes for older adults, but the age groups to which they are offered differs. Two of the countries only offer the vaccine to older adults with certain chronic conditions or who live in long-term care facilities.

What did we find?

RSV infection is very common in Ireland with outbreaks every winter. More than 7,000 people are diagnosed with RSV infection each year, with over 2,000 requiring hospital admission, mostly infants and young children. Most of these hospital admissions happen between October and December. This makes it very challenging for hospitals and disrupts routine care, such as planned surgeries for children.

The highest number of reported RSV cases are in children less than two years of age. They account for up to seven out of every ten reported cases. Across all ages, babies aged less than six months are the most likely to need medical care, including admission to hospital or to intensive care. The burden in older adults is much lower than in small children. Among older adults, nearly half of all recorded cases and hospitalisations occur in those aged 80 years and older.

RSV immunisation is safe to use in infants, pregnant women and older adults. Serious side effects are rare. However, minor reactions are common. These include pain where the injection was given, tiredness, and muscle pain. We found that immunisation reduces the chances that infants and older adults will need to see a doctor if they catch the virus. It also reduces the risk that they require hospital care. Although immunisation is effective when individuals first receive it, the benefit decreases over time.

We looked at the impact of providing immunisation for infants and older adults. Immunisation would reduce the number of people that require medical care and hospital care. However, it would also cost a lot of money, even after considering savings because fewer people have to go to their GP or are admitted to hospital. If immunisation is offered to all infants, it would cost the HSE an extra €50 to 60 million over the first five years. If offered to adults aged 80 years and older, it would cost the HSE an extra €70 million over the first five years.

Unless the price the HSE pays for the RSV interventions is a lot lower than the expected prices, offering immunisation to infants or older adults would not be an efficient use of resources. While making immunisation available to all would be more equitable, it could create unfairness in other ways. The health service needs to aim for a fair distribution of benefits and burdens for the whole population of Ireland.

List of abbreviations used in this report

ACER	average cost-effectiveness ratio
ACIP	Advisory Committee on Immunization Practices (US)
ADR	adverse drug reaction
AE	adverse event
AESI	adverse event of special interest
AIDS	acquired immunodeficiency syndrome
AMSTAR	A MeaSurement Tool to Assess Systematic Reviews
ARI	acute respiratory illness
BIA	budget impact analysis
BMI	body mass index
CAD	Canadian Dollar
CCPA	combined cost of purchasing and administration
CDC	Centers for Disease Control and Prevention
CDM	chronic disease management
CEAC	cost-effectiveness acceptability curve
CHF	congestive heart failure
CHI	Children's Health Ireland
CHMP	Committee for Medicinal Products for Human Use

CI	confidence interval
COPD	chronic obstructive pulmonary disease
CSO	Central Statistics Office
CUA	cost-utility analysis
EAG	expert advisory group
ECDC	European Centre for Disease Prevention and Control
ED	emergency department
EEA	European Economic Area
EHL-mAb	extended half-life monoclonal antibody
EMA	European Medicines Agency
EQ-5D	EuroQol five-dimension
ESRI	Economic and Social Research Institute
EU	European Union
EUnetHTA	European Network of Health Technology Assessment
FDA	Food and Drugs Administration (US)
GA	gestational age
GBP	British Pound Sterling
GBS	Guillain-Barré syndrome
GP	general practitioner

GRADE	Grading of Recommendation, Assessment, Development and Evaluation
HIPE	Hospital In-Patient Enquiry
HIQA	Health Information and Quality Authority
HIV	human immunodeficiency virus
HPO	Healthcare Pricing Office
HPRA	Health Products Regulatory Authority
HPSC	Health Protection Surveillance Centre
HSE	Health Service Executive
HSUV	health state utility value
HTA	health technology asessment
ICER	incremental cost-effectiveness ratio
ICU	intensive care unit
IM	intramuscular
IQR	interquartile range
IRR	incidence rate ratios
ITT	intention-to-treat
IV	intravenous
JBI	Joanna Briggs Institute

JCVI	Joint Committee on Vaccination and Immunisation (UK)
JPY	Japanese Yen
KDOQI	kidney disease outcomes quality initiative
LRTD	lower respiratory tract disease
LRTI	lower respiratory tract infection
LTCF	long-term care facilities
LTCH	long-term care homes
mAb	monoclonal antibody
MA	medically attended
MH	Mantel-Haenszel
MHRA	Medicines and Health Regulatory Agency
MN-CMS	Maternal and Newborn Clinical Management System
mRNA	Messenger ribonucleic acid
MV	maternal vaccine
NCCS	National Cold Chain Service
NIAC	National Immunisation Advisory Committee
NICU	neonatal intensive care unit
NIIS	National Immunisation Information System
NIO	National Immunisation Office

NOCD	new onset chronic disease
NOK	Norwegian Krone
NRSI	non-randomised study of intervention
NYHA	New York Heart Association
OECD	Organisation for Economic Cooperation and Development
OR	odds ratio
OWSA	one-way sensitivity analysis
PC	primary care
PCCU	paediatric critical care unit
PCR	polymerase chain reaction
PCRS	Primary Care Reimbursement Service
PICOS	population, intervention, comparator, outcome, study design
PICU	paediatric intensive care unit
pIMD	potential immune-mediated disease
PPD	price per dose
PPPD	purchasing price per dose
PRISMA	Preferred Reporting Items for Systematic reviews and Meta-Analyses
QALY	quality-adjusted life year

RCT	randomised controlled trial
ROBINS-I	Risk of Bias in Non-randomized Studies of Interventions
RNA	ribonucleic acid
RR	risk ratio
RSV	respiratory syncytial virus
RSVpreF	respiratory syncytial virus prefusion F vaccine
RSVPreF3	respiratory syncytial virus prefusion F3 vaccine
RT-PCR	reverse transcription polymerase chain reaction
SAE	serious adverse event
SD	standard deviation
SmPC	Summary of Product Characteristics
Tdap	tetantus, diphtheria, and acellular pertussis vaccine
UK	United Kingdom
VE	vaccine efficacy / vaccine effectiveness
VISION	Virtual SARS-CoV-2, Influenza and Other respiratory viruses Network
VPD	vaccine-preventable disease
wGA	weeks' gestational age
WHO	World Health Organization

WTP	willingness to pay

1 Introduction

1.1 Background to the request

Respiratory syncytial virus (RSV) is a common pathogen and major contributor to acute lower respiratory tract infection (LRTI) among infants, young children and older adults. RSV is a seasonal virus; in temperate climates, outbreaks typically occur during the winter months, with the virus continuing to circulate until early spring.[1]

RSV is typically a self-limiting disease in otherwise healthy individuals. In some children, RSV may progress to bronchiolitis, pneumonia and laryngotracheitis (alternatively referred to as 'croup'). Children at highest risk of severe RSV-associated lower respiratory tract disease (LRTD) include infants aged under six months, premature infants (that is, infants born before 37 completed weeks of gestation), children aged under two years with congenital heart or chronic lung disease, children who are immunocompromised and children with respiratory or neuromuscular disorders.[2] In older children and adults, symptoms are generally either absent or confined to the upper respiratory tract. However, older adults, those who are immunocompromised, and those with certain chronic underlying medical conditions, such as chronic obstructive pulmonary disease (COPD), congestive heart failure (CHF), diabetes, and asthma, are also at increased risk of severe RSV-associated LRTD.[3] Older adults residing in long-term care facilities (LTCFs) are further identified as an important subset of the older adult population with increased susceptibility to infection and severe disease outcomes due to a combination of risk factors such as advanced age, multimorbidity, frailty and close living quarters which can contribute to the spread of infection.[4]

Historically, authorised interventions to reduce the burden associated with RSV were limited to palivizumab (Synagis®), a short-acting monoclonal antibody which was authorised by the European Medicines Agency (EMA) in 1999 for the immunisation of the subset of infants and children aged up to two years at high risk of serious RSV-associated LRTD.[5] Since October 2022, a number of new interventions have been authorised by the EMA for the protection of infants and older adults in the general population. These can broadly be classified as:

- enhanced half-life monoclonal antibodies (EHL-mAbs) for the passive immunisation of infants[6]
- RSV vaccines for the passive immunisation of infants through maternal vaccination[7]
- active immunisation of adults.[7-9]

Following a request from the Department of Health, HIQA completed a rapid HTA of alternative strategies for the immunisation of infants and older adults against RSV in Ireland, to inform an interim policy decision on the most appropriate immunisation strategy for the 2025/26 season. The rapid HTA was published in August 2024.[10] For the 2024/25 season, the HSE implemented a publicly-funded Pathfinder Programme, which offered immunisation with the long-acting mAb, nirsevimab, to all infants born between September 2024 and February 2025.[11] Immunisation with nirsevimab was also extended to infants and children up to two years of age at high risk of severe disease who would previously have been eligible for palivizumab. The Department of Health also requested that, following the completion of the rapid HTA, HIQA conduct a full HTA of alternative strategies for the immunisation of infants infant and older adults against RSV to inform a longer-term policy decision (for the 2026/27 and subsequent RSV seasons).

1.2 Terms of reference

This HTA will be submitted as advice to inform decision making by the Minister for Health and Health Service Executive (HSE) regarding immunisation against RSV in Ireland. With consideration specifically to the immunisation of children aged less than two years identified to be at high risk of severe disease, children aged less than one year in the general population, and adults aged 65 years and older, the terms of reference of this HTA are to:

- describe the forms of RSV immunisation authorised for use (that is, monoclonal antibodies and RSV vaccines)
- describe the epidemiology and burden of disease associated with RSV in Ireland
- describe the population-level immunisation strategies against RSV in EU/EEA countries and the UK
- review the current evidence of the clinical effectiveness and safety of authorised interventions indicated for protection against RSV
- review the methodology for economic modelling studies of RSV immunisation strategies
- assess the cost effectiveness and budget impact of alternative RSV immunisation strategies
- consider any potential organisational and resource implications of the alternative RSV immunisation strategies
- consider any ethical, patient and social implications that RSV immunisation strategies may have for individuals, the general public and the healthcare system in Ireland

- based on the findings of this assessment, provide advice to inform a decision on the most appropriate RSV immunisation strategy for the 2026/27 RSV season and subsequent seasons.

1.3 Overall approach

Following an initial scoping of the available evidence, the terms of reference of this assessment were agreed between HIQA and the Department of Health. HIQA appointed an evaluation team comprising staff from the HTA Directorate to carry out the assessment.

HIQA convened an expert advisory group (EAG) comprising representation from relevant stakeholders, including patient representation, decision makers, clinical experts, public health experts and methodological expertise. The role of the EAG is to inform and guide the process, provide expert advice and information, and to provide access to data where appropriate. A full list of the membership of the EAG is available in the EAG membership section of this report.

The terms of reference for the EAG are to:

- contribute to the provision of high-quality and considered advice by HIQA to the Department of Health
- contribute fully to the work, debate and decision-making processes of the group by providing expert guidance, as appropriate
- be prepared to provide expert advice on relevant issues outside of group meetings, as requested
- provide advice to HIQA regarding the scope of the analysis
- support the Evaluation Team led by HIQA during the assessment process by providing expert opinion and access to pertinent data, as appropriate
- review the project plan outline and advise on priorities, as required
- review the draft report from the Evaluation Team and recommend amendments, as appropriate
- contribute to HIQA's development of its approach to HTA by participating in an evaluation of the process upon the conclusion of the assessment.

The protocol of the HTA, which outlined the terms of reference and the methodology for the HTA, was circulated for review by the EAG. Following incorporation of feedback from the EAG, the protocol was published on the HIQA website on 28 January 2025.[12] For this HTA, two EAG meetings took place. The draft chapters of the HTA were circulated to the EAG in advance of the meetings and discussed at the

meetings. Following revisions, as appropriate, a draft report was prepared for public consultation. After the public consultation, a final draft version of the report and the advice to the Minister for Health and HSE will be circulated for review by the EAG. The report will then be submitted to the Board of HIQA for approval. Following its approval, the completed assessment will be submitted to the Minister for Health and HSE as advice, and published on the HIQA website.

2 Description of Technology

Key Points

- Respiratory syncytial virus (RSV) is a highly contagious virus that is transmitted through airborne respiratory droplets, such as by coughing, sneezing or breathing. Primary infection with RSV can cause lower respiratory tract disease (LRTD) in infected individuals.
- In Ireland, where RSV has been a notifiable disease since 2012, the RSV season typically lasts about six months, running from approximately September/October through February/March.
- In healthy individuals, infection with RSV is usually self-limiting and can be managed without medical attendance. However, in those at increased risk of RSV-related disease, such as infants and older adults, RSV infection can cause more severe illness and lead to hospitalisation or even be fatal.
- Non-pharmacological strategies for preventing RSV infection include encouraging behaviours to reduce virus transmission, such as limiting social contacts for symptomatic individuals, and practicing good hand and respiratory hygiene.
- As of October 2025, three pharmaceutical interventions are authorised, or have had a positive recommendation for authorisation for the passive immunisation of the general population of infants against RSV-related LRTD in Europe:
  - Nirsevimab (Beyfortus®) and clesrovimab (Enflonsia®) are extended half-life monoclonal antibodies (EHL-mABs), which are administered by intramuscular injection to the infant, with a single dose sufficient to confer protection against RSV for that season.
  - RSVpreF (Abrysvo®) is a recombinant bivalent vaccine, which is administered to pregnant women between 24 and 36 weeks' gestation to provide passive protection of infants from birth to six months of age through transplacental antibody transfer.
- Considering specifically the subset of infants and children aged up to two years at high risk of serious RSV-associated LRTD, the short-acting monoclonal antibody palivizumab (Synagis®) has been authorised by the

EMA since 1999, with nirsevimab also authorised for this cohort since June 2024.

- Considering the target adult population in this HTA (adults aged 65 years and older), as of October 2025, there are three vaccines authorised in Europe for their active immunisation against RSV-related LRTD:
  - recombinant bivalent vaccine, RSVpreF (Abrysvo®)
  - recombinant adjuvanted vaccine, RSVPreF3 (Arexvy®)
  - RSV mRNA vaccine (mRESVIA®).
- With the exception of palivizumab, all currently-authorised RSV interventions are subject to additional monitoring requirements by the European Medicines Agency, owing to the fact that they contain new active substances, and are new biological medicines.
- In Ireland, as a temporary measure for the 2024/25 RSV season, the HSE implemented a publicly-funded Pathfinder Programme, which offered immunisation with nirsevimab to all infants born between September 2024 and February 2025. Nirsevimab was also offered to all infants at high-risk of severe RSV disease and previously eligible for palivizumab, including those born prior to the start of the RSV season, as well as all children at high risk of RSV disease entering their second RSV season. The programme has continued for the 2025/26 RSV season with an expansion of the eligible cohort to include a catch-up programme for infants aged less than six months entering their first RSV season. As of September 2025, no RSV maternal vaccine or older adult immunisation programme is in place.
- A review of nationally-funded immunisation programmes against RSV among EU/EEA countries and the UK was carried out, with the following summarising the funding arrangements as of 19 November 2025:
  - Twenty-two countries, including Ireland, have publicly-funded immunisation programmes against RSV for the general infant population, with differences noted between the programmes:
    - Seventeen countries, including Ireland, fund nirsevimab for those born during the RSV season, of which 15 also provide a catch-up for infants born outside the RSV season, with countries differing with regard to the eligibility criteria for the catch-up cohort.

- Twelve countries fund the maternal vaccine either as an alternative to nirsevimab (Cyprus, Belgium, France, Italy, Liechtenstein, Luxembourg) or as their only option (Denmark, Greece, Poland, Romania, Slovenia and the UK). Eight countries (Cyprus, Czech Republic, Belgium, France, Greece, Denmark, Liechtenstein and Luxembourg) restrict eligibility based on the expected due date while two (Slovenia and the UK) offer year-round vaccination. No such eligibility information was identified for Italy or Romania. The countries also differ with respect to the recommended timing of maternal vaccination.

- Eight countries (Belgium, Cyprus, Denmark, France, Germany, Greece, Poland and the UK) and the Italian region of Sicily, were identified as funding RSV vaccination for older adults. The programmes differ in terms of the RSV vaccine(s) offered and the population eligible for vaccination:

  - Two programmes have age-based criteria only, with Poland funding vaccination for all those aged 65 years and older and the UK funding vaccination for those turning 75 years (with an additional one-year catch-up for those aged 75 to 79 years in 2024).

  - Five programmes fund vaccination for all those aged 75 years (Sicily) or 75 years and older (Cyprus, France, Germany, Greece) in addition to having risk-based funding for those aged either 60 years and older (Cyprus, Germany, Greece, Sicily) or 65 years and older (France), with differences noted between programmes in terms of their risk-based criteria (Cyprus: chronic disease or residing in a nursing home; France: chronic respiratory or cardiac disease; Germany: underlying disease or residing in a nursing home; Greece: chronic disease; Sicily: health conditions or residing in a long-term care facility (LTCF)).

- Two programmes fund vaccination only for those at increased risk of severe disease, specifically Denmark (aged ≥60 years with COPD) and Belgium (aged ≥65 years who are residing in a LTCF or who are otherwise classified at increased risk).

- It is likely that there will continue to be updates to national practices for the 2025/26 RSV season and subsequent seasons, as further evidence becomes available for the authorised interventions and given the number of products in development.

2.1 Introduction

The purpose of this chapter is to describe forms of immunisation authorised for use in Ireland, to protect infants and older adults against respiratory syncytial virus (RSV). This chapter provides a brief background of RSV's potential as a pathogen to cause disease, with further detail provided in Chapter 3 (burden of disease). This chapter also provides a brief overview of the current treatment and prevention of RSV in Ireland, as well as a summary of the latest international practice with respect to the immunisation of infants and older adults against RSV in EU/EEA countries and the UK. This chapter can be considered as an update to the corresponding chapters in HIQA's *Rapid HTA of immunisation against respiratory syncytial virus (RSV) in Ireland*, published in August 2024.[10] A more in-depth description of the pathology of RSV can be found in Chapter 2 of the previously published rapid HTA.

2.2 Pathogen and disease

RSV is a common pathogen and major contributor to lower respiratory tract disease (LRTD) in children and older adults. RSV is a negative sense, single-stranded ribonucleic acid (RNA) virus belonging to the *Orthopneumovirus* genus of the family *Pneumoviridae*.[13] RSV has one serotype with two major antigenic subgroups, A and B, with additional antigenic variability within RSV A and RSV B. This antigenic variability (that is differences in proteins expressed by the virus subgroups) plays a significant role in the virus' potential to cause disease and evade the immune system.[3] Both RSV subgroups may co-circulate during a season, alternating in predominance. A systematic review of the global distribution of RSV A and B infections from 2022 found that RSV A has been the predominant strain in most years, but regional and seasonal differences are common.[14] Of the 11 viral proteins encoded by the RSV genome, the glycoprotein F, which is involved in fusion of the viral envelope with the host cell membrane, is highly conserved across RSV A and B subgroups.[3] As a result, glycoprotein F is the focus of existing pharmaceutical interventions against RSV.

RSV infection occurs seasonally, typically during the winter months in temperate climates.[1] In Ireland, where RSV has been a notifiable disease since 2012, the RSV season typically lasts about six months, running from approximately

September/October through February/March.[15] RSV is a highly contagious pathogen, with an estimated basic reproductive number of 3.0.[16] It is transmitted through contact with aerosolised viral particles generated through coughing and sneezing, or from contaminated surfaces. The incubation period for RSV ranges from four to seven days.[3] Infected individuals remain contagious as long as the virus is being shed, with differences in the duration of the infectious period depending on age, severity of infection and health status. In general, infants shed the virus for up to 14 days in mild infections; however, the period during which virus is shed can be extended for up to 3 to 4 weeks for young infants with severe infection or people with compromised immune systems. Infants typically experience mild to moderate nasal congestion and low-grade fever within a few days of exposure, followed by a productive cough. Viral bronchiolitis is one of the most common viral illnesses that occurs in infants as a result of RSV infection. In older adults, the symptom profile is similar to that seen in infants, although there is increased likelihood of lower respiratory tract involvement.[3]

2.3 Treatment

In healthy individuals, RSV typically presents as a self-limiting disease. Most symptoms of RSV are mild, such as a runny nose, coughing and sneezing. People usually recover within 2 to 3 weeks without treatment or the need to see a GP.[17] Hospitalisation may be necessary in more severe cases, or where dehydration or serious secondary infection is suspected. Additional oxygen,[15] and or intravenous (IV) fluids,[18] may be required in such instances, while severe cases may also require mechanical ventilation.[18]

In Ireland, there are currently no antivirals authorised for the treatment of LRTD caused by RSV. As such, the mainstay of management focuses on infection prevention and supportive therapy.[17, 19]

2.4 Prevention

To reduce transmission of RSV, measures such as maintaining good hand and respiratory hygiene are encouraged, and those who suspect they may have RSV are advised to isolate at home if they are symptomatic or feel unwell.[17] In a hospital setting, additional preventive measures could include avoiding overcrowding on wards, managing RSV-positive patients in the same ward, ensuring appropriate infection control measures are followed by staff, and restricting visiting where necessary.[15]

2.4.1 Immunisation for prevention of severe RSV disease

Since October 2022, a number of pharmaceutical interventions have been authorised by the European Medicines Agency (EMA) for the prevention of RSV-associated LRTD in infants and older adults in the general population. These interventions are described in Table 2.1.

As of October 2025, two interventions are authorised for the immunisation of infants in the general population during their first RSV season: a maternal vaccine RSVpreF (Abrysvo®)[7] which was authorised in August 2023 for the passive protection of infants from birth through six months of age via maternal vaccination, and the extended half-life monoclonal antibody (EHL-mAb) nirsevimab (Beyfortus®)[6] which was authorised in October 2022. A second EHL-mAb, clesrovimab (Enflonsia®), received a positive recommendation for authorisation in September 2025.[20] Considering specifically the subset of infants and children aged up to two years at high risk of serious RSV-associated LRTD, the short-acting monoclonal antibody palivizumab (Synagis®) has been authorised by the EMA since 1999,[5] with nirsevimab also authorised for this cohort since June 2024.[6] This subset includes those requiring treatment for bronchopulmonary dysplasia, having haemodynamically-significant congenital heart disease, or who were born at 35 weeks' gestation or less and who are aged less than six months at the onset of the RSV season.[10]

Considering the target adult population in this HTA, that is adults aged 65 years and older, as of October 2025, there are three vaccines authorised by the EMA for the active immunisation of this population: RSVpreF (Abrysvo®),[7] RSVPreF3 (Arexvy®),[8] and the RSV mRNA vaccine (mRESVIA®).[9] RSVpreF is indicated for those aged 18 years and older and RSVpreF3 and the mRNA vaccine are authorised for adults aged 60 years and older. RSVpreF3 is additionally authorised for those aged 50 to 59 years at increased risk of severe disease.

Table 2.1 Summary of the key characteristics of medicinal products authorised or recommended for authorisation by the EMA for the immunisation of infants and older adults in the general population against RSV, as of 17 October 2025

Trade name	Beyfortus®[6]	Enflonsia®[21]	Abrysvo®[7, 22]	Arexvy®[8]	mRESVIA®[9]
Active substance	Nirsevimab (extended half-life monoclonal antibody)	Clesrovimab (extended half-life monoclonal antibody)	RSVpreF (recombinant, bivalent vaccine)	RSVPreF3 (recombinant, adjuvanted vaccine)	Single-stranded 5' capped mRNA encoding the RSV glycoprotein F stabilised in the prefusion conformation (mRNA vaccine)
Marketing authorisation holder	Sanofi Winthrop Industrie+	Merck Sharp & Dohme	Pfizer Europe MA EEIG	GlaxoSmithKline Biologicals SA	Moderna Biotech Spain SL
EMA marketing authorisation	31 October 2022	N/A~	23 August 2023	06 June 2023	27 June 2024
Therapeutic indication and dose	Indicated for the prevention of LRTD caused by RSV in: ▪ neonates and infants during their first RSV season as a single IM dose of: – 50 mg (0.5mL) if body weight <5Kg – 100mg (1mL) for infants with body weight ≥5Kg ▪ children up to 24 months of age who	Indicated for the prevention of LRTD caused by RSV in: ▪ neonates and infants during their first RSV season	Indicated as a single IM injection of 0.5mL for: ▪ passive protection against LRTD caused by RSV in infants from birth through to six months of age following maternal immunisation during pregnancy ▪ active immunisation of adults aged ≥ 18 years for the prevention of LRTD caused by RSV.	Indicated as a single IM injection of 0.5mL for active immunisation for the prevention of LRTD caused by RSV in: ▪ adults aged ≥ 60 years ▪ adults aged 50 through 59 years of age at increased risk for RSV disease.	Indicated as a single IM injection of 0.5mL for: ▪ active immunisation for prevention of LRTD caused by RSV in adults aged ≥ 60 years.

	remain vulnerable to severe RSV disease through their second RSV season as a single IM dose of 200mg given as 2 x 100mg injections.				
Formulation	▪ Pre-filled syringe containing one dose of either: – 50mg nirsevimab[¥] in 0.5mL (100mg/mL); or – 100mg nirsevimab[¥] in 1mL (100mg/mL)	▪ Pre-filled syringe containing: – 105mg clesrovimab[*] in 0.7mL	▪ After reconstitution, one dose (0.5mL) contains: – RSV subgroup A stabilised prefusion F antigen[‡], 60µg – RSV subgroup B stabilised prefusion F antigen[‡], 60µg	▪ After reconstitution, one dose (0.5mL) contains: – RSVPreF3 antigen[‡,§], 120µg.	▪ Pre-filled syringe containing one dose (0.5mL) of: – 50µg of RSV mRNA[±] vaccine (nucleoside modified) encapsulated in lipid nanoparticles.
Contraindications / Special warnings and precautions for use		Hypersensitivity to the active substance or to any of the excipients			
	▪ Serious hypersensitivity reactions have been reported following nirsevimab administration. ▪ Anaphylaxis has also been observed with human immunoglobulin G1 (IgG1) monoclonal antibodies.		▪ RSVpreF has not been studied in pregnant individuals less than 24 weeks of gestation. Since protection of the infant against RSV depends on transfer of maternal antibodies across the placenta, RSVpreF should be administered between weeks 24 and 36 of gestation.		

	Should be given with caution to individuals with thrombocytopenia or any coagulation disorder since bleeding or bruising may occur following an intramuscular administration to these individuals.
Additional monitoring	This medicine is or will be under additional monitoring owing to the fact that it is a new active substance and new biological medicine.[23]

Key: EMA – European Medicines Agency; LRTD – lower respiratory tract disease; mRNA – messenger ribonucleic acid; N/A – not applicable; RSV – respiratory syncytial virus

Notes: ~On 18 September 2025, the Committee for Medicinal Products for Human Use (CHMP) adopted a positive opinion, recommending the granting of a marketing authorisation for the medicinal product Enflonsia. ⁺AstraZeneca AB led on development, and are responsible for the manufacture of nirsevimab (Beyfortus®). Sanofi Winthrop Industrie are responsible for marketing activities and commercialisation of nirsevimab, and, as such, hold the marketing authorisation for nirsevimab in Europe.[6, 24] ¥Human immunoglobulin G1 kappa monoclonal antibody produced in Chinese hamster ovary (CHO) cells by recombinant DNA technology. *Human immunoglobulin G1 kappa (IgG1κ) neutralising monoclonal antibody with a triple amino acid substitution in the Fc region which increases binding to the neonatal Fc receptor leading to an extended serum half-life. ‡Glycoprotein F stabilised in the prefusion conformation. Produced in Chinese hamster ovary cells by recombinant DNA technology. §Adjuvanted with AS01E containing: plant extract Quillaja saponaria Molina, fraction 21, 25µg; and 3-O-desacyl-4'-monophosphoryl lipid A from Salmonella minnesota, 25µg ±Single-stranded 5' capped mRNA encoding the RSV-A glycoprotein F, stabilised in the prefusion conformation.

2.4.2 Co-administration with other vaccines

Information on co-administration of RSV immunisations with other vaccines was obtained from the summary of product characteristics (SmPC) for each product published by the EMA as part of the relevant European Public Assessment Report. This was supplemented by information from published summaries of opinion from the Committee for Medicinal Products for Human Use and information communicated by the marketing authorisation holders.

In each instance where information on concomitant administration with another vaccine was identified, it was specified that separate syringes and different injection sites should be used.

With regard to nirsevimab, no interaction studies have been performed.[6] However, it is considered unlikely that nirsevimab, as a monoclonal antibody, would have direct or indirect significant interaction potential, and it is not expected to interfere with the active immune response to co-administered vaccines. As such, nirsevimab can be given concomitantly with childhood vaccines.[6]

RSVPreF3 can be administered concomitantly with the following inactivated seasonal influenza vaccines: standard dose unadjuvanted, standard dose adjuvanted, and high dose unadjuvanted. Compared with separate administration, numerically lower neutralising titres for RSV A and B and haemagglutination inhibition titres for influenza A and B were observed, although this was not consistent across studies, and the clinical relevance of these findings is unknown.[8]

RSVpreF can be administered concomitantly with:[7]

- seasonal influenza vaccines, either standard dose adjuvanted or high dose unadjuvanted
- COVID-19 mRNA vaccines, with or without high dose unadjuvanted influenza vaccine administered concomitantly.

A minimum interval of two weeks is recommended between administration of RSVpreF and administration of a tetanus, diphtheria and acellular pertussis (Tdap) vaccine. A lower immune response to the pertussis components was noted on co-administration compared with separate administration; however, the clinical relevance of this finding is unknown.[7]

With regard to the RSV mRNA vaccine, the SmPC states that no interaction studies with other medicinal products have been performed, and concomitant administration of this vaccine with other vaccines has not been studied.[9] Based on data from co-administration studies that were presented to the US Advisory Committee on Immunization Practices (ACIP), the updated 2024 ACIP recommendations suggest

that administration of RSV vaccines with other adult vaccines during the same visit is acceptable.[25]

2.4.3 Strategies for prevention of RSV in Ireland

NIAC recommendations for immunisation against RSV in infants

In October 2023, the National Immunisation Advisory Committee (NIAC) published recommendations for the passive immunisation of all infants against RSV during their first RSV season.[26] It was noted that both nirsevimab and the maternal vaccine (RSVpreF) had acceptable safety and efficacy profiles, with no preferential recommendation regarding the choice of RSV passive immunisation strategy. However, NIAC did recommend that nirsevimab should replace palivizumab for infants and children aged between 1 to 2 years who were eligible to receive palivizumab.

In April 2024, NIAC published updated recommendations in relation to the immunisation of infants with nirsevimab for the 2024/25 RSV season and summarised these in Chapter 18a (updated in July 2024) of the NIAC Immunisation Guidelines.[27, 28]

In this update, they recommended the passive immunisation with nirsevimab of:

- all infants born during the RSV season, preferably prior to discharge home from a maternity hospital
- high-risk infants (eligible for palivizumab) aged 12 months or younger at the start of their first RSV season.

NIAC advised that these two groups of infants should be prioritised for nirsevimab in the event of short supply or programmatic limitations. They also advised that nirsevimab administration take place prior to the start of the RSV season for all recommended groups born outside of the RSV season; additional risk groups recommended to receive passive immunisation with nirsevimab included:[27, 28]

- infants aged six months or younger at the start of the RSV season
- all ex-preterm infants aged younger than 24 months with chronic lung disease in their second RSV season
- infants who will be severely immunocompromised during the RSV season, in consultation with their treating specialist
- newborns with prolonged hospitalisation from birth, administered before discharge from hospital if being discharged during or shortly before the RSV season.

NIAC advised that if no catch-up programme was planned, an earlier start to the programme should be considered to capture those who will be aged under three months at the peak of the RSV season with the definitive end date for the programme determined by levels of circulating RSV.[27, 28]

NIAC recommendations for immunisation against RSV in older adults

In October 2023, NIAC recommended vaccination for adults aged 65 years or older with either RSVPreF3 or RSVpreF, advising that vaccine administration should aim to take place prior to the anticipated start of the RSV season, where possible. The groups to be prioritised, in case of limited vaccine supply, were those at high risk of RSV disease, namely:

- older adults of more advanced age
- those with significant comorbidities
- older adults living in long-term care facilities.

Of note, these recommendations were published prior to the EMA issuing marketing authorisation for the RSV mRNA vaccine (mRESVIA®) in August 2024.[26]

In October 2025, NIAC published updated recommendations for this cohort which considered updated epidemiology and pharmacovigilance data related to these vaccines.[29] NIAC considered the vaccines to be generally well tolerated, with some uncertainty over potential serious adverse events like Guillain-Barré Syndrome, although it was noted that these events remain rare. NIAC also advised that uncertainty around how long protection lasts supports vaccinating individuals just in advance of the age of highest likely risk. Given the potential for very rare adverse events and the uncertainty about duration of protection and effect of revaccination, NIAC concluded that the greatest benefits of RSV vaccines are expected in the oldest adults and those with risk factors, due to their higher disease burden. For adults aged 60 to 74 years, especially those without risk factors, NIAC noted that the benefits are less clear as the burden of RSV disease in adults increases with increasing age and is highest in those 75 years of age and older. The epidemiology of RSV and the burden of disease in Ireland is explored in Chapter 3 and the clinical efficacy, effectiveness and safety of the RSV vaccines are reviewed in Chapter 4 of this HTA.

The updated NIAC recommendations advise vaccination with either RSVPreF3, RSVpreF, or the RSV mRNA vaccine of:

- older adults aged 75 years or older

- older adults aged 60 to 74 years with any additional risk factors for severe RSV disease
- older adults aged 60 years and older living in long-term care facilities.

NIAC advise that a single dose is recommended as the need for booster doses has not yet been established.

Pathfinder

During the 2024/25 RSV season, the HSE implemented a publicly-funded Pathfinder Programme, which offered immunisation with nirsevimab to all infants born between September 2024 and February 2025.[11] All infants at high-risk of severe RSV disease previously eligible for palivizumab including those born out of RSV season that is, those born between the end of March 2024 and the beginning of September 2024, as well as all children at high risk of RSV disease entering their second season (year two of their life), were also offered nirsevimab.[30] More information regarding the 2024/25 RSV season in Ireland, and preliminary results from the Pathfinder Programme, are provided in Chapter 3. The RSV 2.0 Immunisation Pathfinder Programme is being provided for the 2025/26 RSV season and the eligible cohort has been expanded to include a catch-up for infants aged less than six months entering their first RSV season. The programme also provides for the continued immunisation of children who are severely immunocompromised or ex-preterm with chronic lung disease aged less than 24 months during the RSV season.[31] As of September 2025, no RSV maternal vaccine or older adult immunisation programme is in place.

2.4.4 Strategies for the prevention of RSV internationally

In HIQA's rapid HTA of immunisation against RSV in Ireland,[10] published on 12 August 2024, a review of international practice regarding immunisation of infants and older adults against RSV in EU/EEA countries and the UK was conducted, with searches up to 1 July 2024. The section in this current report provides a summary of nationally-funded immunisation programmes against RSV among countries of the EU/EEA and the UK, as of 19 November 2025.

To gather information on nationally-funded programmes, the websites of ministries of health, state medicines agencies and public health agencies in EU/EEA countries and the UK were searched on 15 September 2025. The search was updated again on the 19 November 2025 after cross checking against a published European Centre for Disease Prevention and Control (ECDC) assessment.[32]

Google Translate and or DeepL Translate professional software were used to obtain translations of non-English sources.[33, 34]

Publicly-funded immunisation against RSV for infants in EU/EEA countries and the UK as of 19 November 2025

As outlined in Table 2.1, there are three forms of immunisation against RSV which are currently authorised or have had a positive recommendation for authorisation in Europe for the general infant population: nirsevimab, authorised in October 2022,[6] clesrovimab, which received a recommendation for authorisation on 18 September 2025[20], and RSVpreF (subsequently referred to in the context of maternal vaccination as the maternal vaccine), authorised in August 2023.[7] Table 2.2 lists the relevant countries for which information was identified with respect to national immunisation programmes against RSV for the general infant population, including the cohorts identified as eligible to receive immunisation against RSV.

As of 19 November 2025, 17 countries, including Ireland, were identified as funding (or reimbursing) nirsevimab as part of an immunisation programme against RSV.[11, 29, 35-49] Of these 17 countries, all provide immunisation for those born during the RSV season, and all except Greece and Sweden include some degree of a catch-up programme. Thirteen countries offer a catch-up for all infants[29, 32, 35, 37, 42, 50-52] or those aged six months or less[40, 45, 53, 54] in the general population entering their first RSV season. In Portugal, catch-up before the season is limited to infants born since the previous June,[55] while in Finland, infants in risk groups are prioritised and it is stipulated that administration of nirsevimab to healthy infants born during the season along with a catch-up for those under three months old is dependent on obtaining sufficient stock.[36]

Twelve countries were identified as funding the maternal vaccination of pregnant women to passively protect infants against RSV.[29, 32, 37, 40, 52, 56-62] Of these countries, six (Denmark, Greece, Poland, Romania, Slovenia and UK) offer only the maternal vaccine, and do not fund a nirsevimab programme,[32, 56-59, 61] while six countries (Cyprus, Belgium, France, Italy, Liechtenstein, Luxembourg) fund both the maternal vaccine and nirsevimab as alternate strategies.[29, 37, 40, 47, 52, 60, 62] Slovenia and UK offer year-round RSV maternal vaccination programmes.[56, 57] Cyprus, Greece, Denmark, France, Luxembourg are funding the maternal vaccine for those with an expected due date during the RSV season[32, 37, 40, 59, 63] while Belgium specify it is for those with an expected due date between September and March.[29] Liechtenstein is funding administration of the vaccine between October and February, for those with an expected due date is before the end of March.[52] Italy and Romania are noted to include the maternal vaccine in the national vaccination schedule from the 2025/26 RSV season onwards, but no further details were identified.[32, 60] The countries differ with respect to the recommended timing of the maternal vaccination. While in Poland and Slovenia vaccination is recommended as per the EMA authorised timing between 24 to 36 weeks' gestation, other countries

recommend a shorter administration window. In Belgium, vaccination is recommended between 28 and 36 weeks' gestation; in Cyprus, Denmark, France, Greece, Liechtenstein and Luxembourg vaccination is recommended between 32 and 36 weeks' gestation; and in the UK vaccination is recommended from 28 weeks' gestation (with no upper limit noted).

As listed in Table 2.2, several countries specify that infants and or children aged less than two years of age considered to be at increased risk of RSV-related disease are eligible to receive nirsevimab as part of their respective immunisation programmes. The eligible cohorts differed across countries. Conditions that categorise an infant as of increased risk (where identified) are included in appendix A2.1. In addition, as described in the rapid HTA published in August 2024, it is possible that other countries continue to fund palivizumab for children up to two years of age at high risk of severe RSV-related disease, and or may fund nirsevimab for this cohort, but do so outside of a specific immunisation programme.

Table 2.2 Summary of nationally-funded practices with respect to immunisation against RSV in the general infant population aged less than two years in EU/EEA countries and the UK, as of 19 November 2025

Country	Nirsevimab	Maternal Vaccine	Additional notes
Austria[35, 64]	▪ Born during RSV season ▪ Catch-up for those born April through September (fromFebruary 2025) ▪ Children at risk age <24 months	X	Newborns were immunised starting from December 2024. A catch-up was delayed due to stock availability. From 30 January 2025, infants <5Kg who did not receive prophylaxis after birth were also eligible (usually those born from November 2024 onwards). Infants >5 Kg (who require a higher dosage) were eligible to receive prophylaxis from mid-February 2025.
Belgium[29, 65]	▪ Born during RSV season ▪ Catch-up for those born from 19 February 2025 through September 2025 administered before start of first RSV season ▪ Premature infants residing at NICU (<13 months old and born before February 19, 2025) that did not previously receive nirsevimab ▪ Children at risk aged <24 months*	28-36 weeks' gestation Due date between September and March	Nirsevimab reimbursed for a trial period of two years (RSV seasons 2024/25 and 2025/26) Catch-up during the previous 2024/25 season included infants born from April 2024 through September 2024. The maternal vaccine is almost fully reimbursed as of 01 January 25. The patient cost is €12 or €8 if eligible for increased reimbursement. If the maternal vaccine is chosen, the newborn is generally^ no longer eligible for reimbursement of nirsevimab.
Cyprus[32, 47, 62]	▪ Born during RSV season ▪ Catch-up for infants entering their first RSV season	32-36 weeks' gestation Due date during season	RSV vaccine is for pregnant women is listed in the National Vaccination Programme for adults from 2024.

			The Cyprus Health Ministry announced the inclusion of nirsevimab in the state health system on the 3 October 2025.
Czech Republic[32, 49]	▪ Born during RSV season ▪ Catch-up for infants entering their first RSV season	X	The Czechia State Institute for Drug Control had a positive decision for reimbursement of nirsevimab the Czechia State Institute for Drug Control on 30th April 2025 with a positive decision for reimbursement of nirsevimab.
Denmark[58, 63, 66]	X	32-36 weeks' gestation Due date between July and March	The maternal vaccine has been funded from October 2025. On 29 January 2025, the Danish Medicines Council previously recommended nirsevimab for premature infants and infants at increased risk. However the manufacturer would not supply nirsevimab in Denmark as it was not recommended for the majority of infants.
Finland[36, 67, 68]	▪ Born during RSV season ▪ Catch up for those <3 months old during RSV season ▪ <12 months with increased risk*	X	It was noted that for the 2025/26 season nirsevimab is prioritised for infants <12 months who are in a risk group. Only if stock availability is sufficient, will it also be administered to infants born during the season and infants <3 months of age at the beginning of the season.
France[37, 69]	▪ Born from 1 September 2025 until the end of the RSV season ▪ Catch-up in September for children born between February and August 2025. ▪ Children at risk aged <24 months	32-36 weeks' gestation Due date during season	Catch-up during the previous 2024/25 season included infants born those born after 1 January 2024. Nirsevimab is free in the maternity ward. If collected in a pharmacy the cost is 30% reimbursed by national health insurance and the remainder

			may be covered by supplementary health insurance companies.
Germany[38, 50]	▪ Born during RSV season ▪ Catch-up for infants born from April through September (<6 months) ▪ In children with known risk factors, the use of palivizumab or nirsevimab can be decided on an individual basis.	X	Since June 2024, the Standing Committee on Vaccination (STIKO) has recommended a single dose of nirsevimab before or in their 1st RSV season for the included cohorts. Immunisations are covered by all health insurance providers if recommended by the STIKO.
Greece[48, 59, 70]	▪ Born during RSV season ▪ Infants aged <6 months with risk* for severe RSV infection and a mother who was not vaccinated ▪ Infants and children aged 6 to <24 months with risk* for severe RSV infection	Between 32-36+6 weeks' gestation Due date between October and March	The maternal vaccine has been funded from March 2025. It is noted that revaccination may be necessary in subsequent pregnancies. Newborns whose mothers were not vaccinated against RSV during pregnancy are eligible for nirsevimab from October 2025.
Iceland[46, 54]	▪ All infants <6 months from October 2025 until the end of the winter	X	Nirsevimab to be offered for the 2025/26 and 2026/27 seasons. At the end of the contract for the purchase of the antibody in 2027, the impact will be assessed.
Ireland[11, 30, 53]	▪ Born during RSV season ▪ Catch-up for babies ≤6 months at the start of RSV season ▪ <24 months previously eligible for palivizumab	X	The second year of Pathfinder expanded the eligible cohort to include a catch-up with appointments available during September until the first week in October 2025. Additional clinics offered from 17 November to 12 December 2025.
Italy[43, 51, 60, 71]	▪ Born between October and March ▪ Catch-up for those born from April 2025 to September 2025 to be administered in October 2025. ▪ <24 months with risk factors.	From the 2025/26 RSV season included in the national vaccination schedule	During the 2024/25 season nirsevimab was offered to infants born from November 2024. Catch-up during the previous 2024/25 season included infants born those born up to 100 days before November 2024.

			The Minister of Health advised that two regions, Sicily and Molise, have already initiated maternal vaccination on their own initiative, and from the 2025/26 RSV season the maternal vaccine will be included in the national vaccination schedule.
Liechtenstein (39, 52, 72)	▪ Born during RSV season ▪ Catch-up for infants born from April through September (<6 months) ▪ ≤24 months beginning their second RSV season with increased risk*	Between 32-36 weeks' gestation Administration between October and February, if due date is before the end of March.	Liechtenstein follows the Swiss immunisation schedule. The maternal vaccine was approved for reimbursement from July 2025.
Luxembourg(40)	▪ Born during RSV season ▪ Catch-up for those <6 months old during the RSV season ▪ <24 months with increased risk*	32-36 week's gestation Due date during season	
The Netherlands (45, 73)	▪ Born from 8 September 2025 to the end of the RSV season ▪ Catch-up for babies born April 2025 in September 2025 before the start of the RSV season	X	Funded immunisation with nirsevimab began in the 2025/26 season. From 2026 onwards, it is intended to offer passive immunisation to all infants <12 months at the start of the RSV season
Poland(32, 61)	X	24-36 weeks' gestation Due date during season	The maternal vaccine is free since August 2025
Portugal(41, 55, 74)	▪ Born between 16 September 2025 and 31 March 2026 ▪ Catch-up for children born between 1 June and 15 September 2025.	X	During the 2024/25 season nirsevimab was offered to infants born from August 2024 through March 2025. Pre-term infants born from January 2024 through July 2024 were eligible during the 2024/25 season.

	▪ <24 months with increased risk* entering their first or second RSV season		Pre-term infants born from April 1 and May 31, 2025 were eligible during the 2025/26 season or born between 1 January and 31 March 2025, if not been previously immunised. Funding was expanded during the 2025/26 season to include a catch-up.
Romania[32]	X	Details of the programme were not identified.	The ECDC reported in November 2025 that Romania has implemented a fully funded RSV vaccination for pregnant women. The report advises that the timing of the programme (year-round or seasonal) is still under discussion. Information on the recommended gestational timing of vaccination during pregnancy was not provided.
Slovenia[57]	X	24-36 weeks' gestation Year-round	The maternal vaccine is free since September 2024 via compulsory health insurance to pregnant women
Spain [42, 75, 76]	In order of priority: ▪ All premature babies (<35 wGA) aged <12 months at the start of the RSV season ▪ Children aged <24 months at increased risk* ▪ All children born from April 2024 through March 2025, beginning in October 2024 (to be repeated for 2025/26)	X	
Sweden[44, 77]	▪ Born from 10 September 2025 during the RSV season	X	Funded immunisation with nirsevimab began in the 2025/26 season.

United Kingdom [56]	X	≥28 weeks' gestation Year-round	The maternal vaccine is free since September 2024 Although not funded for healthy infants, the Joint Committee on Vaccination and Immunisation advised on 1st February 2023 that palivizumab should be replaced by nirsevimab for the currently eligible cohort.

Key: NICU – Neonatal Intensive Care Unit; RSV – respiratory syncytial virus; wGA – weeks' gestational age**.**

Note: RSV season can vary yearly in different countries. It commonly circulates in Europe from September/October to February/March.

*Conditions that categorise an infant as of increased risk (where identified) are included in appendix 2.1. ^Administration of nirsevimab to infants born from vaccinated mothers could be considered in cases of infants with sufficiently increased risk for severe RSV disease, infants from vaccinated mothers born within the two weeks following administration, pregnant women expected to have an inadequate immune response to vaccination or decreased transplacental antibody transfer and infants who have undergone cardiopulmonary bypass or neonatal blood exchange leading to loss of maternal antibodies.

WHO position paper on immunisation to protect infants against RSV

Recommendations on the use of maternal RSV vaccines and extended half-life RSV monoclonal antibodies to prevent severe RSV disease in infants were issued by the World Health Organization (WHO) Strategic Advisory Group of Experts on immunisation in September 2024.[78] Following the meeting, a position paper on immunisation to protect infants against RSV was published in May 2025.[79] While the WHO recommends that all countries introduce products for the prevention of severe RSV disease in young infants, it notes that decisions to use maternal RSV vaccination and or long-acting mAbs should consider factors such as cost, cost effectiveness, financing, supply, anticipated coverage and feasibility of implementation within the existing health system. For countries deciding to use the maternal vaccine as the primary preventive strategy, the WHO recommends administering a single dose of RSVpreF in the third trimester of pregnancy, as defined in the local context (≥28 weeks' gestation in most settings). No upper limit of week of gestation for vaccination is recommended except for women in active labour. It advises that although a year-round approach is likely to enhance programmatic feasibility, in countries with documented clear and consistent seasonal peaks in RSV circulation, a seasonal approach can be considered on the basis of programmatic and cost considerations. For countries deciding to use an extended half-life monoclonal antibody as the primary preventive strategy, WHO recommends a single dose at birth, or at the earliest opportunity thereafter if year-round administration is adopted. In a seasonal approach, administration of a single dose of an extended half-life monoclonal antibody is recommended for infants and should begin shortly before the start of the RSV season, as well as at birth or the earliest opportunity thereafter for infants born during the RSV season. While noting that the greatest impact in preventing severe RSV disease will be achieved by administering the monoclonal antibody to infants aged less than six months, the WHO advises that there is still potential benefit among infants up to 12 months of age.[79]

Publicly-funded immunisation against RSV in older adults in EU/EEA countries and the UK as of 19 November 2025

Considering the target population for this HTA (adults aged 65 years and older), as outlined in Section 2.4.1, as of 15 September 2025 there are three available vaccines authorised for the prevention of LRTD caused by RSV: RSVPreF3 (Arexvy®),[8] RSVpreF (Abrysvo®),[7] and Respiratory Syncytial Virus mRNA vaccine (mRESVIA®).[9].

As listed in Table 2.3, as of 19 November 2025, eight countries (Belgium,[80] Cyprus,[62] Denmark,[81] France,[82] Germany[83], Greece,[84] Poland[61] and the UK[56]) and the region of Sicily in Italy were identified to publicly fund RSV vaccination for older adults, with two of these (Belgium and Poland) newly offering vaccination for

the 2025/2026 season. While three countries (France, Germany, Greece) fund vaccination with any of the three authorised vaccines, information for Poland and the Italian region of Sicily suggest that only RSVpreF or RSVPreF3 are funded, although it is noted that the Sicilian decree was published prior to the authorisation of the RSV mRNA vaccine. Two countries (Denmark and Belgium) fund RSVPreF3 while the UK funds only RSVpreF. Information with regard to which RSV vaccines are funded in Cyprus was not identified.

The cohorts eligible to receive RSV vaccination differed across the countries, with only two countries (Poland and the UK) using age-based criteria only. Poland is the only country identified as funding vaccination for the general population aged 65 years and older. In the UK, since 1 September 2024, free RSV vaccination with RSVpreF vaccine is offered to adults turning 75 years old.[56] A once-off catch-up campaign for those already aged 75 to 79 years old on 1 September 2024 was undertaken for the first year of the programme.

Five of the programmes offer vaccination to all those aged 75 years (Sicily) or 75 years and older (Cyprus, France, Germany, Greece) in addition to providing funding for those with risk factors for severe disease aged 60 years and older (Cyprus, Germany, Greece, Sicily) or 65 years and older (France). Differences were noted between countries in terms of these risk factors. For example, France limits eligibility to those with chronic respiratory or cardiac disease while Cyprus includes those with chronic disease or residing in a nursing home; Germany includes those with underlying disease or residing in a nursing home; Sicily includes those with health conditions or residing in a long-term care facility; and Greece includes those with chronic disease.

Two countries fund vaccination only for subsets of the older adult population with specific risk factors. That is, Denmark funds vaccination for individuals aged 60 years or older with chronic obstructive pulmonary disease (COPD),[81] while Belgium funds vaccination for adults aged 65 years and older who are residing in a LTCF or who are classified as at increased risk.[80]

The focus of this section has been countries in which nationally-funded immunisation programmes for RSV vaccination were identified. There may be additional countries in which RSV vaccination may be available on an individual basis at full or partial reimbursement, such as in the Czech Republic, where partial reimbursement is available for individuals through health insurance,[85, 86] or where vaccination is additionally partly funded for another group (for example, Poland where a 50% discount is available on the cost of these vaccines for those aged 60-64 years).[61]

Table 2.3 Summary of nationally funded practices with respect to immunisation against RSV in older adults in EU/EEA countries and the UK, as of 19 November 2025

Country	Eligible groups	Conditions classified as increasing risk	RSVPreF (Abrysvo®)	RSVPreF3 (Arexvy®)	RSV mRNA vaccine (mRESVIA®)
Belgium[80]	▪ ≥65 years and residing in a LTCF ▪ ≥65 years with increased risk	Chronic respiratory disease, chronic heart failure with NYHA class II – IV, chronic kidney disease with KDOQI score 3-5, diabetes, obesity (with body mass index ≥ 30) and immunodeficiency due to disease or treatment.	X	✓	X
Cyprus[62]	▪ ≥75 years ▪ ≥60 years with increased risk or living in a nursing home	Chronic cardiovascular disease (e.g., heart failure, coronary artery disease, or congenital heart disease, excluding isolated arterial hypertension). Chronic lung or respiratory disease (e.g., COPD, emphysema, asthma, interstitial lung disease, or cystic fibrosis). End-stage renal disease or dependence on dialysis or other renal replacement therapy. Diabetes mellitus complicated by chronic kidney disease, neuropathy, retinopathy, or other end-organ damage or requiring treatment with insulin or more than 2 antidiabetic tablets. Neurological or neuromuscular diseases causing impaired airway clearance or respiratory muscles weakness (e.g., dysphagia after stroke, amyotrophic lateral sclerosis, or muscular dystrophy). Chronic liver disease (e.g. cirrhosis). Chronic hematologic conditions (e.g. sickle cell disease or thalassemia). Severe obesity (body mass index ≥40 kg/m2). Moderate or severe immunodeficiency. Nursing home residence.	*	*	*
Denmark[81]	▪ ≥60 years with COPD	N/A	X	✓	X
France[82]	▪ ≥75 years ▪ ≥65 years with increased risk	Chronic respiratory pathologies (particularly COPD) or cardiac pathologies (particularly heart failure) likely to decompensate during an RSV infection.	✓	✓	✓§
Germany[83, 87]	▪ ≥75 years ▪ ≥60 with increased risk or living in a nursing home	Serious underlying disease including severe forms of chronic respiratory diseases, chronic cardiovascular and kidney diseases, chronic neurological and neuromuscular diseases, hemato-oncological diseases, diabetes mellitus (with complications) and severe congenital or acquired immunodeficiency.	✓	✓	✓

Greece[84, 88]	▪ ≥75 years ▪ 60-74 with increased risk	Chronic serious cardiovascular diseases; chronic respiratory diseases; chronic renal failure stage 4 or 5 (on dialysis); diabetes mellitus with target organ damage; severe morbid obesity with BMI ≥40Kg/m2; moderate or severe immunosuppression; neurological or neuromuscular conditions that affect swallowing or the cough reflex, or cause weakness of the respiratory muscles; chronic liver failure; severe hemoglobinopathies; residing in institutions for the chronically ill or elderly care units; another chronic disease or condition where, in the judgement of the treating physician, RSV may cause serious illness or complications.	✓	✓	✓
Italy (Region of Sicily)[89-91]	▪ 75 years ▪ ≥60 with increased risk	COPD and bronchial asthma, following a risk assessment by a health professional; previous serious lower respiratory tract infections, caused by an agent other than RSV; type I or type II diabetes mellitus, subject to risk assessment by a health professional; cardiovascular disease, subject to risk assessment by a health professional; congenial/acquired immunodeficiency or expecting immunosuppressive therapy; chronic renal failure and on dialysis; living in long-term care facilities for people with physical and or mental disabilities.	✓	✓	NI~
Poland[61]	▪ ≥65 years	N/A	✓	✓	X
United Kingdom[56]	▪ 75 years ▪ Catch up 75-79 years¥	N/A	✓	X	X

Key: BMI – body mass index; COPD – chronic obstructive pulmonary disease; KDOQI – kidney disease outcomes quality initiative; N/A – not applicable; NYHA – New York Heart Association; NI – not identified; RSV – respiratory syncytial virus

Note: Reimbursed in Denmark, France, Italy and Greece; covered by health insurance providers in Germany (as recommended by STIKO Ständigen Impfkommission [Standing Committee on Vaccination]) and free in the United Kingdom for eligible groups. Poland introduced funding of the older adult vaccine for those over 65 from August 2025 and with a 50% discount for those aged 60-64 years.

¥A one-off catch-up campaign for those already aged 75 to 79 years old on 1 September 2024 for the first year of the programme.

§Approved for reimbursement in October 2024.

~Decree by the Health Councillor was published on 11 June 2024, prior to the authorisation of the RSV mRNA vaccine in Europe.

* Information on which specific RSV vaccines were funded was not obtained.

2.5 Discussion

RSV is a highly transmissible respiratory infection.[15] Certain populations are at a higher risk of LRTD and associated complications following RSV infection, including infants, young children and older adults, and those with compromised immune systems or with certain co-morbidities of the heart and lungs.[15] Given the seasonal nature of RSV transmission, and potential for co-infection with other respiratory diseases, the seasonal burden on healthcare systems can be considerable.[92, 93] Immunisation against RSV may reduce the risk and or severity of infection and transmission, thereby potentially reducing the annual seasonal burden on the healthcare system.

Until recently, preventive interventions to reduce the burden of RSV were limited to palivizumab for infants and children up to two years at increased risk of severe disease. Since 2022, several new preventive interventions have been authorised that aim to reduce the burden of RSV in the general infant and older adult populations. As such, overall, international practice with respect to the implementation of immunisation programmes against RSV for infants and older adults is a rapidly changing area. One expected change reported by the American Academy of Pediatrics is the discontinuation of palivizumab in the US from 31 December 2025.[94] The decision by Swedish Orphan Biovitrum AB (the rights holder to Synagis® in the US) to voluntarily remove the product from the market follows the approval of new forms of RSV immunisation. The previous review of international practice, from 1 July 2024, which was conducted as part of the rapid HTA, identified five EU/EEA countries and the UK as having publicly-funded immunisation programmes for the general population of infants (that is, either providing nirsevimab or a maternal vaccine) planned or in place for the 2024/25 RSV season.[10] As of 19 November 2025, this number had risen to 22 countries offering at least one type of immunisation for the general population of infants, with six of these countries offering both nirsevimab and the maternal vaccine. Similarly, the number of countries identified as providing a funded programme of immunisation against RSV for older adults for the 2024/25 RSV season increased between 1 July 2024 and 19 November 2025. Whereas in the previous review of international practice,[10] the UK was the only country identified to have planned a publicly-funded formal immunisation programme, this updated review identified that eight additional EU/EEA countries and the region of Sicily in Italy are funding programmes of vaccination of older adults against RSV based on specific age and or risk-based criteria. International polices are changing rapidly and it is likely that there will continue to be updates to national practices for the 2025/26 RSV season and subsequent seasons, as further evidence becomes available for the authorised interventions and given the number of products in development.

Evidence relating to the efficacy, effectiveness and safety of these interventions are discussed in Chapter 4, while the cost of alternate strategies for the immunisation of infants and older adults against RSV are explored in Chapter 6.

3 Epidemiology and burden of disease

Key Points

- RSV is a common seasonal virus and a leading cause of acute respiratory infections in both young children and older adults. RSV is a self-limiting disease in otherwise healthy individuals. Groups vulnerable to serious complications include infants, young children and older adults. Protective immunity from prior exposure to RSV is not lifelong and therefore a large proportion of the population is susceptible to RSV infection each season.
- RSV has been a notifiable disease in Ireland since 2012. RSV incidence data were sourced from the Health Protection Surveillance Centre in Ireland for RSV seasons from 2018/19 to 2024/25 inclusive. RSV-associated hospital utilisation data were sourced from the Hospital In-Patient Enquiry (HIPE) system for 2018 to Q1 2025 inclusive. Acute bronchiolitis data were also sourced from HIPE for those aged less than two years for the same period.
- The observed RSV-related morbidity and mortality are in the context of the HSE's Pathfinder Programme which offered immunisation with nirsevimab to all infants born in the six-month period between 1 September 2024 and 28 February 2025. This immunisation was also extended to infants and children up to two years of age at high risk of severe disease who would previously have been eligible for palivizumab. The cumulative national uptake rate of the programme for the 2024/25 RSV season was 83%.
- Excluding 2020/21 (due to the influence of the COVID-19 pandemic), HPSC data indicate that for the RSV seasons from 2018/19 to 2024/25, the RSV burden was consistently and substantially higher among those aged less than two years, with this cohort accounting for 41% to 69% of all notified cases each year.
- In children aged less than two years, seasonal rates ranged from:
  - 1,211.8 to 2,225.7 per 100,000 for notified RSV cases
  - 286.6 to 990.6 per 100,000 for RSV-related emergency department (ED) visits among notified cases

  - 643.8 to 1,063.9 per 100,000 RSV-related hospital admissions among notified cases.

- In the 2024/25 season:
  - there were marked reductions in the notified case rate, and rates of RSV-related ED visits and hospitalisations in those aged less than six months, with the largest difference seen in those aged less than three months
  - those aged less than six months accounted for 23% of the total notified cases, 24% of RSV ED visits and 26% of RSV hospitalisations in those aged less than two years compared with 55%, 53% and 57%, respectively, of such cases between 2019/19 and 2023/24.
- In adults aged 65 years and older, seasonal rates from 2018/19 to 2024/25 (excluding 2020/21) ranged from:
  - 47.1 to 284.3 per 100,000 for notified RSV cases (adults aged 80 years and older accounted for 47% of these cases)
  - 9.4 to 77.4 per 100,000 for notified RSV ED visits (adults aged 80 years and older accounted for 46% of these visits)
  - 18.3 to 93.4 per 100,000 for RSV-related hospital admissions (adults aged 80 years and older accounted for 48% of these admissions).
- HIPE data also highlight the substantial burden associated with RSV in those aged 0 to 2 years. From 2018 to 2024 (excluding 2020) in those with a primary diagnosis of RSV:
  - on average, there were 1,633 (range 1,342 to 2,195) discharges that did not include an ICU stay (infants less than one year accounted for 86% of these discharges). The mean annual length of stay (LOS) was 3.3 days, and the mean total bed days associated with these discharges was 5,359 (range: 2,946 to 7,059) per annum
  - on average, there were 133 (range 67 to 191) discharges that included an ICU stay (infants less than one year accounted for 91% of these discharges). The mean annual LOS was 8.3 days, and the

mean total bed days associated with these discharges was 1,099 (range: 462 to 1,450) per annum.

  - the highest proportion of discharges with or without an ICU stay each year occurred in Q4 (October – December) ranging, for example, from 69% to 88% among infants aged less than one year for discharges without an ICU stay
  - there was a substantial reduction in discharges in those aged less than one year in Q4 of 2024 (n = 533) compared with 2018 to 2023 (range: 785 to 1,601).

- HIPE data indicate that in adults aged 65 years and older, the number of discharges is relatively low. From 2018 to 2024 (excluding 2020) in those aged 65 years and older with a primary diagnosis of RSV:
  - for discharges that did not include an ICU stay, the total number ranged from 8 to 130 per annum, the mean annual hospital LOS ranged from 8.4 to 16.3 days, and the total bed days associated with these discharges ranged from 130 to 1,825 per annum
  - discharges that included an ICU stay were uncommon, and cannot be reported due to data suppression of quarterly data by age band over this time period.
- For the period 2018 to 2024 (excluding 2020), the total cost of inpatient stays for all age groups with a primary diagnosis of RSV ranged from €2.2 to €6.2 million per annum for cases that included an ICU stay, and €9.9 to €20.4 million per annum for cases that did not include an ICU stay.
- It is acknowledged that these data are likely an underestimate of the total burden of RSV, particularly in primary care, as not all RSV cases are laboratory confirmed, and some discharges may not be coded. While there is an apparent trend of increasing incidence over time, this may reflect changing testing practices (increased laboratory capacity in hospital settings and updated HSE guidance relating to use of multiplex tests that include RSV in surveillance testing and when testing patients that present with acute respiratory tract infection).

- Uptake of existing immunisation programmes offered to infants, pregnant women and older adults in Ireland were assessed to inform potential uptake of RSV immunisation strategies in these populations:
  - overall uptake of vaccines included in the childhood immunisation programme ranged from 87.2% to 90.0% between 2018 and 2022 for children up to 12 months of age
  - reported uptake of other maternal vaccines in Ireland was estimated at 49.9% for pertussis, and ranged between 42.1% and 62% for the seasonal influenza vaccine and between 6% and 19.6% for COVID-19 vaccines in recent years
  - reported uptake of recommended vaccines for those aged 65 years and older was estimated to be 36% for pneumococcal vaccine, and ranged between 54.5% and 76.5% for seasonal influenza vaccine and between 46.4% and 61% for COVID-19 in recent years.
- In summary, RSV places a significant burden on young children, older adults and secondary healthcare services, with the highest burden seen in children aged less than two years. RSV poses a particular challenge for paediatric healthcare services, as a high proportion of hospital discharges occur in Q4 each year. However, the introduction of a pilot immunisation programme for those born during the 2024/25 RSV season appears to have had a positive impact with reductions seen in notifications. Increased testing capacity and changes in testing practices have likely contributed to improved ascertainment; however, the identified data are likely an underestimate of the total burden, particularly in primary care, as not all RSV cases are laboratory confirmed and some discharges may not be coded.

3.1 Introduction

This chapter describes the epidemiology of respiratory syncytial virus (RSV) and the burden of disease in Ireland, EU/EEA countries and the UK among children and older adults (that is, those aged 65 years and older). The previously published rapid HTA described the epidemiology of RSV and the burden of disease in detail covering the period 2013 to 2023. This chapter provides an update on the epidemiological and burden of disease data, including where available, data relating to the 2024/25 RSV season. Additionally, this chapter focuses on the data required for the development of a de novo economic evaluation of RSV immunisation and a budget impact analysis for Ireland described in Chapter 6.

3.2 Natural history of RSV

As introduced in Chapter 2, RSV is a common seasonal virus and a leading cause of acute respiratory infections in both young children and older adults. In temperate climates, RSV activity generally peaks during the winter months (mostly between December and January); however, peaks can occur earlier. Approximately 50% to 70% of children are infected by RSV during their first year of life, with almost all children infected by two years of age.[95] Children born prematurely (<35 weeks gestational age) and those with pre-existing chronic conditions such as chronic lung disease (CLD), congenital heart disease (CHD), neuromuscular disease, and immunodeficiency are at increased risk of severe RSV-associated disease.[15] Similarly, adults at highest risk of severe RSV disease include older adults (that is, those aged 65 years and older), particularly those with significant comorbidities such as cardiorespiratory and endocrine or metabolic conditions (such as chronic obstructive pulmonary disease (COPD), congestive heart failure, and diabetes), and those living in long-term care facilities.[3, 4]

RSV is highly contagious with an estimated basic reproductive number (R0) of 3.0 which means that in a completely susceptible population, one case of RSV would infect on average three other individuals.[16] RSV is spread by large droplets and secretions from contact with an infected person. It can also survive on hard surfaces such as worktops and doorknobs for up to six hours. RSV first infects the upper respiratory tract, with clinical symptoms typically occurring after the incubation period of two to eight days. Infants typically experience mild to moderate nasal congestion and low-grade fever within a few days of exposure, followed by a productive cough. Viral bronchiolitis is one of the most common viral illnesses that

occurs in infants as a result of RSV infection. In older adults, the symptom profile is similar to that seen in infants, although there is increased likelihood of lower respiratory tract involvement. Healthy adults are more likely to be asymptomatic than older adults, those who are immunocompromised, and other patients at high risk of severe disease. The duration of the infectious period depends on age, severity of infection and health status. Following infection, adults typically shed virus for three to seven days. Infants shed the virus for up to 14 days in mild infections; however, in those with severe infection or in those aged less than six months, the virus may shed for up to three weeks. The duration of the infectious period can be protracted in immunocompromised individuals who may shed the virus for several months following infection.[3]

The majority of young children will experience at least one primary RSV infection by the second or third year of life.[96, 97] Moreover, reinfection with RSV is common throughout life. A 2016 Finnish follow-up study of 216 children found that RSV seropositivity increased from 37% by age 13 months to 68% and 86% by 24 and 36 months, respectively.[96] The same Finnish study reported an RSV reinfection rate of approximately 35%.[96] While protective immunity arising from prior exposure to RSV is short lived, disease severity tends to be reduced with repeated exposure.[19] An older longitudinal cohort study (1986) from the USA followed children from birth up to 12 months of age (n=125) in the Houston Family Study, with 92 followed up to five years of age.[97] The authors reported that approximately 50% of children experienced a reinfection by two years of age; however, reinfection-related illnesses were generally mild, compared with primary infection. High rates of reinfection were also noted in a 2012 report of a birth cohort of 635 children in Kenya, monitored for RSV infections from 2002 to 2005, which estimated a period of protection of approximately six months following primary and or secondary RSV infection.[98] The rate of secondary infection was estimated to be 70% lower during the first six months after primary infection while the rate of tertiary infection was 60% lower following secondary infection. No statistically significant differences in infection rates were noted for any time period beyond six months after infection. Of note, the study authors reported that the incidence of RSV infection was lowest in infants aged less than six months, which they suggested could be influenced by the protective effect of maternal antibodies in these infants, as well as low mixing rates, although this was not specifically evaluated.[98] This six-month age group with low incidence aligned with the duration of protection conferred by primary or secondary infection in the same study.

In addition to acute disease, RSV is also associated with long-term complications such as recurring or persistent wheezing and the development of asthma, though the causal links are not yet established.[99] Data suggest that compared with RSV non-infected infants, RSV-infected infants are three times more likely to develop wheezing illnesses that may persist up to adolescence,[100] while children who had RSV-induced bronchiolitis during the first two years of life are seven times more likely to develop asthma during their school-years compared with healthy infants.[101] In older adults who survive a severe RSV infection, late complications can include sustained loss of general function and independence, development or worsening of heart failure, cardiovascular events, decline in lung function, greater use of medications, impaired quality of life, fatigue, and readmission to hospital. In immunocompromised adults, late complications can include progressive lung disease and chronic infection with viral evolution.[102]

3.3 Data sources

In Ireland, RSV has been a notifiable disease since 2012 under the Infectious Disease Regulations. The Health Protection Surveillance Centre (HPSC) monitors RSV activity year round through different surveillance systems.[15] Surveillance of all confirmed RSV notifications, including hospitalisations, ICU admissions, deaths and outbreaks, are reported through the Irish Computerised Infectious Disease Reporting system (CIDR) notification system. The HPSC also monitors RSV activity through sentinel GP acute respiratory infection (ARI) and non-sentinel respiratory specimen surveillance. A network of sentinel general practices report on clinical consultations of acute respiratory infection (ARI) and influenza-like illness (ILI) on a weekly basis.[103] Sentinel GPs systematically sample five patients presenting to their practice each week with symptoms of ARI or ILI and send combined nose and throat swabs from these patients to the National Virus Reference Laboratory (NVRL) for respiratory virus testing. Since the 2023/24 season, there are 100 sentinel GP sites participating in the programme, representing a population coverage of approximately 11%. The network has expanded since it was first established, increasing sampling capacity in the community for monitoring respiratory viruses and improving the geographical representation of the network. Since the start of the 2023/24 season, improved practice patient denominators are available, with only active patients who have consulted their GP clinic in the past three years included in these denominators. Prior to the 2023/24 season, these denominators were estimated by practice, irrespective of when the patients had last sought care.

Non-sentinel respiratory surveillance began in 2001 and includes specimens referred to the NVRL for testing from a variety of sources including hospitals, GPs (not part of sentinel GP network), nursing homes and other health and care settings. This non-sentinel surveillance is undertaken for clinical or public health reasons and may include more than one specimen from each case.

For this HTA, RSV surveillance data for all age groups were gathered from the sentinel GP network, CIDR and the NVRL, for the RSV seasons (week 40 to week 20) from 2018/19 to 2024/25; these data were provided to HIQA by the HPSC. Data on confirmed RSV cases, hospitalisations, emergency department (ED) cases, ICU admissions and deaths were extracted from CIDR on 15 July 2025. Data on underlying medical conditions among RSV ICU admissions and RSV-positive severe acute respiratory infection (SARI) cases were extracted from CIDR and the SARI surveillance database, respectively, on 1 December 2025. HPSC began surveillance of RSV deaths and ICU admissions in October 2023, and therefore these data are only available from the 2023/24 season onwards. Sentinel GP ARI and non-sentinel respiratory specimen data were extracted from the HPSC sentinel surveillance database on 13 February 2025.

Rates were calculated using Central Statistics Office (CSO) census denominator data for the total and associated age-stratified population of Ireland. Census data from 2016 were used for the 2018/19 RSV analyses.[104] Census data from 2022 were used for the 2018/19 to 2024/25 RSV analyses.[105]

Data from the Hospital In-Patient Enquiry (HIPE) system were also gathered to examine hospital discharges with and without an intensive care unit (ICU) stay for all age groups with a primary or secondary diagnosis of RSV (with ICD-10 codes B97.4, J12.1, J20.5, J21.0).[106] For children aged 0 to 2 years, hospital discharge data with a primary diagnosis of acute bronchiolitis (with ICD-10 codes J21.8 and J21.9) were also obtained. Data provided by HIPE for this assessment also included the total cost of discharges, reported separately for those with and without an ICU stay, for all included diagnoses.

As outlined in Chapter 2, a pilot Pathfinder Programme offering immunisation with nirsevimab was first introduced in the 2024/25 RSV season. In that season, immunisation was offered to all infants born in the six-month period between 1 September 2024 and 28 February 2025 and was subsequently extended to include a catch-up programme for the 2025/26 season for infants aged less than six months entering their first RSV season. Since 2024/25, immunisation with nirsevimab has

also been offered to infants and children up to two years of age at high risk of severe disease who would previously have been eligible for, and offered, palivizumab. The observed RSV-related morbidity and mortality are therefore in the context of these changes to immunisation policy.

3.4 Incidence of RSV

3.4.1 Incidence of RSV in Ireland

Notified RSV incidence per 100,000 from the 2018/19 season to 2024/25 season are reported by age group in Table 3.1, with a more detailed breakdown reported among those aged 0 to 2 years in Table 3.2 and among those aged 65 years and older reported in Table 3.3.

Between the 2018/19 and 2024/25 RSV seasons there was a general trend of increasing incidence, with the highest reported incidence in the 2024/25 season (148.7 per 100,000). There was an abrupt decline in RSV notifications in the 2020/21 RSV season, likely due to the implementation of non-pharmacological measures to limit transmission of SARS-CoV-2, which also limited transmission of other respiratory pathogens. Increased notifications in the subsequent year may have been influenced by immunity depletion.[107] Caution is also required in inferring temporal trends from the data presented for the following reasons. There has been a substantial increase in testing capacity since 2016, and changes in testing patterns since the COVID-19 pandemic (such as increased used of multiplex reverse transcriptase polymerase chain reaction (RT-PCR) assays), both of which have likely contributed to increased RSV notifications to the HPSC. Further improvement in the reporting of notified cases has also been achieved through the modernisation of information systems, using a Robotic Process Automation solution to process notifications.[108] Moreover, as highlighted in Section 3.2, the Pathfinder programme was introduced for the 2024/25 RSV season providing RSV immunisation for infants born between 1 September 2024 and 28 February 2025, with the impact of the programme more clearly demonstrated in Table 3.2.[109]

Across all seasons examined in this HTA, the proportion of seasonal notified RSV cases was consistently and substantially higher in children aged 0 to 2 years compared with all other age bands. This cohort accounted for the largest proportion of notified cases per annum, ranging from 41% (2022/23) to 69% (2018/19). Over the same time period, adults aged 65 and older represented 9% (2021/22) to 29% (2024/25) of all RSV notifications. Similarly, notification rates were consistently

highest in those aged 0 to 2 years, followed by the notification rates in those aged 3 to 4 years. Excluding 2020/21 (COVID-19), rates ranged from 1,211.8 to 2,225.7 per 100, 000 in those aged 0 to 2 years compared with 92.9 to 514.8 per 100,000 in those aged 3 to 4 years. In comparison, notification rates in those aged 65 years and older ranged from 47.1 to 284.3 per 100,000.

Table 3.1 Notified RSV cases in Ireland from 2018/19 season to 2024/25 season, reported by age band

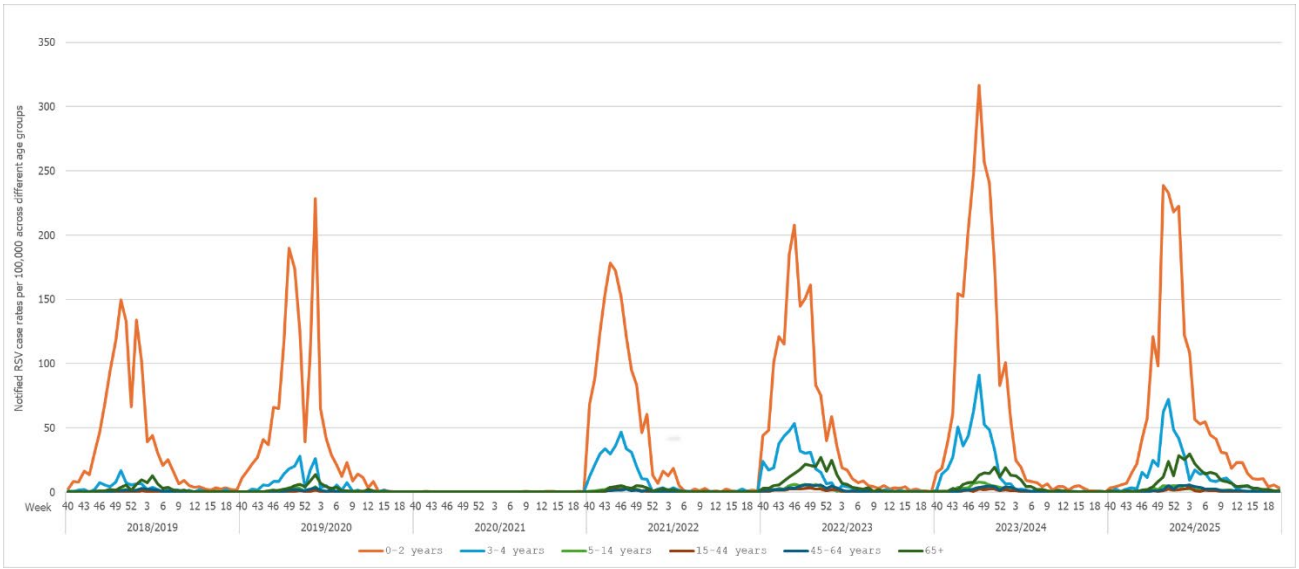
RSV season~	0-2 years		3-4 years		5-14 years		15-44 years		45 - 64 years		65+		Total	
	n (%)	Rate per 100,000	n (%)	Rate per 100,000	n (%)	Rate per 100,000	n (%)	Rate per 100,000	n (%)	Rate per 100,000	n (%)	Rate per 100,000	n	Rate per 100,000
2018/19	2,334 (69)	1,211.8	129 (4)	92.9	94 (3)	13.9	154 (5)	7.8	222 (7)	19.6	471 (14)	73.9	3,404	71.5
2019/20	2,609 (64)	1,504.4	230 (6)	188.5	179 (4)	25	223 (5)	10.8	273 (7)	21.1	552 (14)	71.1	4,066	79.0
2021/22	2,489 (61)	1,435.2	406 (10)	332.8	210 (5)	29.3	383 (9)	18.5	205 (5)	15.9	366 (9)	47.1	4,059	78.8
2022/23	2,899 (41)	1,671.6	498 (7)	408.2	373 (5)	52	645 (9)	31.2	763 (11)	59	1,892 (27)	243.7	7,070	137.3
2023/24	3,860 (53)	2,225.7	628 (9)	514.8	405 (6)	56.5	435 (6)	21.0	545 (8)	42.1	1,353 (19)	174.3	7,226	140.3
2024/25	3,385 (44)	1,951.8	556 (7)	455.9	339 (4)	47.4	500 (7)	23.8	680 (9)	52.7	2,207 (29)	284.3	7,657	148.7

Note: ~RSV season corresponds from week 40 of the first year to week 20 of the following year. Data for the 2020/21 season were excluded as there was a very low number of events during this period, due to the influence of COVID-19.
Source: Health Protection Surveillance Centre.

The notified RSV case rates by age band were also examined by epidemiological weeks (Figure 3.1). As expected, seasonal outbreaks occurred each year, with increased notifications typically from September through to the end of February (Weeks 40 to 12), albeit with slight variation both in the onset of RSV activity and the timing of peak notifications. In particular, an early increase in RSV activity was seen in the 2021/22 and 2022/23 seasons.[110] Across all seasons, the highest notification rates were observed in the 0 to 2 years age group, with a disproportionate burden in this age group compared with all other age groups. The next highest notification rates were consistently seen in the 3 to 4 years age group, followed by the 65 years and older age group.

Across the period 2018/19 to 2024/25, notification levels in the 0 to 2 years and 3 to 4 years age groups typically increased sooner and peaked earlier (1 to 2 months earlier) compared with notifications in older adults (65+ years) (Figure 3.1). Increased notifications in these younger age groups were generally observed from Week 40 of the epidemic year to Week 12 of the following year, compared with Week 47 to Week 7 in older adults.

Figure 3.1 Notified RSV case rate per 100,000 in the total population in Ireland, reported by age band and epidemiological weeks



Source: Health Protection Surveillance Centre.

HPSC data in relation to specimens received from primary care (sentinel GP practices) were reviewed to assess the volume of testing in primary care for those aged 0 to 4 years and in those aged 65 years and older. Further disaggregation of

these data was not available. Between the 2018/19 and 2023/24 RSV seasons, and excluding the 2020/21 season, the total number of specimens from sentinel practices tested for RSV generally increased over time with concerted efforts made to improve sentinel GP swabbing since 2022. In children aged zero to four years, the total number of specimens tested per season was 225, 359 and 278 in 2022/23, 2023/24 and 2024/25, respectively, while in those aged 65 years and older, the total number was 424, 615 and 690 in 2022/23, 2023/24 and 2024/25, respectively. For the latest season of 2024/25, the percentage positivity from the sentinel services was 14.4% among those aged 0 to 4 years and 5.8% among those aged 65 years and older.

Compared with the pre-COVID season (2018/19), the total number of specimens tested from non-sentinel GP practices has decreased among those aged 0 to 4 years (4,388 in 2018/19 vs 1,613 in 2024/25). In contrast, testing has increased in those aged 65 years and older (1,641 in 2018/19 vs 4,412 in 2024/25). For the latest season of 2024/25, a similar pattern of higher percentage positivity in the youngest cohort was seen for specimens from the non-sentinel practices, that is 20.1% among those aged 0 to 4 years and 8.4% among those aged 65 years and older.

3.4.2 Incidence of RSV in Ireland (those aged 0 to 2 years)

Notified RSV incidence rates per 100,000 for those aged 0 to 2 years disaggregated by three-month age band are reported in Table 3.2. As noted previously, data from the 2020/21 RSV season are not considered representative due to the influence of the COVID-19 pandemic.

Between the 2018/19 and 2023/24 RSV seasons (excluding 2020/21), infants aged less than six months accounted for 55% of all notified RSV cases among those aged 0 to 2 years. Specifically, infants aged less than three months accounted for the largest proportion (range 30-39%) of seasonal notified RSV cases in those aged 0 to 2 years between the 2018/19 and 2023/24 RSV seasons. In contrast, in the latest season of 2024/25, infants aged less than six months accounted for 23% of cases in this age band. In the 2024/25 season the lowest proportion (9%) of reported cases was in those aged 0 to 3 months, while the proportion of cases in those aged 3 to 6 months also declined compared with previous years (14% vs. a range of 18% to 21%). This likely indicates the impact of the 2024/25 RSV Pathfinder programme which offered nirsevimab to infants born during the six-month period from 1 September 2024 to 28 February 2025. Moreover, the notified case rate in those aged 0 to 3 months reported for 2024/25 season was the lowest observed since 2018/19,

with the notified rate approximately 60 to 70 percent lower than that observed in previous years (2,166 per 100,000 vs a range of 5,635 to 7,959 per 100,000) in this age group. As the notified cases reported from 2024/25 include infants born before the RSV season, the true impact among the infants eligible for Pathfinder was likely greater.

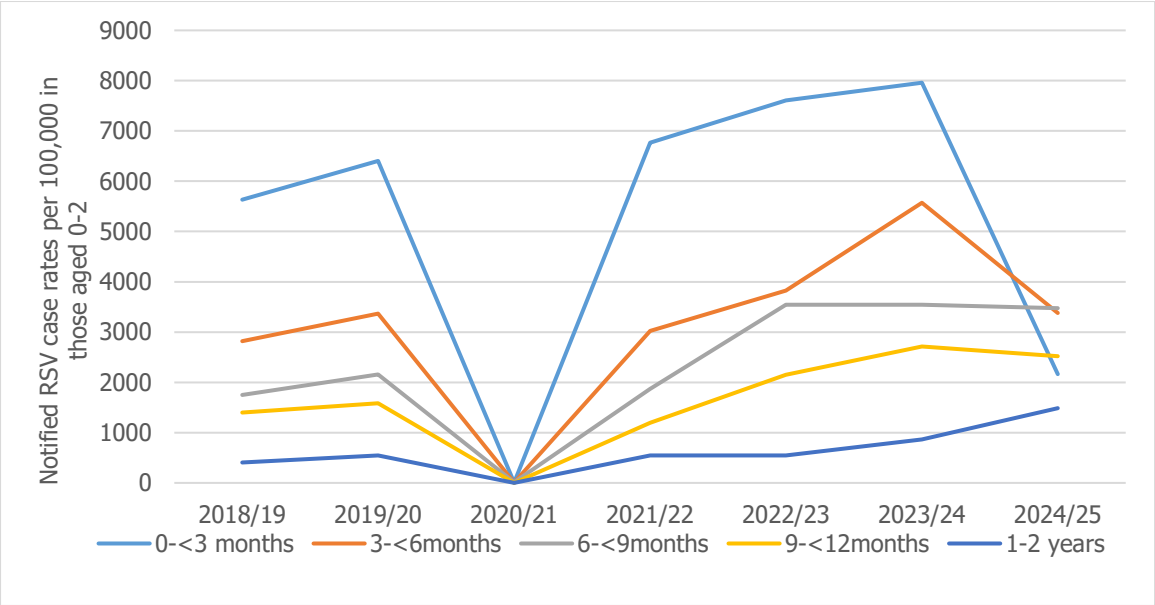
Table 3.2 Notified RSV cases for those aged 0 to 2 years in Ireland, reported by age band

RSV season~	0-2 years		0-<3 months		3-<6months		6-<9months		9-<12months		1-2 years	
	n	Rate per 100,000	n (%)	Rate per 100,000	n (%)	Rate per 100,000	n (%)	Rate per 100,000	n (%)	Rate per 100,000	n (%)	Rate per 100,000
2018/19	2,334	1,211.8	877 (38)	5,634.8	439 (19)	2,820.6	272 (12)	1,747.6	218 (9)	1,400.7	528 (23)	405.1
2019/20	2,609	1,504.4	925 (35)	6,401.8	486 (19)	3,363.6	336 (13)	2,325.4	229 (9)	1,584.9	633 (24)	547.4
2021/22	2,489	1,435.2	978 (39)	6,768.6	437 (18)	3,024.4	270 (11)	1,868.6	173 (7)	1,197.3	631 (25)	545.7
2022/23	2,899	1,671.6	1,099 (38)	7,606.1	553 (19)	3,827.3	303 (10)	2,097.0	311 (11)	2,152.4	633 (22)	547.4
2023/24	3,860	2,225.7	1,150 (30)	7,959.0	805 (21)	5,571.3	512 (13)	3,543.5	392 (10)	2,713.0	1,001 (26)	865.7
2024/25	3,385	1,951.8	313 (9)	2,166.4	488 (14)	3,377.3	502 (15)	3,474.1	364 (11)	2,519.1	1,718 (51)	1,485.9

Note: ~RSV season corresponds from week 40 of the first year to week 20 of the following year. Data for the 2020/21 season were excluded as there was a very low number of events during this period, due to the influence of COVID-19.**Source:** Health Protection Surveillance Centre.

The notified RSV rates per 100,000 for those aged 0 to 2 years are presented by age band and RSV season in Figure 3.2. Overall, incidence rates typically decreased with increasing age, with the highest rates observed in infants aged 0 to 3 months followed by those aged 3 to 6 months up until the 2024/25 season, when the notified rates within these age bands decreased substantially. As noted, this likely reflects the impact of the Pathfinder immunisation programme for those born during the 2024/25 RSV season. Aside from this group, there appears to be a general trend of increasing notified RSV case rates.[110] However as noted, caution is required in inferring temporal trends based on the data presented given changes in testing capacity and patterns, and the potential influence of the COVID-19 pandemic on behaviour and immunity levels.

Figure 3.2 Notified RSV case rate per 100,000 in those aged 0 to 2 years in Ireland, reported by age band and season



Note: RSV season corresponds from week 40 of the first year to week 20 of the following year.
Source: Health Protection Surveillance Centre.

3.4.3 Incidence of RSV in Ireland (those aged 65 years and older)

Notified RSV incidence per 100,000 for adults aged 65 years and older and disaggregated by five-year age band are reported in Table 3.3. As before, data from the 2020/21 RSV season are not considered representative due to the influence of the COVID-19 pandemic.

The notified case rate reported for the 2024/25 season (284.3.5 per 100,000) was the highest observed across all seven seasons examined for this HTA. When disaggregated by five-year age-band, the highest notification rates were consistently observed among those aged 80 years and older, with notification rates approximately six times those reported in those aged 65 to 69 years. Moreover, those aged 80 years and older consistently accounted for the highest proportion of notified cases (range 41% to 52%) annually, equating to 47% of all cases across these seasons, while those aged 75 years and older accounted for 68% of all cases.

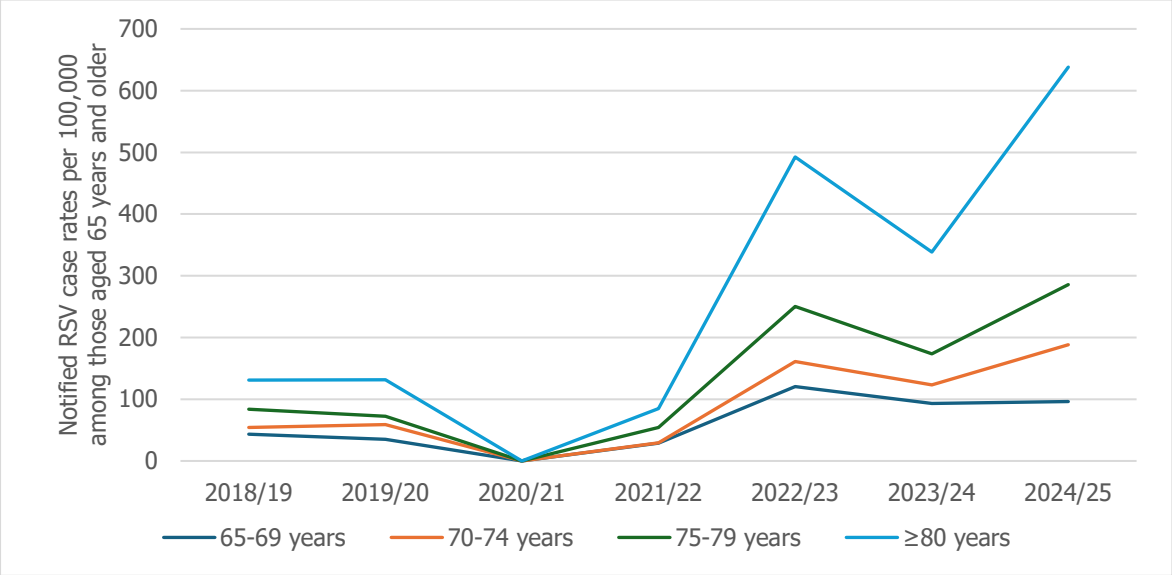
These data are presented graphically in Figure 3.3. Notification rates typically increased with increasing age, with as noted, the highest rates observed among adults aged 80 years or older across all seasons. Since 2022/23, notification rates in all age groups are higher than in the pre-COVID-19 period, however it is not possible to make inferences about temporal trends given the limited data available and changes in testing practices.

Table 3.3 Notified RSV cases for those aged 65 years and older in Ireland, reported by age band

RSV season~	≥65 years		65-69 years		70-74 years		75-79 years		≥80 years	
	n	Rate per 100,000	n (%)	Rate per 100,000	n (%)	Rate per 100,000	n (%)	Rate per 100,000	n (%)	Rate per 100,000
2018/19	471	73.9	91 (19)	43.1	88 (19)	54.2	97 (21)	84	195 (41)	131.2
2019/20	552	71.1	83 (15)	34.9	119 (22)	58.7	112 (20)	72.6	238 (43)	131.5
2021/22	366	47.1	68 (19)	28.6	60 (16)	29.6	84 (23)	54.5	154 (42)	85.1
2022/23	1,892	243.7	287 (15)	120.5	327 (17)	161.2	386 (20)	250.2	892 (47)	492.7
2023/24	1,353	174.3	222 (16)	93.2	250 (18)	123.2	268 (20)	173.7	613 (45)	338.6
2024/25	2,207	284.3	229 (10)	96.0	382 (17)	188.0	441(20)	285.7	1,155 (52)	638.1

Note: ~RSV season corresponds from week 40 of the first year to week 20 of the following year. Data for the 2020/21 season were excluded as there was a very low number of events during this period, due to the influence of COVID-19.
Source: Health Protection Surveillance Centre.

Figure 3.3 Notified RSV case rate per 100,000 in those aged 65 years and older in Ireland, reported by age band and year



Source: Health Protection Surveillance Centre.

RSV outbreaks in Ireland

HPSC data on RSV outbreaks across a range of healthcare and non-healthcare settings were requested from the 2022/23 season onwards, with the number of outbreaks per RSV season reported in Table 3.4, along with the data for a number of residential settings. Across these seasons, the highest number of outbreaks were reported in nursing homes, with this setting accounting for more than half (53%) of the 97 reported outbreaks in the 2024/25 season.

Table 3.4 Number of RSV outbreaks by RSV season and for specific residential settings

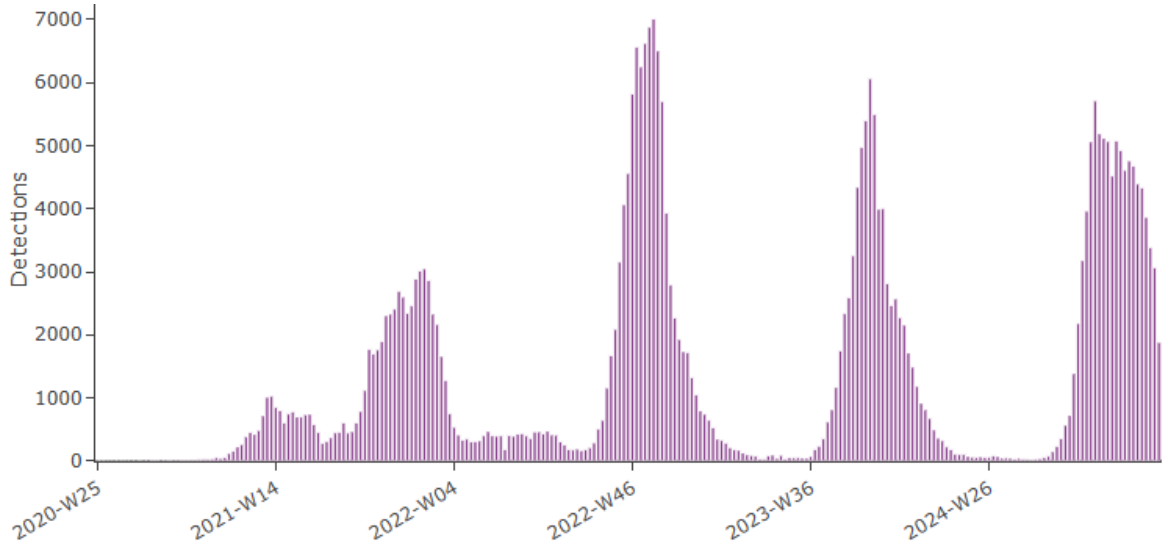
RSV season~	Total outbreaks (all settings)*	Nursing homes	Residential institutions	Community hospitals /long-stay units
2022/23	58	22	4	10
2023/24	37	15	4	2
2024/25	97	51	13	4

Source: Health Protection Surveillance Centre.
Note: ~RSV season corresponds from week 40 of the first year to week 20 of the following year. *All settings include nursing homes, residential institutions, community hospitals /long-stay units, hospitals, other healthcare services and non-healthcare settings. Residential Institutions include residential disability services, residential mental health facilities, hospices, homeless hubs/hostels, prisons, direct provision centres, etc.

3.4.4 Incidence of RSV in EU/EEA countries and the UK

RSV is currently not a mandatory reportable disease at an EU level. As of 2022, RSV was a notifiable disease in 12 countries.[111] The European Centre for Disease Prevention and Control (ECDC) and WHO Regional Office for Europe have jointly developed the European Respiratory Virus Surveillance Summary (ERVISS) which provides a weekly integrated epidemiological summary for respiratory viruses including RSV for the EU/EEA and the WHO European Region. ERVISS reflects the surveillance data from the 53 countries of the WHO/Europe Region (which includes the 30 EU/EEA countries). The data in ERVISS are not disaggregated into age cohorts relevant for this HTA, that is, those aged 0 to 2 years and adults aged 65 years or older. Total counts of aggregate weekly laboratory detections of RSV in all EU/EEA countries from week 25, 2020 to week 14, 2025 are shown in Figure 3.4. These data highlight the seasonal nature of RSV, with outbreaks occurring each year.

Figure 3.4 Aggregate weekly laboratory-based detections of RSV in all EU/EEA countries reported by epidemiological week and year



Source: European Respiratory Virus Surveillance Summary

A 2024 systematic literature review of the burden of RSV in young children up to five years of age included 19 studies (in North America and Europe) and reported RSV incidence rates in primary care settings and emergency departments (EDs).[112] Due to differences in contextual and methodological factors including the lack of a

uniform case definition for RSV, pooled estimates could not be calculated and instead medians and ranges were presented. While acknowledging the limitations in the data, the authors concluded that though estimates vary widely, a substantial number of children aged less than five years attend primary care and EDs each year due to RSV infections. Specifically, in primary care, the yearly incidence rates in all age categories ranged from 0.8 to 330 (median = 109) per 1,000 population, while incidence rates in EDs ranged from 7.5 to 133.0 (median 48) per 1,000 population. Incidence rates were highest in the youngest age categories with annual incidence rates per 1,000 population in primary care ranging from 7.2 to 330 (median = 202) for infants under six months of age, 14.2 to 263 (median = 176) for infants under one year of age, 19 to 263 (median = 109) for children under two years of age, and 0.8 to 212 (median = 35) for children under five years of age. Similarly, incidence rates in EDs decreased with increasing age, ranging from 74.8 to 144.0 (median =112) and 7.5 to 40.4 (median = 28) per 1,000 population per year for those aged less than six months and those aged less than five years, respectively.[112]

A 2023 European prospective birth cohort (with sites in Spain, Finland, England, Scotland, and the Netherlands) examined the burden of RSV in a healthy term-born infant birth cohort. Infants born between 1 July 2017 and 31 July 2020 were followed up during the first year of life.[113] Among 993 nested active surveillance cohort participants, the incidence (as the proportion of infants experiencing the event at least once during their first year of life) of RSV infection confirmed by diagnostic assay was 26.2% (95% CI 24.0–28.6) and was 14.1% (95% CI 12.3–16.0) for medically attended RSV infection. The corresponding incidence rates were 23.7 per 1,000 infant-months and 12.1 per 1,000 infant-months for RSV infection and medically attended RSV infection, respectively.[113]

The 2021 prospective, observational cohort study conducted by the REspiratory Syncytial virus Consortium in EUrope (RESCEU) assessed the community burden of laboratory-confirmed symptomatic RSV infection in Europe in older adults aged 60 years, and older recruiting 1,040 participants in the 2017/18 and 2018/19 RSV seasons.[114] Participants reported weekly about symptoms of acute respiratory tract infection (ARTI) during one RSV season, with an estimated 4.2% and 7.2% experiencing RSV-related illness (diagnosis via PCR and or serology) in the 2017/18 and 2018/19 RSV seasons, respectively.[114]

3.4.5 Incidence of RSV in high-risk groups

Limited co-morbidity data are available for Ireland. Combined HPSC data from the 2023/24 and 2024/25 seasons (that is from week 40 of the first year to week 20 of the following year) indicate that among RSV cases that were admitted to the ICU (n=250), the proportion of underlying clinical conditions was substantially higher among older adults compared with children. Among RSV cases admitted to ICU, all those aged 60 to 74 years (n=18/18) and 73% (n=8/11) of those aged 75 years and older were individuals with at least one documented underlying medical condition. By comparison, only 2% of RSV-related ICU admissions among infants and 8% of admissions among those aged 1 to 2 years occurred in patients with at least one underlying clinical condition.

SARI surveillance data from the 2024/25 season (week 40 2024 to week 39 2025) show that underlying conditions are common among RSV cases. The 2024/25 season data are based on three sentinel hospital sites; St Vincent's University Hospital, Dublin and St. James's Hospital, Dublin, both reporting on SARI cases aged 15 years and older; and University Hospital Limerick, reporting on SARI cases aged under 15 years of age only. Among older patients, 96% (n=22/23) of those aged 60-74 years and 99% (n=64/65) of those aged 75 years and older had at least one underlying medical condition. In children under two years of age, 33% (n=14/42) of infants and 29% (n=14/48) of those aged 1 to 2 years had at least one underlying medical condition. It is important to note that these proportions are based on small numbers and may vary from season to season.

When considering the paediatric population specifically, it is noted that premature infants, infants (especially those aged six months and younger), children less than two years of age with congenital heart or chronic lung disease (CLD), children with weakened immune systems due to a medical condition or medical treatment and children with neuromuscular disorders are deemed to be at high risk of severe RSV disease.[15] As outlined in section 3.4.2 above, the available Irish notification data confirm a pattern of higher notification rates in those aged less than six months. Data on the incidence of RSV in community or outpatient settings among children at high risk of severe disease are limited, while data on the burden of severe disease in these sub-groups (as measured hospitalisation and mortality rates) are discussed in sections 3.5.1 and 3.5.3.

A 2010 retrospective cohort study from a national US claims database documented rates of outpatient RSV lower respiratory tract infection (LRTI) visits among infants.[115] The study methods assumed that between 50% to 80% of reported

bronchiolitis visits and 30% of reported pneumonia visits were due to RSV. This database analysis reported that infants with CLD had the highest rates of all outpatient RSV LRTI visits ranging from 189.1 to 241.0 per 1,000 children for ambulatory care settings as compared with 115.2 to 154.8 per 1,000 for full term infants without CLD. However, this analysis found no discernible trend in rates of medical encounters for RSV LRI among pre-term infants based on gestational age. Another 2025 US study utilising claims data found that the incidence of RSV-associated LRTI in outpatient setting for infants was similar across gestational age groups at 54.0 per 1,000 person years for infants under one year of age born at less than 29 weeks' gestation, and 51.6 per 1,000 person years for infants under one year born at 37 weeks or more gestation.[116]

A 2022 systematic review was identified on the burden of RSV in developed countries that reported data relating to laboratory-confirmed RSV cases in adults aged 60 years and older and those aged 18 years or older at risk of infection due to a range of underlying conditions.[117] The majority of the data related to high-risk and medically-attended populations. An overall incidence (based on three studies each) was estimated for two of the included risk groups, immunodeficiency and cardiopulmonary disease. For the immunodeficiency risk group, the estimated annual and seasonal incidence of RSV cases per 1,000 person-years were 36.88 (95% CI 17.82–76.33) and 260.89 (95% CI 82.33–826.65), respectively. In those with cardiopulmonary disease, the seasonal incidence was estimated at 19.15 (95% CI 6.06–60.49) RSV cases per 1,000 person-years. The review also included a study which reported on institutionalised older adults, with an incidence of 9.78 (95% CI 3.18–20.04) RSV cases per 1,000 person-years.[118]

A systematic review published in 2024 examined the burden of RSV among adults in nursing and care homes.[119] It included 13 studies reporting on incidence rates, incidence proportions and prevalence estimates in nursing home residents.[119] Reported annual RSV incidence ranged from 0.5 to 14%. Two included studies reported RSV-positive acute respiratory infection, with similar annual incidence rates of 4,582 (95% CI: 3,259–6,264)[120] and 4,785 (95% CI: 2,258–10,141) per 100,000 person-years, while one also reported the annual incidence of RSV-positive lower respiratory tract infections at 3,040 (95% CI: 1,986–4,454) cases per 100,000 person-years.

A 2024 literature review of the incidence of RSV in adults also reported on incidence among high risk sub-groups.[121] Overall, the review included 37 primary studies and

reported that RSV incidence estimates were highly variable within and between geographic regions. The review included 15 studies that specifically considered RSV incidence in adult populations with underlying conditions. Differences in case definitions, diagnostic testing and surveillance strategies were noted between studies, which may have contributed to the substantial differences in incidence rates across populations and within and between geographical regions. The authors reported that overall, RSV incidence in adults tended to increase with age and was highest in older adults with underlying conditions. Specific risk groups identified within the review included transplant recipients and patients with COPD, congestive heart failure (CHF), haematological malignancies and solid organ tumours, with the highest RSV incidences observed in populations with a history of transplantation and in populations with severe underlying cardiopulmonary conditions.[121]

3.5 Burden of RSV

3.5.1 Complications and hospitalisations (those aged 0 to 2 years)

RSV-related emergency department visits

Notified RSV emergency department (ED) visit rates per 100,000 for those aged 0 to 2 years are reported in Table 3.5 and graphically in Figure 3.5 by age band and RSV season for the RSV seasons 2018/19 to 2024/25. These data are limited to ED cases that were not reported to have been admitted to hospital; the number of notified ED cases does not therefore include all cases attending ED. As before, data from the 2020/21 RSV season are excluded from the subsequent reporting as they are not considered representative due to the influence of the COVID-19 pandemic.

Between the 2018/19 and 2023/24 RSV seasons (excluding 2020/21), there was a mean of 1,163 (range 552 to 1,718) RSV ED visits per season, with the highest notified RSV ED visit rate (990.6 per 100,000) observed in the 2023/24 season. Up until the 2024/25 season, when disaggregated by age band, ED notification rates consistently decreased with increasing age, with a substantially higher burden seen in infants aged less than three months (range: 1,394 to 3,543 per 100,000) followed by those aged 3 to 6 months (range: 661.8 to 2,36.9 per 100,000). The data for the 2024/25 season indicate a substantial decline in RSV ED visit rates in those aged less than three months, and in those aged between three and six months, while notified visit rates for those aged 9 to 12 months and 1 to 2 years were the highest reported since 2018/19.

The distribution of ED visits among those aged 0 to 2 years changed in the 2024/25 RSV season. Infants aged less than six months accounted for 24% of RSV ED visits in the 2024/25 season compared with 53% of such visits between the 2018/19 and 2023/24 seasons. The most notable change was in those aged less than three months who had consistently accounted for the largest proportion of RSV ED visits each season (range 23% to 40%) but instead accounted for the lowest proportion (9%) in the 2024/25 season. This change in the distribution is possibly due to the positive impact of the Pathfinder programme in the context of a general trend of improved ascertainment due to increased testing.

Table 3.5 Notified RSV emergency department visits for those aged 0 to 2 years in Ireland, reported by age band

RSV season~	0-2 years		0-<3 months		3-<6months		6-<9months		9-<12months		1-2 years	
	n	Rate per 100,000	n (%)	Rate per 100,000	n (%)	Rate per 100,000	n (%)	Rate per 100,000	n (%)	Rate per 100,000	n (%)	Rate per 100,000
2018/19	552	286.6	217 (39)	1,394.2	103 (19)	661.8	53 (10)	340.5	52 (9)	334.1	127 (23)	97.4
2019/20	782	450.9	235 (30)	1,626.4	143 (18)	989.7	115 (15)	795.9	79 (10)	546.8	210 (27)	181.6
2021/22	1,021	588.7	412 (40)	2,851.4	189 (19)	1,308	119 (12)	823.6	73 (7)	505.2	228 (22)	197.2
2022/23	1,332	768.1	512 (38)	3,543.5	253 (19)	1,751	144 (11)	996.6	139 (10)	962	284 (21)	245.6
2023/24	1,718	990.6	402 (23)	2,782.2	381 (22)	2,636.9	260 (15)	1,799.4	178 (10)	1231.9	497 (29)	429.8
2024/25	1,575	908.2	139 (9)	961.7	242 (15)	1,674.6	236 (15)	1,633.1	193 (12)	1,335.2	765 (49)	661.3

Note: ~RSV season corresponds from week 40 of the first year to week 20 of the following year. Data for the 2020/21 season were excluded as there was a very low number of events during this period, due to the influence of COVID-19.
Source: Health Protection Surveillance Centre
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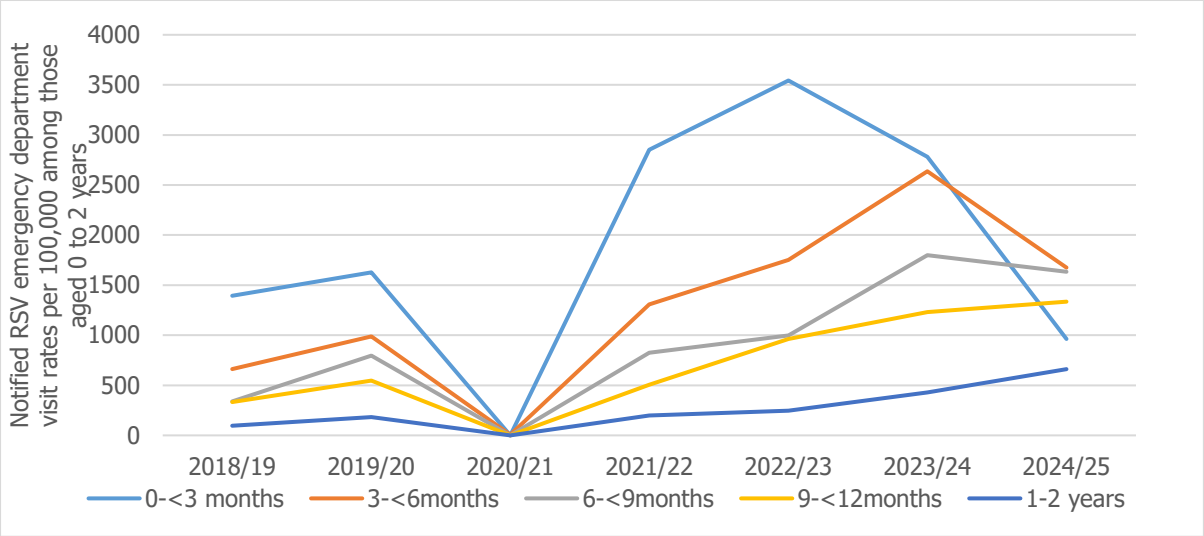
Figure 3.5 Notified RSV emergency department visit rates per 100,000 for those aged 0 to 2 years in Ireland, reported by age band and season



Note: RSV season corresponds from week 40 of the first year to week 20 of the following year.
Source: Health Protection Surveillance Centre

RSV related hospital admissions

Notified RSV hospital admissions for those aged 0 to 2 years are reported in Table 3.6 and graphically in Figure 3.6 by age band and RSV season for the period 2018/19 to 2024/25. As before, the data for 2020/21 are not considered representative due to the influence of the COVID-19 pandemic and are excluded from the reporting below.

Between the 2018/19 and 2023/24 RSV seasons (excluding 2020/21), the total number of RSV hospital admissions per season in those aged 0 to 2 years ranged from 1,205 to 1,845, with the highest notified RSV hospital admission rate (1,063.9 per 100,000) reported for the 2023/24. When disaggregated by age band for the period up to 2023/24, admission rates were noted to consistently decrease with increasing age. Infants aged less than six months accounted for 57% of these admissions across seasons and infants aged less than three months consistently accounted for the highest rates of RSV-related hospital admissions (range: 3,001 to 4,713 per 100,000) and the largest proportion of seasonal RSV hospital admissions (range 37% to 40%).

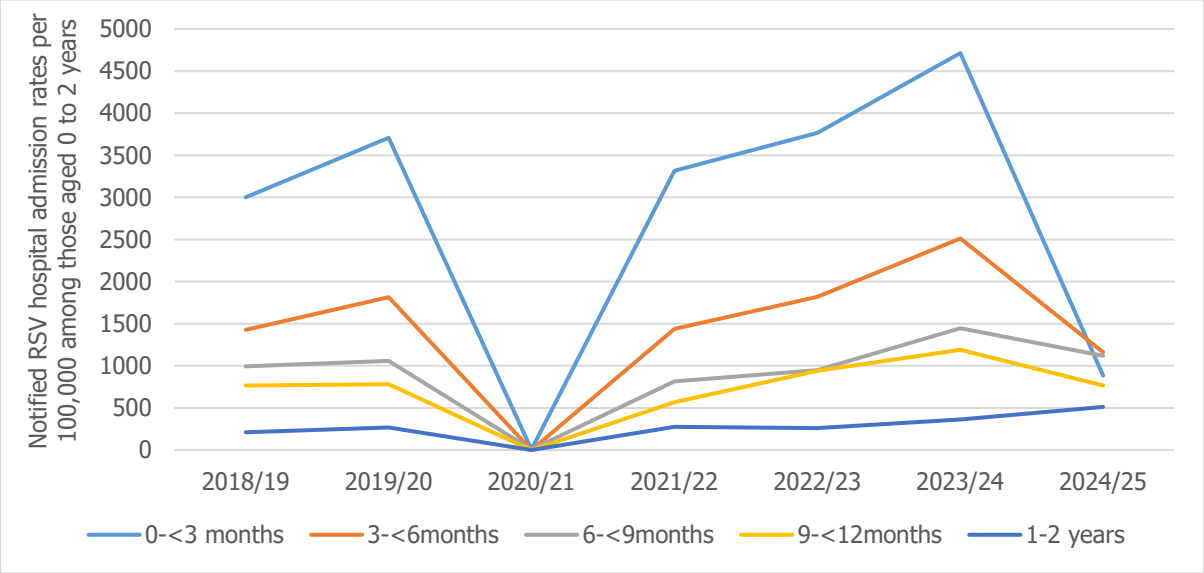
In contrast, this trend appears to have changed in the 2024/25 RSV season, with a lower proportion (11%) of RSV hospital admissions among infants aged less than three months (11%) and those aged three to six months (15%) compared with previous years. This is likely due to the positive effects of the Pathfinder programme with the impact among those specifically eligible for the programme likely greater. In contrast, the admission rate in those aged 1 to 2 years (512.4 per 100,000) was the highest reported since 2018/19, with this age band accounting for 51% of all RSV hospital admissions in those aged 0 to 2 years.

Table 3.6 Notified RSV hospital admissions for those aged 0 to 2 years in Ireland, reported by age band and season

RSV season~	0-2 years		0-<3 months		3-<6months		6-<9months		9-<12months		1-2 years	
	n	Rate per 100,000	n (%)	Rate per 100,000	n (%)	Rate per 100,000	n (%)	Rate per 100,000	n (%)	Rate per 100,000	n (%)	Rate per 100,000
2018/19	1,240	643.8	467 (38)	3,000.5	222 (18)	1,426.4	155 (13)	995.9	119 (10)	764.6	277 (22)	212.5
2019/20	1,375	792.8	536 (39)	3,709.6	262 (19)	1,813.3	153 (11)	1,058.9	113 (8)	782.1	311 (23)	269
2021/22	1,205	694.8	479 (40)	3,315.1	208 (17)	1,439.5	118 (10)	816.7	82 (7)	567.5	318 (26)	275
2022/23	1,381	796.3	544 (39)	3,765	263 (19)	1,820.2	137 (10)	948.2	136 (10)	941.2	301 (22)	260.3
2023/24	1,845	1,063.9	681 (37)	4,713.1	363 (20)	2,512.3	209 (11)	1,446.5	172 (9)	1,190.4	420 (23)	363.2
2024/25	1,161	669.4	128 (11)	885.9	168 (15)	1,162.7	162 (14)	1,121.0	111 (10)	768.0	592 (51)	512.4

Note: ~RSV season corresponds from week 40 of the first year to week 20 of the following year. Data for the 2020/21 season were excluded as there was a very low number of events during this period, due to the influence of COVID-19.
Source: Health Protection Surveillance Centre

Figure 3.6 Notified RSV hospital admission rates per 100,000 for those aged 0 to 2 years in Ireland, reported by age band and season

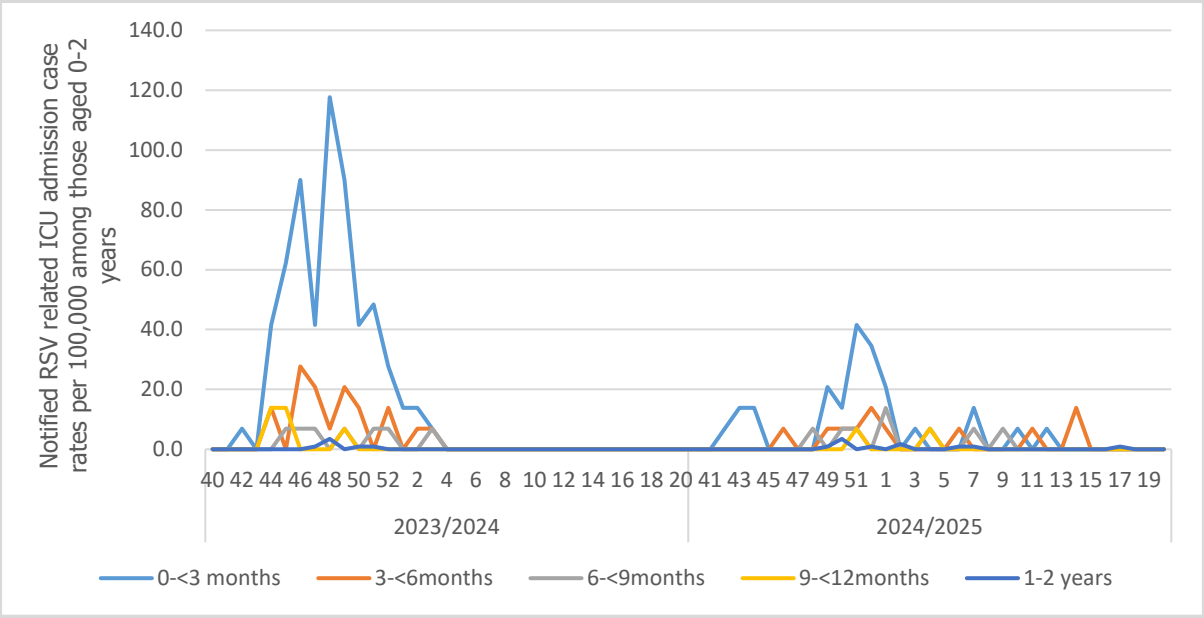


Note: RSV season corresponds from week 40 of the first year to week 20 of the following year.
Source: Health Protection Surveillance Centre

ICU admissions related to RSV

Data on notified RSV ICU admissions for those aged 0 to 2 years are only available for the 2023/24 (n= 125) and the 2024/25 RSV (n= 61) seasons. These RSV-related ICU admission rates are presented by age band and epidemiological week in Figure 3.7. In the 2023/24 season, infants aged less than six months accounted for 85% (n=106) of the total ICU admissions in children aged less than two years, with 70% of this burden in infants aged less than three months (n=87). In the latest season of 2024/25, there was a significant reduction in the ICU admissions among those aged less than three months (n=29). Considering these very limited data, in 2024, weekly ICU admission rates among those aged less than three months and those aged between 3 to 6 months from week 40 to 52 were typically lower compared with the equivalent period in 2023. The peak rate was lower in the 2024/25 season (5.2 vs 12.7 ICU admissions per 100,000) and occurred slightly later than in the 2023/24 season (week 51 vs week 48).

Figure 3.7 Notified RSV related ICU admission rates per 100,000 for those aged 0-2 years in Ireland, reported by epidemiological weeks per season and by age band



Source: Health Protection Surveillance Centre.

Burden on tertiary hospitals

A retrospective, observational cohort study evaluating the impact of the Pathfinder programme on RSV related paediatric intensive care unit (PICU) admissions in Ireland (comprising data from Children's Health Ireland (CHI) at Crumlin and CHI at Temple Street) compared data across two RSV seasons (before and after implementation of the Pathfinder programme) as shown in Table 3.7. [122] The study concluded that the administration of nirsevimab to infants born during the 2024/25 RSV season was associated with a substantial reduction (more than 50%) in PICU admissions for severe RSV bronchiolitis in Ireland (155 vs 70). There was also a statistically significant increase in the median age at admission between RSV seasons, with a marked shift towards older infants and children following implementation of Pathfinder, which is consistent with protection of the youngest infants.

The study also reported a subgroup analysis by age band showing a statistically significant reduction among neonates (aged <1 month), with a total of seven admissions compared with 35 admissions in 2023/24. A reduction was also observed

for infants between one month up to six months of age (although this outcome was underpowered for statistical significance).

Table 3.7 RSV-related PICU admissions for those aged 0-2 years

	2023/24 RSV season	2024/25 RSV season
Age band	**n (% of all PICU admissions)**	**n (% of all PICU admissions)**
<1 month	35 (22.6%)	7 (10.0%)
≥1- <6 months	83 (53.5%)	33 (47.1%)
≥6 months- <1 year	11 (7.1%)	11 (15.7%)
1 - <2 years	9 (5.8%)	10 (14.3%)
≥ 2 years	17 (10.9%)	9 (12.8%)
Total PICU admissions	155	70
Incidence	2.8 per 1,000 live births	1.29 per 1,000 live births
Median age at admission	1.91 months IQR: 1.07-5.54 months	4.56 months IQR: 1.73-13.43 months

Key: IQR – interquartile range; RSV – respiratory syncytial virus; PICU - paediatric intensive care unit.
Note: Data were gathered for the 2023/24 RSV season from 1 October 2023 to 9 January 2024 (100 days) and for the 2024/25 RSV season from 1 September 2024 to 17 March 2025 (197 days).
Source: Children's Health Ireland

The authors observed that there were differences in the clinical characteristics of PICU patients between the two RSV seasons. A significant increase in the incidence of viral co-infections was observed in those admitted in the 2024/25 RSV season, with over 40% of RSV-related PICU admissions diagnosed with at least one additional respiratory virus, compared with 27.7% in the preceding season. In addition (although this finding was underpowered for statistical significance) it is notable that in the 2024/25 RSV season, infants with underlying conditions and or prematurity constituted a higher proportion (37.1%) of admissions as compared with admissions from the previous RSV season (25.2%). The total PICU bed days attributable to RSV were reported as having declined by 70% compared with the 2023/24 season.

RSV discharges and bed days (primary diagnosis)

Data from the HIPE system in Ireland were used to examine hospital discharges with and without an ICU stay for those aged 0 to 2 years with a primary or secondary diagnosis of RSV (with ICD-10 codes B97.4, J12.1, J20.5 and J21.0) or acute bronchiolitis (with ICD-10 codes J21.8 and J21.9). A HIPE discharge record is created when a patient is discharged from or dies in hospital. This record contains information for a discrete episode of care. An episode of care begins at admission to hospital, as a day patient or inpatient, and ends at discharge from (or death in) that hospital.[106] These data are not available by RSV season, but instead were provided quarterly by year and are reported below separately for RSV and acute bronchiolitis. Q4 (October to December) and Q1 (January to March) broadly approximate the reporting period for the RSV season (2024/25, week 40 to week 20: week beginning 30 September 2024 to week beginning 12 May 2025).

Table 3.8 provides an overview of inpatient discharges with a primary diagnosis of RSV in those aged 0 to 2 years, from 2018 to Q1 2025 presented by age band and quarter. Data suppression due to low count numbers limit some comparisons; however, overall, the number of hospital discharges with a primary diagnosis of RSV (regardless of whether the patient had a stay in ICU) was substantially higher in infants aged less than one year as compared with those aged between 1 to 2 years. Further disaggregation within these age bands was not possible using the HIPE data. In addition, Q4 accounted for the greatest proportion of annual discharges with or without an ICU stay (excluding data from 2020 due to the influence of the COVID-19 pandemic) in all years for which there were complete data. Specifically, considering infants aged less than one year, 69% to 88% of all hospital discharges without an ICU stay occurred in Q4.

Table 3.8 Hospital discharges for those aged 0 to 2 years with a primary diagnosis of RSV (2018 to 2024) reported by age band and quarter

Year	Year Quarter (Q)	Hospital discharges without an intensive care unit stay (% of annual discharges)		Hospital discharges with an intensive care unit stay (% of annual discharges)	
		<1 year	1-2 years	<1 year	1-2 years
2018	Q1	299 (26)	37(^)	34 (^)	- (-)
	Q2	36 (3)	- (-)	- (-)	0 (0)
	Q3	10 (1)	- (-)	- (-)	0 (0)
	Q4	785 (69)	175 (^)	59 (^)	10 (^)
2019	Q1	321 (26)	40 (^)	26 (^)	- (-)
	Q2	15 (1)	- (-)	- (-)	0 (0)
	Q3	23 (2)	- (-)	- (-)	0 (0)
	Q4	857 (70)	185 (^)	97 (^)	7 (^)
2020	Q1	264 (^)	58 (^)	35 (^)	- (-)
	Q2	- (-)	0 (0)	- (-)	0 (0)
	Q3	- (-)	- (-)	0 (0)	0 (0)
	Q4	0 (0)	- (-)	0 (0)	0 (0)
2021	Q1	- (-)	0 (0)	0 (0)	0 (0)
	Q2	0 (0)	- (-)	0 (0)	0 (0)
	Q3	108 (^)	31 (^)	- (-)	- (-)
	Q4	1261 (^)	232 (^)	108 (^)	18 (^)
2022	Q1	65 (3)	- (-)	9 (^)	- (-)

Year	Year Quarter (Q)	Hospital discharges without an intensive care unit stay (% of annual discharges)		Hospital discharges with an intensive care unit stay (% of annual discharges)	
		<1 year	1-2 years	<1 year	1-2 years
	Q2	39 (2)	6 (^)	- (-)	- (-)
	Q3	164 (9)	41 (^)	10 (^)	0 (0)
	Q4	1601 (86)	279 (^)	163 (^)	9 (^)
2023	Q1	155 (8)	28 (^)	20 (^)	- (-)
	Q2	24 (1)	- (-)	0 (0)	0 (0)
	Q3	47 (3)	- (-)	- (-)	0 (0)
	Q4	1598 (88)	307 (^)	148 (^)	12 (^)
2024	Q1	203 (27)	34 (^)	15 (^)	33 (^)
	Q2	15 (2)	6 (^)	0 (0)	0 (0)
	Q3	12 (2)	- (-)	- (-)	0 (0)
	Q4	527(70)	226 (^)	40 (^)	12 (^)
2025	Q1	329 (*)	121 (*)	28 (*)	- (-)

Note: Hospital discharges associated with a primary diagnosis of RSV from the specified list of diagnosis codes. For reasons of confidentiality, counts are suppressed for cells where the number of discharges is between 1 and 5 (and replaced by -). To ensure that the values in these suppressed cells are not disclosed, further suppression of other cells may be necessary. Where this is the case, the number is replaced by ^. *Q1 data only available for 2025.
Source: Hospital In-Patient Enquiry System

Table 3.9 reports the annual hospital discharges, annual bed days and mean length of stay for those aged 0 to 2 years with a primary diagnosis of RSV (from 2018 to 2024), disaggregated into two age bands (<1 year vs 1 to <2 years) and reported separately for those with and without an ICU stay. The data highlight the considerable burden associated with RSV in those aged 0 to 2 years. Excluding 2020, the total number of hospital discharges in those aged 0 to 2 years (with and without and ICU admission) ranged from 1,098 (in 2024) to 2,386 (in 2022), per annum, with total bed days ranging from 3,407 (2024) to 8,453 (2022) per annum. From 2018 to 2024 (excluding 2020), on average, there were 1,633 (range 1,031 to

2,195) discharges that did not include an ICU stay per annum. The mean annual length of stay of 3.3 days and the mean total bed days per annum associated with these discharges was 5,359 (ranged 2,946 to 7,059). There were 133 (range 67 to 191) discharges that included an ICU stay. The mean annual length of stay was 8.3 days and the mean total bed days per annum associated with these discharges was 1,099 (range 462 to 1,450). It is not possible to ascertain from these data what proportion of the stay occurred in the ICU.

Irrespective of whether or not the discharge included a stay in ICU, across all years the total number of hospital discharges was substantially higher in those aged less than one year, who accounted for approximately 91% and 86% of discharges with and without an ICU stay in those aged less than two years. Considering specifically the years 2018 to 2023 (excluding 2020), the number of discharges without an ICU stay was 5 to 6 times higher in those aged less than one year (range 1,130 to 1,869) compared with discharges in those aged between one and two years (range 212 to 335). In 2024, there was a substantial reduction in the number of such discharges among children aged less than one year (n=763) compared with previous years; however, it is noted that the number of discharges was still almost three times higher than for those aged between one and two years (n=268). The mean annual length of stay in 2024 (2.9) for those aged less than one year was also the lowest reported since 2018 (range: 3.2 to 3.6).

A similar pattern was seen for discharges that included an ICU stay, with a substantially higher number of discharges in those aged less than one year (range 93 to 182) compared with discharges in those aged between one and two years (range 7 to 18) for the years 2018 to 2023 (excluding 2020). A considerable reduction in such discharges was seen in 2024 (n=55) for those aged less than one year, with a reduction also noted in the mean annual length of stay (6.9 days) compared with previous years (range: 7.3 to 10.3 days).

Table 3.9 Annual hospital discharges, annual bed days and mean length of stay for those aged 0 to 2 years with a primary diagnosis of RSV (with and without an ICU stay from 2018 to 2024) reported by age band

Without an intensive care unit stay						
	<1 year			1-2 years		
Year	Annual hospital discharges (n)*	Bed days per annum (n)*	Mean annual length of stay (days)*	Annual hospital discharges (n)*	Bed days per annum (n)*	Mean annual length of stay (days)*
2018	1,130	4,071.6	3.6	212	725.5	3.4
2019	1,216	4,380.7	3.6	225	687	3.1
2020	264	924	3.5	58	162.4	2.8
2021	1,369	4,874.4	3.6	263	779.7	3.0
2022	1,869	6,106	3.3	326	953.3	2.9
2023	1,824	5,761.5	3.2	335	871.1	2.6
2024	763	2,200.9	2.9	268	745	2.8
With an intensive care unit stay						
	<1 year			1-2 years		
Year	Annual hospital discharges (n)*	Bed days per annum (n)*	Mean annual length of stay (days)*	Annual hospital discharges (n)*	Bed days per annum (n)*	Mean annual length of stay (days)*
2018	93	954.3	10.3	10	120	12.0
2019	123	1,062.2	8.6	7	70.7	10.1
2020	35	311.5	8.9	-	-	-
2021	108	831.6	7.7	18	248.4	13.8
2022	182	1,323	7.3	9	70.2	7.8
2023	168	1,374.4	8.2	12	75.6	6.3
2024	55	377.5	6.9	12	84	7.0

Note: Hospital length of stay associated with a primary diagnosis of RSV from the specified list of diagnosis codes. Data from 2020 are not considered representative due to the influence of the COVID-19 pandemic.
*For reasons of confidentiality, counts are suppressed where the number of discharges is between 1 and 5, and or where an associated cell discloses the value of a suppressed cell. Where quarterly data were suppressed, they were excluded when calculating summary statistics. For the older age cohort annual data has also been suppressed in 2020 (and replaced by -).
Source: Hospital In-Patient Enquiry System

For the period 2018 to 2024 (excluding 2020), the total annual cost of inpatient stays for those with a primary diagnosis of RSV ranged from €2.2 (in 2024) to €6.2 million (in 2023) per annum for discharges that included an ICU stay, and from €9.9 (in 2024) to €20.4 million (in 2022) for discharges that did not include an ICU stay. In the most recent two years, for those with a primary diagnosis of RSV, the estimated total annual cost of discharges without an ICU stay was €20.3 million and €9.9 million in 2023 and 2024, respectively, while costs for discharges that included an ICU stay were €6.2 million and €2.2 million, respectively. The difference in costs between those two years was likely largely driven by the substantial reduction in the number of hospital discharges among children aged less than one year in 2024.

Note that these aggregate costs are for all age groups with a primary diagnosis of RSV, including adults, as disaggregated cost data by age group were unavailable. Moreover, costs for the most recent year available have been applied retrospectively to all years to facilitate comparisons. ICU costs are bundled into the overall average costs; due to this, any cost differential seen between discharges that include or do not include an ICU stay is mainly driven by differences in length of stay, the total number of patients in each group and assignment of diagnosis-related groups.

RSV discharges (secondary diagnosis)

Data were also sought in relation to inpatient discharges with a secondary diagnosis of RSV in those aged 0 to 2 years. Table 3.10 provides an overview of hospital discharges with a secondary diagnosis of RSV, from 2018 to 2024, presented by age band. In contrast to the discharge data for those with a primary diagnosis of RSV, the number of hospital discharges with a secondary diagnosis of RSV (regardless of whether the patient had a stay in ICU) was typically lower in those aged less than one year compared with data for those aged 1 to 2 years.

For the period 2018 to 2024 (excluding data for 2020 due to the influence of COVID-19), in infants aged less than one year, the annual number of discharges ranged from 8 to 22 and from 66 to 150 discharges for those with and without an ICU stay, respectively. In contrast, in those aged between one and two years, the annual number of discharges ranged from 6 to 12 and from 89 to 445 for those with and without an ICU stay, respectively.

Table 3.10 Hospital discharges for those aged 0 to 2 years with a secondary diagnosis of RSV (2018 to 2024) reported by age

Year	Hospital discharges without an ICU stay		Hospital discharges with an ICU stay	
	<1 year	1-2 years	<1 year	1-2 years
2018	66	89	15	6
2019	80	129	8	11
2020	26	-	11	-
2021	127	270	16	12
2022	148	352	22	7
2023	150	445	21	10
2024	109	317	10	10

Note: Hospital discharges associated with a secondary diagnosis of RSV from the specified list of diagnosis codes. For reasons of confidentiality, counts are suppressed for cells where the number of discharges is between 1 and 5 (and replaced by -).
Source: Hospital In-Patient Enquiry System

Acute bronchiolitis discharges (primary diagnosis)

It is possible that not all individuals presenting with symptoms of RSV are tested and confirmed as a case. Children with acute RSV infection frequently present with bronchiolitis, with RSV noted as the most common cause of acute bronchiolitis in children.[123] For this reason, data in relation to discharges with a primary diagnosis of bronchiolitis were also sought. Table 3.11 provides an overview of inpatient discharges with a primary diagnosis of acute bronchiolitis in those aged 0 to 2 years, from 2018 to 2025 presented by age band and quarter.

It is difficult to determine a clear pattern in the distribution of discharges with an ICU stay for those with a primary diagnosis of acute bronchiolitis due to the suppression of data for reasons of confidentiality (that is, where the number of discharges in a cell was between one and five). For discharges without an ICU stay, the number of discharges with a primary diagnosis of acute bronchiolitis were consistently higher in infants aged less than one year.

For discharges without an ICU stay, the highest proportions occurred in Q4 for each year between 2018 and 2024 (excluding data for 2020 due to the influence of COVID-19). The proportion of such discharges in Q4 ranged from 39% to 69% and from 30% to 65% of annual discharges of infants aged under one year, and infants aged between one and two years, respectively.

Data from HIPE for the period 2018 to 2024 (excluding 2020) shows the total annual cost of inpatient stays for those with a primary diagnosis of acute bronchiolitis ranged from €0.8 million (in 2021) to €3.8 million (in 2022) for cases with an ICU stay, and from €7.3 million (in 2021) to €13.1 million (in 2018) for cases without an ICU stay. For the most recent year, the total annual cost of inpatient stays for those with a primary diagnosis of acute bronchiolitis was €2.8 million for cases with an ICU stay, and €12.9 million for cases without an ICU stay in 2024. Note that costs for the most recent year available have been applied retrospectively to all years for a comparative analysis and these costs are for all age groups with a primary diagnosis of acute bronchiolitis. ICU costs are bundled into the overall average costs. As such any cost differential seen between the ICU and non-ICU discharges is driven mainly by differences in length of stay and assignment of DRGs.

Table 3.11 Hospital discharges for those aged 0 to 2 years with a primary diagnosis of acute bronchiolitis (2018 to 2024) reported by age band and quarter

Year	Year Quarter (Q)	Hospital discharges without an intensive care unit stay (% of annual discharges)		Hospital discharges with an intensive care unit stay (% of annual discharges)	
		<1 year	1-2 years	<1 year	1-2 years
2018	Q1	476 (31)	47 (25)	- (-)	- (-)
	Q2	260 (17)	32 (17)	- (-)	- (-)
	Q3	113 (7)	28 (15)	- (-)	- (-)
	Q4	672 (44)	81 (43)	- (-)	- (-)

Year	Year Quarter (Q)	Hospital discharges without an intensive care unit stay (% of annual discharges)		Hospital discharges with an intensive care unit stay (% of annual discharges)	
		<1 year	1-2 years	<1 year	1-2 years
2019	Q1	431 (29)	48 (27)	- (-)	- (-)
	Q2	200 (13)	21 (12)	8 (^)	- (-)
	Q3	146 (10)	14 (8)	- (-)	- (-)
	Q4	724 (48)	96 (54)	20 (^)	9 (^)
2020	Q1	309 (61)	49 (^)	16 (^)	- (-)
	Q2	17 (3)	- (-)	- (-)	0 (0)
	Q3	70 (14)	- (-)	- (-)	- (-)
	Q4	112 (22)	25 (^)	10 (^)	- (-)
2021	Q1	40 (5)	6 (4)	- (-)	0 (0)
	Q2	69 (8)	11 (7)	7 (^)	0 (0)
	Q3	166 (19)	38 (25)	8 (^)	- (-)
	Q4	604 (69)	100 (65)	18 (^)	- (-)
2022	Q1	255 (20)	33 (19)	15 (^)	- (-)
	Q2	284 (22)	36 (20)	- (-)	- (-)
	Q3	232 (18)	31 (18)	- (-)	- (-)
	Q4	508 (40)	76 (43)	19 (^)	- (-)
2023	Q1	457 (32)	37 (26)	- (-)	- (-)

Year	Year Quarter (Q)	Hospital discharges without an intensive care unit stay (% of annual discharges)		Hospital discharges with an intensive care unit stay (% of annual discharges)	
		<1 year	1-2 years	<1 year	1-2 years
	Q2	289 (20)	33 (23)	13 (^)	- (-)
	Q3	199 (14)	30 (21)	11 (^)	- (-)
	Q4	469 (33)	42 (30)	- (-)	- (-)
2024	Q1	452 (30)	54 (26)	21(^)	- (-)
	Q2	406 (27)	52 (25)	17 (^)	6 (-)
	Q3	190 (13)	31 (15)	6 (^)	- (-)
	Q4	436 (29)	71 (34)	23 (-)	- (-)
2025	Q1	350 (*)	34 (8)	8 (*)	- (-)

Note: Hospital discharges associated with a primary diagnosis of acute bronchiolitis from the specified list of diagnosis codes. For reasons of confidentiality, counts are suppressed for cells where the number of discharges is between 1 and 5 (and replaced by -). To ensure that the values in these suppressed cells are not disclosed, further suppression of other cells may be necessary. Where this is the case, the number is replaced by ^. *Q1 data only available for 2025.

Source: Hospital In-Patient Enquiry System

3.5.2 Complications and hospitalisations (older adults)

RSV-related emergency department visits

Notified RSV ED visit rates per 100,000 for adults aged 65 years and older are reported in Table 3.12 and graphically in Figure 3.8 by age band and RSV season. As noted previously, ED cases exclude those who presented to the ED, but who were reported as being admitted to hospital; the number of notified ED cases does not therefore include all cases attending ED. In those aged 65 years and older, the notified ED visit rate reported for the 2024/25 RSV season (77.4 per 100,000) was the highest observed across all seven seasons of data examined in this HTA.

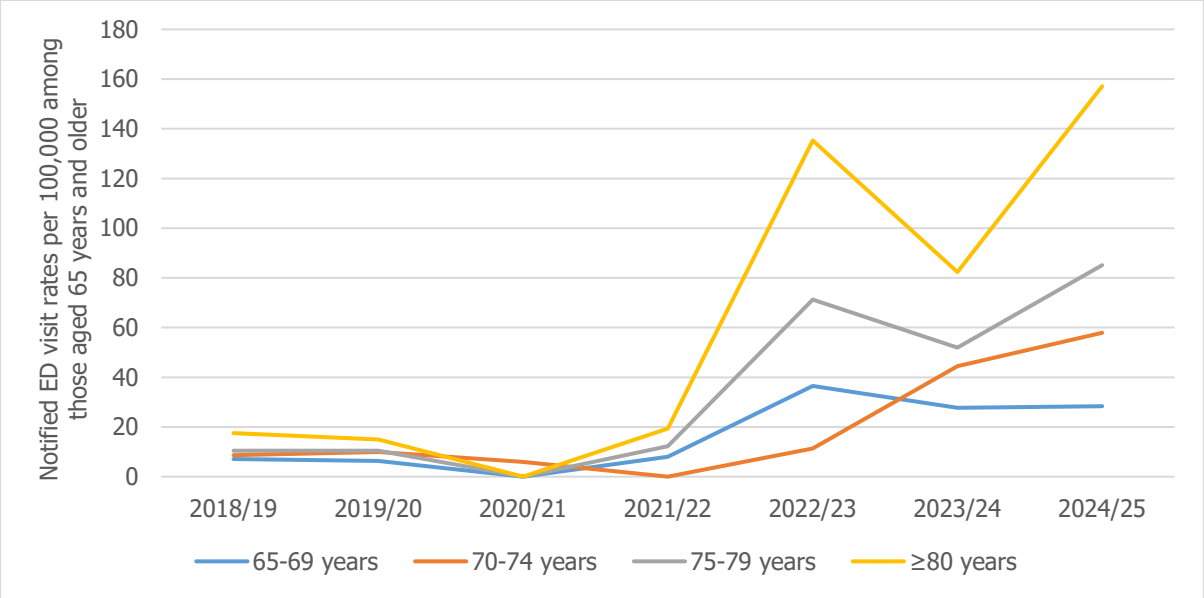
Across all seasons (excluding 2020/21 due to the influence of COVID-19), ED visit rates generally increased with increasing age and were consistently highest in those aged 80 years and older (range: 14.9 to 157.1 per 100,000), with this subgroup accounting for a mean of 45% (range: 35% to 53%) of all seasonal ED visits in older adults. Moreover, there appears to be a general trend of increasing ED visit rates over time in all age bands, although as noted previously, these data must be considered in the context of a change in testing practices since the COVID-19 pandemic.

Table 3.12 Notified RSV emergency department visits for those aged 65 years and older in Ireland, reported by age band

RSV season~	≥65 years		65-69 years		70-74 years		75-79 years		≥80 years	
	n	Rate per 100,000	n (%)	Rate per 100,000	n (%)	Rate per 100,000	n (%)	Rate per 100,000	n (%)	Rate per 100,000
2018/19	67	10.5	15 (22)	7.	14 (21)	8.6	12 (18)	10.4	26 (39)	17.5
2019/20	78	10	15 (19)	6.3	20 (26)	9.9	16 (21)	10.4	27 (35)	14.9
2021/22	73	9.4	19 (26)	8	0 (0)	0	19 (26)	12.3	35 (48)	19.3
2022/23	465	59.9	87 (19)	36.5	23 (5)	11.3	110 (24)	71.3	245 (53)	135.3
2023/24	385	49.6	66 (17)	27.7	90 (23)	44.4	80 (21)	51.9	149 (39)	82.3
2024/25	601	77.4	68 (11)	28.4	117 (20)	57.9	132 (22)	85.1	284 (47)	157.1

Note:
~ RSV season corresponds to week 40 of the first year to week 20 of the following year. Data for the 2020/21 season were excluded as there was a very low number of events during this period, due to the influence of COVID-19.
Source: Health Protection Surveillance Centre.

Figure 3.8 Notified RSV emergency department visit rates per 100,000 for those aged 65 years and older in Ireland, reported by age band and season



Source: Health Protection Surveillance Centre

RSV related hospital admissions

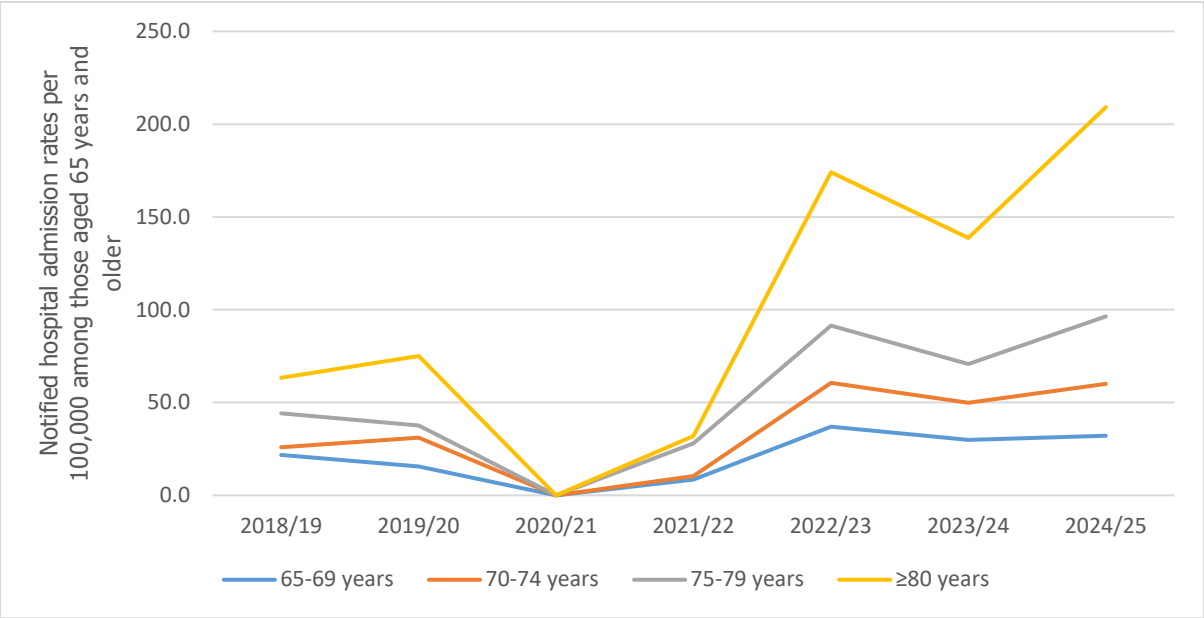
Notified RSV hospital admission rates per 100,000 for adults aged 65 years and older are reported in Table 3.13 and graphically in Figure 3.9 by age band and season. In those aged 65 years and older, the notified hospital admission rate reported for the 2024/25 RSV season (93.4 per 100,000) was the highest observed across all the seasons examined in the HTA. Rates of hospital admissions generally increased with increasing age and were consistently highest in those aged 80 years and older, with notified admission rates ranged from 32.0 to 209.1 per 100,000 in the 2021/22 and 2024/25 RSV seasons, respectively (excluding 2020/21 due to the influence of COVID-19 pandemic). Overall, those aged 80 years and older accounted for 48% (range 40% to 52%) of all RSV hospital admissions among those aged 65 years and older across these seasons. As with the RSV-related ED visit rates, there appeared to be a general trend of increasing hospitalisation rates over time, with increases seen in all age bands.

Table 3.13 Notified RSV hospital admissions for those aged 65 years and older in Ireland, reported by age band

RSV season~	≥65 years		65-69 years		70-74 years		75-79 years		≥80 years	
	n	Rate per 100,000	n (% of ≥65 years)	Rate per 100,000	n (% of ≥65 years)	Rate per 100,000	n (% of ≥65 years)	Rate per 100,000	n (% of ≥65 years)	Rate per 100,000
2018/19	233	36.5	46 (20)	21.8	42 (18)	25.9	51 (22)	44.2	94 (40)	63.3
2019/20	294	37.9	37 (13)	15.5	63 (21)	31.1	58 (20)	37.6	136 (46)	75.1
2021/22	142	18.3	20 (14)	8.4	21 (15)	10.4	43 (30)	27.9	58 (41)	32.0
2022/23	667	85.9	88 (13)	37.0	123 (18)	60.6	141 (21)	91.4	315(47)	174.0
2023/24	532	68.5	71 (13)	29.8	101 (19)	49.8	109 (20)	70.7	251 (47)	138.7
2024/25	725	93.4	77 (11)	32.2	121 (17)	60.0	149 (21)	96.4	378 (52)	209.1

Note: ~RSV season corresponds from week 40 of the first year to week 20 of the following year. Data for the 2020/21 season were excluded as there was a very low number of events during this period, due to the influence of COVID-19.
Source: Health Protection Surveillance Centre.

Figure 3.9 Notified RSV hospital admission rates per 100,000 for those aged 65 years and older in Ireland, reported by age band and season



Source: Health Protection Surveillance Centre

ICU admissions related to RSV

HPSC data on notified RSV ICU admissions are only available for the 2023/24 and 2024/25 seasons. ICU admissions related to RSV in those aged 65 years and older were uncommon, with a total of seven and 13 such admissions reported in the 2023/24 and 2024/25 RSV seasons, respectively.

RSV discharges and bed days (primary diagnosis)

HIPE data were used to examine hospital discharges with and without an ICU stay in those aged 65 years and older years that had a primary or secondary diagnosis of RSV. Table 3.14 provides an overview of the discharges with a primary diagnosis of RSV that did not include an ICU stay. Excluding 2020 (due to the influence of COVID-19), there were a total of 409 discharges between 2018 and 2024, while provisional data indicate that there were 118 discharges in Q1 2025 alone. Adults aged 80 years and older accounted for 67% (n=273) of all discharges between 2018 and 2024. Due to data suppression, it was not possible to calculate mean annual length of stay in all age bands, but where data were available to support comparisons, it was generally highest in those aged 80 years and older, ranging

from 8 to 16 days in this cohort. Discharges that included an ICU stay were uncommon for this diagnosis, resulting in data suppression when disaggregated by five-year age band.

Table 3.14 Total hospital discharges and length of stay (without an ICU stay) in adults aged 65 years and older with a primary diagnosis of RSV from 2018 to 2024 (excluding 2020) reported by age band and year

	≥65 years*			65-69 years*		70-74 years*		75-79 years*		≥80 years*	
Year	**Total hospital discharges**	**Bed days per annum**	**Mean annual length of stay in days**	**Total hospital discharges (%)**	**Mean annual length of stay in days**	**Total hospital discharges (%)**	**Mean annual length of stay in days**	**Total hospital discharges (%)**	**Mean annual length of stay in days**	**Total hospital discharges (%)**	**Mean annual length of stay in days**
2018	8	130.4	16.3	0	0	-	-	-	-	8	16.3
2019	28	235.2	8.4	-	-	-	-	-	-	28	8.4
2021	16	146.2	9.1	-	-	6	8.2	-	-	10	9.7
2022	122	1121.8	9.2	21	5.9	14	7.4	27	10.9	60	10.0
2023	130	1825.0	14.0	12	5.5	-	-	15	7.4	103	16.0
2024	105	975.2	9.3	8	5.5	18	7.6	15	5.6	64	11.1
2025 (Q1)	118			-	-	18	8.5	21	12.3	79	14.9
2018-2024	**409**	**4,433.8**		**41 (10)**		**38 (9)**		**57 (14)**		**273 (67)**	

Note: Hospital discharges associated with a primary diagnosis of RSV from the specified list of diagnosis codes. Data from 2020 are excluded as they were not considered representative due to the influence of the COVID-19 pandemic. Data for 2025 (Q1) are provisional. For reasons of confidentiality, counts are suppressed for cells where the number of discharges is between 1 and 5, and or where an associated cell discloses the value of a suppressed cell (and replaced by -). Further suppression of other cells may also be necessary.
*Where suppressed data were present, they were excluded when calculating summary statistics.
Source: Hospital In-Patient Enquiry System

RSV discharges (secondary diagnosis)

Data were also sought in relation to annual inpatient discharges with a secondary diagnosis of RSV in those aged 65 years and older which are presented in Table 3.15 by age band for the period 2018 to 2025 (provisional data for Q1 only). The data indicate a substantial increase in the number of discharges with RSV as a secondary diagnosis across all age groups from 2022 onwards, possibly as a consequence of a change in testing practices following the COVID-19 pandemic. The number of hospital discharges with a secondary diagnosis of RSV was consistently highest in those aged 80 years and older, with this cohort accounting for an annual average of 46% (range: 42% to 50%) of all such diagnoses in those aged 65 years and older. Preliminary data show that in 2025 there were 525 such discharges in those aged 65 years and older in Q1 alone, with 52% of this burden in those aged 80 years and older.

Table 3.15 Hospital discharges for adults aged 65 years and older with a secondary diagnosis of RSV reported by age band

	≥ 65 years	65-69 years	70-74 years	75-79 years	≥80 years
Year	**n**	**n (% ≥ 65 years)**	**n (% ≥ 65 years)**	**n (% ≥ 65 years)**	**n (% ≥ 65 years)**
2018	106	16 (15)	19 (18)	20 (19)	51 (48)
2019	165	25 (15)	35 (21)	35 (21)	70 (42)
2020	126	18 (14)	28 (22)	26 (21)	54 (43)
2021	77	16 (21)	10 (13)	16 (21)	35 (46)
2022	601	86 (14)	114 (19)	125 (21)	276 (46)
2023	602	82 (14)	102 (17)	118 (20)	300 (50)
2024	522	61 (12)	83 (16)	122 (23)	256 (49)
2025 (Q1)	525	58 (11)	84 (16)	112 (21)	271(52)

Note: Hospital discharges associated with a secondary diagnosis of RSV from the specified list of diagnosis codes. Data include discharges with and without an ICU stay. Data for 2025 (Q1) are provisional.
Source: Hospital In-Patient Enquiry System

3.5.3 Mortality in Ireland

RSV-related mortality data were obtained from the HPSC and HIPE. Data on notified RSV-related deaths, are only available for the 2023/24 and 2024/25 RSV seasons from the HPSC. As such data are contingent on RSV being listed as a cause of death on a death certificate, mortality related to RSV in Ireland is underestimated in all patient cohorts. Note that deaths may not be recorded as related to RSV even when RSV infection may have been the cause of a deterioration of an underlying condition or increased susceptibility to a secondary infection. Mortality data could not be ascertained from the data obtained from HIPE due to suppression of the majority of data due to small count numbers.

Children aged less than two years

According to HPSC data, the mortality rate among notified cases of RSV in the 2023/24 season was very low (0.6 per 100,000) in children aged less than two years. For the 2024/25 season, no deaths were reported among this cohort.

Older adults aged 65 years and older

In those aged 65 years and older, there were 38 deaths reported among notified cases of RSV, indicating a mortality rate of 4.9 per 100,000 in the 2023/24 season, with 66% of these deaths occurring in adults aged 80 years and older. For the 2024/25 season, there were 47 deaths (6.1 per 100,000) reported among those aged 65 years and older, with 68% of these deaths in those aged 80 years and older.

3.5.4 Burden in EU/EAA countries and the UK

The ECDC and WHO Regional Office for Europe have jointly developed the European Respiratory Virus Surveillance Summary (ERVISS) which provides an epidemiological summary for respiratory viruses including RSV.[124] ERVISS reported that the 2024/25 winter respiratory virus epidemiology in the EU/EEA included an RSV epidemic that had a big impact on secondary care for children aged under five years. Overall, respiratory virus activity observed in the EU/EEA during the 2024/25 winter season was characterised by intense influenza activity and the co-circulation of RSV which placed pressure on healthcare systems and hospital capacity.[124] The December 2024 ECDC epidemiological update on acute respiratory infections reported that children aged up to four years, and in particular young infants, had the highest risk of hospitalisation for RSV with over 40% of tests among severe acute respiratory infections (SARI) admissions in this age group positive for RSV from week 47, 2024. This age group, followed by those aged 65 years and older, accounted for 83% and 11%, respectively, of the RSV-positive SARI admissions

between weeks 40-49 in 2024. Subsequent ICU admissions occurred most commonly in infants, while reported deaths tended to be concentrated in older age groups.[125]

The UK yearly overview of seasonal respiratory viruses for the 2023/24 RSV season used sentinel surveillance system data and reported that RSV activity was consistent with the 2022/23 and other recent pre-pandemic seasons. Overall in the UK, the highest burden was seen in children aged under five years with high hospitalisation rates noted, while the next highest burden was seen in those aged over 65 years.[126] In England, the RSV hospitalisation rate for children aged under five peaked at 44.83 per 100,000 in week 48, 2023. The rate for those aged over 65 years peaked at 6.43 per 100,000 in week 52, 2023, while considering specifically those aged over 85 years, the rate peaked at 17.26 per 100,000 in week 52, 2023. Age-stratified hospitalisation rates were not provided for Scotland, Northern Ireland or Wales in the 2023/24 overview. A July 2025 overview of UK surveillance of RSV during the 2024/25 season reported that in England the RSV hospital admission rate (excluding ICU or HDU) was highest among those aged five years or under, peaking at 46.17 per 100,000 in week 48, 2024.[127] Those aged 85 years or more had the next highest rate, peaking at 18.78 per 100,000 in week 51, 2024. For most weeks in the 2024/25 season, the majority of the cases in the cohort aged less than five years were aged less than six months. Age-stratified hospitalisation rates were not provided for the other countries in the UK, but it was noted that in Scotland RSV hospital admissions were also highest among those aged five years or under. Vaccination programmes to protect against RSV began on 1 September 2024 in England, Wales, and Northern Ireland, and on 1 August 2024 in Scotland. Early vaccine impact analyses in England and Scotland indicate a reduction in expected RSV-related hospitalisation rates among eligible older adults aged 75 to 79-years-old. This was estimated as a 33% (95% CI 23% to 39%) and a 62% (95% CI 35% to 80%) reduction in England and Scotland, respectively. It was noted that the difference in impact may reflect the differences in vaccination coverage and programme start dates between England and Scotland. An impact assessment of the UK maternal RSV vaccination programme has not yet been published.

3.5.5 Burden among high-risk groups

With the exception of the age-based data presented in sections 3.5.1 to 3.5.3, there are limited Irish data to support the identification of groups that might be at high risk of severe disease and or to estimate the additional burden in these groups relative to the general population. Evidence in relation to infants and for adults at increased risk of severe disease was identified based on a scoping review of the literature and is detailed below.

A 2024 systematic review and meta-analysis of the global burden of disease and risk factors of RSV among infants and young children in 2019 provided evidence on risk factors for severe infections. Underlying medical conditions, including congenital heart disease, tracheostomy, bronchopulmonary dysplasia, chronic lung disease and Down syndrome, were all consistently associated with a higher risk of severe RSV outcomes. RSV-related ALRI and hospitalisation rates were significantly higher in early preterm infants (born before 32 weeks' gestation) compared with infants born at any gestational age, with a significantly higher relative risk of hospitalisation also observed for this cohort in their second year of life. For late preterm infants, while RSV-related ALRI rates were similar to that of all infants aged less than one year, hospitalisation rates were significantly higher in the first six months. Higher chronological age and gestational age were associated with a lower risk for severe outcomes.[128]

NIAC have recommended the passive immunisation with nirsevimab of all infants aged up to 12 months at high risk.[28] Groups categorised as being at high risk of severe disease align with those previously eligible to receive palivizumab prophylaxis. These categories were adapted from the American Academy of Pediatrics (AAP) 2014 guidance[129] and their more recent 2023 technical report[130] on the use of palivizumab which summarise the relevant literature regarding children at the highest risk of severe RSV disease. Chronologic age was noted to be the single most important risk factor for RSV hospitalisation on the basis of the observation that more than 58% to 64% of paediatric RSV hospitalisations occur in the first five months after birth, with most of these hospitalisations occurring in the first 90 days. Aside from chronologic age, the report highlighted that infants with certain risk factors, such as prematurity, chronic lung disease (CLD), or hemodynamically-significant congenital heart disease, have an increased risk of hospitalisation due to RSV, although the degree of risk was found to vary among studies.[130]

Prematurity is an important risk factor for severe RSV disease. Among preterm infants, those born at less than 29 weeks of gestation have one of the highest risks of severe morbidity and hospitalisation from RSV.[130] Overall the data demonstrate a substantial increase in the risk of RSV hospitalisation in infants born at less than 29 weeks' gestation compared with other preterm and term infants. The AAP noted evidence to suggest an increased rate of RSV hospitalisations in preterm infants born at more than 29 weeks' gestation compared with term infants, but this finding was not consistent across studies, with small sample sizes and varying methodology precluding comparisons. Overall, there was a lack of consistent and robust evidence indicating that infants born at more than 29 weeks' gestation without chronic lung disease (CLD) had a higher risk of severe RSV disease as compared with healthy

term infants. Preterm infants with CLD due to prematurity have increased rates of RSV hospitalisation and these elevated rates are noted to be sustained through their second year of life.[130]

Evidence in relation to adults at increased risk from severe disease due to RSV was identified from a number of US-based retrospective and prospective cohort studies in addition to evidence identified based on a search for published systematic reviews. There were differences between the studies in terms of the methodology, population and risk factor definitions; however, there was a general consistency in terms of the populations identified to be at high risk, albeit noting that the reported magnitude of relative risks differed. A study published in 2017 reported the rates of RSV-related hospitalisations in the US from 1997 to 2009 according to risk status. Individuals with chronic obstructive pulmonary disease (COPD), cardiovascular disorders, kidney disorders, diabetes, immunosuppression, liver disorders, stroke or central nervous system disorders were considered to be at high risk of RSV disease. Those without any of these conditions were considered to be at low risk of RSV disease. The rate of hospitalisation was 11.1 times higher in high-risk individuals aged 65 to 74 years compared with low-risk individuals, and five times higher in high-risk individuals aged 75 years and older compared with those at low risk.[131]

A prospective study that followed adults aged 60 years and older for 12 consecutive winter seasons, from 2004/05 through 2015 in the US, reported a significantly higher risk of severe outcomes among individuals with comorbidities. The relative risk of severe outcomes, measured in terms of hospitalisation, was 2.18 times higher among individuals with COPD and 2.38 times higher among those with congestive heart failure, compared with individuals without a comorbid condition. The risk was also elevated among patients with asthma, immunocompromised status, and diabetes, but these associations were not statistically significant. Additionally, the study reported a significantly higher risk of hospitalisation among patients aged 75 years and older compared with those aged 65 to 74 years.[132]

A 2022 systematic review of RSV in developed countries described the burden among those who are at risk of severe outcomes of RSV infection due to underlying comorbidities.[117] The review specifically considered the burden associated with laboratory-confirmed RSV in adults aged 60 years and older and in those aged 18 years or older at increased risk of complications due to a range of underlying conditions. The meta-analysis indicated that (based on 19 included studies with risk groups comprising diabetes, cardiopulmonary disease, asthma, immunodeficiency and institutionalised older adults), 32.8% (95% CI 23.5–43.7%) of RSV-positive patients at high-risk of complications required hospitalisation. Moreover, 26.7% (95% CI 20.4–34.2%) of all RSV-positive patients at high-risk (based on 14 studies with risk groups comprising chronic kidney disease, diabetes, cardiopulmonary

disease and immunodeficiency) were admitted to ICU. Within a subgroup of RSV-positive patients who were immunodeficient, 35.3% (95% CI 29.8–41.3%) developed pneumonia (six studies), 20.6% (95% CI 2.2–74.8%) had respiratory failure (three studies), 24.1% (95% CI 16.4–34.0%) were admitted to ICU (10 studies), 13.7% (95% CI 7.9–22.6%) required ventilatory support (five studies) and 38.3% (95% CI 29.3–48.2%) were hospitalised (13 studies). The estimated case fatality proportion (CFP) was 10.8% (95% CI 6.5–17.6%) in RSV patients with cardiopulmonary disease (six studies), and 9.3% (95% CI 5.4–15.4%) among patients who were immunodeficient (18 studies). In a subgroup analysis restricted to Europe, the CFP among all RSV-positive adults at high-risk was estimated to be 13.0% (95% CI 9.2–18.1%). While this review has limitations, including the combining of studies with medically-attended and community cohort populations, it highlights the significant burden of RSV in adults with comorbidities.[117]

A 2023 systematic review synthesised data from 26 studies to estimate the relative risk of severe RSV disease outcomes (hospitalisation, mortality, LRTI or pneumonia, or a composite measure) in adults by age group, or on the basis of specific comorbidities or living conditions in high-income countries.[133] There was substantial heterogeneity in the magnitude of measured relative risks between studies, likely due to differences in study methodology, risk factor definitions, and population. However, there was evidence that chronic cardiac, pulmonary and kidney diseases, diabetes, immunocompromising conditions and certain living conditions (such as low socioeconomic status and nursing home residence) are associated with an increased risk of severe RSV infection outcomes in adults. Where the data could be compared, the authors noted a similar frequency of severe outcomes among younger adults with comorbidities to that experienced by older adults.

A 2025 systematic review on the burden of RSV in adults with asthma or COPD in high-income countries reported that they are at high risk of developing severe RSV symptoms.[134] In inpatient settings, the pooled prevalence of asthma and COPD among RSV-infected adults was estimated at 19.3% (95% CI: 15.0-24.6) and 30.8% (95% CI: 26.1-36.0), respectively. Additionally, adults with asthma or COPD were more likely to be hospitalised following RSV infection than those without these conditions, with adjusted incidence rate ratios (IRRs) of 6.7-8.2 for asthma and 9.6-9.7 for COPD. Exacerbation of the underlying condition was common following RSV infection, reported in up to 64.9% of those with asthma and up to 83.0% of those with COPD. Moreover, among hospitalised RSV-infected adults, case fatality rates ranged from 2.6%-4.3% in those with asthma and from 2.8%-17.8% in those with COPD.

A 2024 systematic review on the burden of RSV infection among adults in nursing and care homes found the available data on RSV infection among nursing and care

home residents to be largely heterogeneous and limited.[119] However, the review noted that chronic medical conditions were more commonly reported among RSV cases compared with non-RSV cases in nursing and care homes. These chronic medical conditions included (congestive) heart failure, COPD, respiratory allergy, hypertension, diabetes mellitus, kidney dysfunction, malignancy, dementia, cerebrovascular accident, ischemic heart disease, coronary artery disease, end-stage renal disease or multiple comorbidities.

3.6 Size of the target population in Ireland

Population groups considered for this HTA are infants and adults aged 65 years and older. As described in Chapter 2, in October 2023, NIAC recommended the passive immunisation of all infants against RSV during their first RSV season, and the vaccination of adults aged 65 years and older prior to the commencement of the RSV season. [26, 27] In October 2025, NIAC updated its recommendations for older adults to include those aged 60 to 74 years with any additional risk factors for severe RSV disease and those aged 60 years and older living in long-term care facilities, while increasing the recommended starting age of age-based vaccination from 65 to 75 years.[135] The number of people potentially eligible for immunisation are described by group in this section. Data sources of these estimated population sizes included the CSO's reports and population projections, the Healthcare Pricing Office's perinatal statistics report, communications received from the HSE's Pathfinder Programme, the HSE's Primary Care Reimbursement Service (PCRS), the HSE's Structured Chronic Disease Management Treatment Programme in General Practice report and Economic and Social Research (ESRI) projections.

Table 3.17 below summarises the total eligible population for immunisation.

3.6.1 Infants in the general population

In 2024, there were 54,062 registered births in Ireland.[136] Over the past decade, the number of annual registered births decreased from 68,930 in 2013 to 54,678 in 2023. Due to a projected decline in the total fertility rate, the annual average number of births is expected to continue decreasing until 2038. On average, from 2020 to 2022, 50.2% (range 49.8-50.6%) of total births occurred within the months associated with the RSV season (Jan, Feb, Sept-Dec).[137-139]

3.6.2 Infants at high risk of RSV

Data obtained from the PCRS indicate that there were, on average, 249 unique patients aged less than one year, 360 unique patients aged one to less than two years and 66 unique patients older than two years in receipt of palivizumab annually from 2019 to 2023. In 2024, there were four infants aged less than one year, 292 children aged one to less than two years and 70 children older than two years who

received palivizumab; these data relate to the 2023/24 RSV season. After the introduction of the Pathfinder Programme for the 2024/25 RSV season, all babies born between 1 September 2024 and 28 February 2025 were offered nirsevimab; this included infants who would previously have been eligible for palivizumab. For the 2024/25 season, data obtained from the Pathfinder Programme indicate that 395 infants and children at high risk of severe RSV were immunised in the community with additional immunisations of high-risk children also occurring in Children's Health Ireland (CHI) paediatric hospitals.

3.6.3 Older adults in the general population

In April 2024, CSO census data indicate that there were 833,300 people aged 65 years and older living in Ireland, representing an increase of 156,800 since 2018.[140] The cohort aged 65 years and older has increased as a proportion of the total population, from 13.8% in 2018 to 15.5% in 2024. When disaggregated by five-year age band, the highest increase was observed in those aged 75 to 79 years (38%), with the size of this subgroup increasing from 122,600 in 2018 to 169,200 in 2024. Over the same period, the subgroup aged 80 years and older increased by 25% (from 157,300 in 2018 to 198,100 in 2024). The number of people aged 65 years and older is expected to increase rapidly, reaching over 1 million nationally by 2032.[141]

3.6.4 Older adults at high risk of RSV

Adults with chronic conditions

NIAC advice highlights that older adults and adults with co-morbidities including chronic pulmonary disease, chronic cardiac conditions, diabetes mellitus, cerebrovascular disease, chronic kidney disease and other immunocompromising conditions are at increased risk of severe RSV.[26] The size of the population with these chronic conditions aged 60 years and above relevant for this HTA can be approximated from the HSE's Structured Chronic Disease Management (CDM) Treatment Programme in General Practice.[142] The CDM Treatment Programme was launched in January 2020 and initially rolled out to patients aged 70 years and older, and extended to those aged 65 years and older commencing from January 2021 and subsequently to all adults aged 18 years and older from January 2022. The CDM Treatment Programme is open to all adults who have a General Medical Services (GMS) or GP Visit Card, who are registered with a GP that accepts these cards and who have been diagnosed with at least one of the following chronic diseases: type 2 diabetes mellitus, ischaemic heart disease, atrial fibrillation, heart failure, cerebrovascular accident (CVA), transient ischaemic attack (TIA), COPD and asthma. Of note, everyone aged 70 years and older is eligible to register for a GP visit card,

whereas for other age groups, eligibility for both GMS and GP visit cards are based on meeting certain criteria and or are means-tested.

Table 3.16 presents the number of unique individuals aged 60 years and older that enrolled in the programme from 1 January 2020 to 31 December 2023, disaggregated by five-year age group. As illustrated, there were an estimated 333,758 unique individuals that enrolled in the programme during this period. It is noted that individuals are not eligible for the programme if they reside in long-term care facilities. Moreover, once enrolled in the programme, individuals are currently not removed from programme records upon death or entering long-term care, so the provided figures may be inflated.

Table 3.16 Population enrolled in the HSE's Structured Chronic Disease Management Treatment Programme in General Practice from 1 January 2020 to 31 December 2023, reported by age band

Age groups (Years)	Enrolled in Chronic Disease Management Treatment Programme (n)
Total 60+	333,758
60-64*	28,155
65-69	37,569
70-74	75,168
75-79	80,287
80-84	59,605
85-89	36,659
90+	16,315

Note: *Estimated enrolment based on data extraction from the age group distribution reported in Figure 1 of the report.
Source: The third report of the Structured Chronic Disease Management Treatment Programme in General Practice.

As the data are limited to individuals diagnosed with at least one of the specified chronic diseases who have a GMS or a GP visit card and are registered with a participating GP service, they underrepresent the total number of individuals aged 60 years and older with one of these chronic diseases. Considering chronic disease prevalence estimates from the Irish Longitudinal Study on Ageing (TILDA) and Quarterly National Household Surveys, the CDM Treatment Programme estimated that the uptake rate was 89% among eligible people with chronic disease aged 65 years and older. The uptake was estimated to be lower (61%) in those aged 18 to 64 years (61%), but it was highlighted that the programme was only expanded to include this cohort from January 2022.

As noted before, adults with chronic kidney disease (CKD) are another group identified by NIAC to be at high risk of severe RSV disease. Individuals with CKD are not currently eligible for the HSE's CDM Treatment Programme unless they have been diagnosed with at least one other of the specified conditions as a comorbid condition. A report from TILDA and the National Renal Office estimated that 15.6% of Irish adults aged 50 years and older have CKD based on data collected between 2014 and 2015. Further disaggregation of data indicate the estimated national prevalence was 4.9% and 35.8% in people aged 50 to 69 years and 70 years and older, respectively. Hypertension was the most common CKD-related condition in the Irish adult population. The estimated prevalence of CKD among individuals without diabetes and hypertension was 10.0%.[143] Separately, it is noted that 5,404 people

with CKD or kidney failure were treated by dialysis or kidney transplantation in Ireland in 2024.[144]

Residents of long-term care facilities

According to the ESRI report published in 2025, there were a total of 33,324 beds in long-term residential care facilities in 2022, with 29,579 long-stay beds and 3,745 short-stay beds. Furthermore, the report estimated that there were over 29,650 residents across these beds, with the majority (96%, n=28,394) aged 65 years and older.[145] The ESRI report does not include disaggregated data for those aged less than 65 years; however, a 2024 Ombudsman report suggests that 85% of such individuals are aged between 50 and 64 years.[146]

Table 3.17 Size of the target population potentially eligible for RSV immunisation

Potential eligible population for immunisation	Estimated size (n)	Source
Infants born during RSV season	~27,000	CSO, HPO
Infants born outside RSV season	~27,000	CSO, HPO
Infants and children (≤2 years) at high risk of RSV disease	399	Pathfinder Programme
Adults aged ≥65 years	831,921	CSO
Adults aged ≥60 years with at least one chronic condition engaged with healthcare system	333,758#	CDM Treatment Programme
Adults aged ≥60 years living in long-term care facilities	28,750*	ESRI

Key: CDM – Chronic Disease Management; CSO – Central Statistics Office; HPO - Healthcare Pricing Office; RSV – respiratory syncytial virus.
Note: # Once enrolled in the HSE's Structured Chronic Disease Management Treatment Programme in General Practice, individuals are currently not removed from programme records upon death or entering long term care, so the provided figure may be inflated. Figure based on enrollments to December 2023 and includes an estimate for those aged 60 to 64 years. * Population aged 60 to 64 years approximated based on age distribution of nursing home residents aged less than 65 years.[146]

3.7 Treatment of RSV

As described in Chapter 2, in healthy individuals, RSV typically presents as a self-limiting disease. As such, supportive care, such as treating the symptoms of disease with antipyretics (such as paracetamol and ibuprofen) and maintaining adequate fluid intake is often the recommended way to manage the disease.[147] However,

certain individuals have an increased risk of severe disease and may require hospitalisation. These high-risk groups include those with a weakened immune system, infants, young children, those with an underlying lung or heart condition and those aged 65 years or older.[17]

There is currently no medicine specifically authorised to treat RSV or shorten the duration of symptoms. For all ages, treatment for RSV is mainly supportive, aiming to ensure adequate oxygenation, ventilation, nutrition and hydration.[10, 17, 19]

3.8 Immunisation uptake rates

3.8.1 Immunisation uptake rates in Ireland

Pathfinder programme

The Pathfinder immunisation programme commenced in September 2024 and offered nirsevimab to all babies born in the 2024/25 RSV season.[11] The overall cumulative uptake of nirsevimab in maternity hospitals (n=19) and Children's Health Ireland (CHI) in Ireland was 83% (n=22,444 infants) between 1 September 2024 and 28 February 2025. CHI delivers acute paediatric services at Crumlin, Temple Street and Tallaght Hospitals. When disaggregated by setting, the overall cumulative uptake was 82% (range: 69-81%) in maternity hospitals. Among infants at high risk of severe disease (that is, the cohort previously eligible for palivizumab), the uptake was 96% in CHI and 99% in those immunised by TCP Homecare in the community.[148]

In Ireland, vaccines included as part of the primary childhood immunisation schedule are provided free at the point of administration by the HSE. These vaccines are generally administered in the primary care setting, typically by the GP or a practice nurse or administered in schools by immunisation teams. Considering all vaccines offered to children up to 12 months of age, as reported in the 2024 Rapid HTA, the uptake of scheduled vaccines for children up to 12 months of age in Ireland ranged from 87% to 90% between 2018 and 2022. Complete data are not yet available for 2023 or 2024, but the most recent data available for Q4 2024 shows a mean uptake rate of 87% and 89% of scheduled vaccines for children up to 12 and 24 months of age, respectively, in Ireland.[149]

Uptake in other immunisation programmes for maternal and older adults vaccines

Maternal vaccines

In Ireland, there are two vaccines that are routinely recommended during pregnancy: pertussis and the seasonal influenza vaccine. The NIAC recommendation

with respect to the COVID-19 vaccine was updated in May 2025 to suggest that pregnant women may choose to receive the vaccine following discussion with a healthcare provider.[150, 151]

In 2019, Ireland reported a pertussis vaccine coverage rate of 49.9% in pregnant women via Epipulse (the European surveillance portal for infectious diseases).[152] The pertussis vaccine coverage rates for subsequent years are not available as these data were collected through an ad-hoc data call.

The WHO collect data on annual influenza coverage in pregnant women in Ireland reported through the WHO/UNICEF Joint Reporting Form on Immunization. Irish data on influenza vaccine in pregnant women is available from the WHO for 2018 with a coverage rate of 62% and for 2020 with a coverage rate of 42.1%.[153]

Ireland reports data on COVID-19 vaccination coverage to the ECDC. The most recent ECDC surveillance report on interim COVID-19 vaccination coverage in the EU/EEA covering the period from August to November 2024 reported a coverage rate of 6.0% for COVID-19 vaccine in pregnant women in Ireland.[154] A previous report covering the period between 1 September 2023 and July 2024 reported a coverage rate of 19.6% for this cohort.[155]

Older adult vaccines

PPV23

The pneumococcal vaccine (PPV23) is free for those aged 65 years or older and is given as a once-off dose in this age group. Published data suggest that uptake in Ireland is low, though data are limited and not current. National telephone surveys were conducted in 2006, 2010 and 2013, with the 2013 survey noting that 36% (98/271) (95% CI: 30%-42%) of those aged 65 years and older reported ever being vaccinated.[156] More recent published data on pneumococcal vaccination uptake in Ireland for the general population were not identified. Data were identified specifically for adults with chronic disease enrolled in the HSE's Structured Chronic Disease Management Treatment Programme.[157] In the third report of the programme published in January 2025, previous pneumococcal vaccination was self-reported by 70% of those aged 65 years and older. While uptake rates are monitored as part of the childhood schedule, there is currently no similar scheme for routinely monitoring overall pneumococcal vaccine uptake in adults. Uptake of the pneumococcal vaccine adults in Ireland is low compared with the paediatric pneumococcal schedule. This may be because pneumococcal vaccination is part of the primary childhood immunisation schedule whereas in adults, access is more opportunistic.[158] Moreover, while there is no charge for the vaccine, prior to September 2025 patients could be charged an administration fee.[159]

Influenza

From the 2010/11 season to 2019/20 (the last season before the onset of the COVID-19 pandemic) the uptake rate of the influenza vaccine ranged from 54.5% (2016/17 season) to 68.5% (2018/19 season).[160] The uptake rate among those aged 65 years and older was 70.5%, 75.4%, 76.5% and 75.7% in the 2020/21, 2021/22 and 2022/23 and 2023/24 influenza seasons, respectively.[161] These figures reflect the administration of influenza vaccines across all settings — that is, GP practices, community pharmacies, long-term care facilities and healthcare work clinics. For the 2023/24 influenza season the uptake rate in those aged 65 and over was 75.7% with a slight decrease from the previous season.[162] The monthly influenza uptake reporting is still ongoing for the 2024/25 period but the uptake in the 65 years and older age group between 2 September 2024 and 16 February 2025 (74.3%) was slightly lower compared with the same period in 2023/24 (75.5%).[163]

The completeness of the data has differed over time. For example, 2022/23 was the first year in which the vaccinations outside of GP surgeries and pharmacies were included when calculating overall uptake.

According to data from the HSE's Structured Chronic Disease Management Treatment Programme, 98% of all individuals enrolled in the programme were noted as having received an influenza vaccine within the previous 12 months.[157]

COVID-19

As for the other vaccines in the adult programme, it is challenging to predict likely uptake of a long-term immunisation programme for RSV based on patterns of COVID-19 vaccine uptake. Booster uptake data are provided here, but it is unclear if this uptake rate would be applicable to RSV vaccination. The percentage (uptake based on the Census 2022 population) reported by the HPSC in the winter 2024 booster campaign was 27.4% in the 60-69 years age group, 46.4% in the 70-79 years age group and 61.0% in those aged 80 years and older.[164]

3.8.2 Immunisation uptake rate in EU/EEA countries and the UK

As previously discussed in Chapter 2, a review was carried out of nationally-funded immunisation programmes against RSV among countries of the EU/EEA and the UK. RSV immunisation uptake data in this section are informed by available published reports in relation to these programmes.

RSV maternal vaccine uptake

UK

Since 1 September 2024, pregnant women can avail of a free RSV vaccine typically offered at the 28-week antenatal appointment. For those who do not avail of it at this visit, they can contact their GP or midwife to receive it later in pregnancy up until the birth of their infant.

In England, 43% of women giving birth between September and February 2025 had received an RSV vaccine prior to the birth. In Scotland, based on data up to May 2025, it was noted that 50% of pregnant women giving birth since September 2024 had received an RSV vaccine. In Wales, 40% of women giving birth between September 2024 and April 2025 had received an RSV vaccine. (127)

Uptake of the maternal vaccine was noted to have gradually increased in England from the time vaccine was first offered in September 2024, with monthly uptake increasing from 40.5% in September 2024 to 54% in April 2025. Differences in uptake by ethnicity were noted, with a 44 percentage points' difference between the ethnic group with the lowest uptake (Black or Black British – Caribbean, 26%) and highest uptake (Other ethnic groups – Chinese, 71%) over the first eight months of the programme. (165)

RSV long-acting monoclonal antibody uptake

France

Two observational studies from maternity hospitals in France reported nirsevimab uptake among those born during the 2023/24 RSV season who were offered immunisation prior to discharge. A 2024 observational study conducted in three maternity hospitals in Lyon, France reported an 80.1% uptake in those born between 15 September and 31 December 2023.(166) Similarly, a prospective longitudinal cohort study conducted in Lille from 18 September 2023 to 23 January 2024 at Lille University Hospital reported nirsevimab acceptance rates among those that agreed to participate in the study. In total, 27.6% agreed to participate (n=477/1,730 newborns), with an acceptance of 91.6% (95% CI, 89.1%-94.2) within this participating cohort.(167)

Italy

Valle d'Aosta is an Italian region which implemented early adoption of universal prophylaxis with nirsevimab for newborns and infants in the 2023/24 RSV season. A prospective cohort study (n=537) was conducted of eligible infants born in this region between 1 May 2023 and 15 February 2024. Uptake in the catch-up cohort (born between 1 May 2023 and 18 December 2023) was 65%, with immunisation provided by appointment in the city public health office. For infants discharged from the maternity hospital between 20 December 2023 and 15 February 2024,

prophylaxis was provided in the hospital on the day of discharge with an uptake rate of 86%. The study reported that the overall uptake rate of all eligible infants born in this region between 1 May 2023 and 15 February 2024 was 69%.[168]

Luxembourg

A nationwide immunisation programme administering nirsevimab to all infants entering their first RSV season, and children under the age of two years with risk factors for severe respiratory infection, was implemented for the 2023/24 RSV season. It reported an estimated uptake rate of 84% (ranging from 66% to 94%) for infants born from October to mid-December 2023, with immunisation offered in maternity hospitals prior to discharge. Coverage in outpatient settings was not reported.[169]

Spain

Three studies provided regional nirsevimab uptake data relating to the 2023/24 RSV season. One provided uptake data for infants born during the season,[170] one for those born during the season in addition to data for those in catch-up and high-risk groups,[171] while one study provided data for the catch-up cohort only.[172] For those born during the season, nirsevimab was offered in the maternity hospital prior to discharge. For those in the catch-up or high-risk group, immunisation was provided in a public hospital or healthcare centre,[171] or in primary care practices.[172]

The 2023/24 immunisation campaign in Galicia began on 25 September 2023. Infants born during the RSV season were offered immunisation before discharge from hospital. Infants in the catch-up and high-risk groups received electronic appointments to attend a public hospital or healthcare centre for nirsevimab administration. An interim analysis which included data for children born up to 15 December 2023 reported that immunisation coverage with nirsevimab was 95.4%, 89.9%, and 97% for infants born during the RSV season, infants younger than six months at the start of the season (catch-up cohort) and high-risk children younger than two years at the start of the season, respectively.[171] In Catalonia, infants who were less than six months old before the onset of the 2023/24 RSV season (born between 1 April and 30 September 2023) were offered a dose of nirsevimab in primary care practices during October. A case-control study found an 87.2% coverage rate in this cohort. Infants born during the RSV season were not included in this analysis.[172] A population-based study in the Navarre region in Spain, of infants born between October and December 2023 and who were offered nirsevimab at birth in maternity wards, reported a 92% uptake rate.[170]

RSV older adult vaccines uptake

UK

The RSV adult vaccination programme was introduced in England in September 2024 as a single-dose vaccine for adults turning 75 years old, with a catch-up programme covering those up to 79 years of age; the vaccine is administered in primary care by GP practices and participating pharmacies.[173] As of the end of May 2025, the cumulative vaccine coverage among eligible older adults had reached 58.9%, with coverage of 36.4% and 62.4% in the routine and catch-up cohorts, respectively. [127]

Scotland launched its RSV vaccine programme in August 2024, with the RSV vaccine offered to adults aged 75-79 years and those turning 75 years before July 2025. Vaccination is provided by local NHS immunisation teams who initiate contact with eligible individuals to make an appointment. By May 2025, 70.6% of eligible older adults in Scotland had received the vaccine, with coverage of 69.9% and 70.7% in the routine and catch-up cohorts, respectively.[174]

In Wales, RSV vaccination of older adults commenced on 1 September 2024, with eligible individuals invited to attend for vaccination. Vaccination is offered year-round to older adults as they turn 75 years old. A catch-up programme was also started for those aged 75 to 79 years on 1 September 2024. The vaccine is administered in GP practices or in community vaccine centres. Uptake in both the routine and catch-up cohorts increased over time from 15% and 12%, respectively on 22 October 2024[175] to 29.7% and 47.3%, respectively by May 2025.[176]

Differences in uptake by ethnicity and deprivation status in older adults have been noted. Data for England for the first 11 months of the programme indicated a 22 percentage points' difference in coverage between the most deprived (51%) and least deprived (73%). There was a 44 percentage points' difference between the ethnic group with the lowest uptake (Asian or Asian British – Pakistani, 24%) and highest uptake (White British, 68%). [177]

3.9 Economic burden of RSV

In the 2024 Rapid HTA on RSV, a brief overview of relevant literature in children aged 0 to 4 years and adults aged 65 years and older was provided to highlight the considerable economic burden that RSV places on society and healthcare systems.[10] As described in Chapter 4 of that report, both direct (such as those related to providing care for the patient) and indirect (such as productivity losses due to RSV-related illness or death) costs are relevant when considering the economic burden associated with RSV. It should be noted that the cost to patients accessing primary care varies from country to country, and these differences impact how applicable international findings will be to the Irish setting. Moreover, while RSV has been a notifiable disease in Ireland since 2012,[15] as of April 2025, it is not

currently a notifiable disease at a European level, so reporting by individual countries may differ across Europe.[111] In addition, estimating the burden of RSV in secondary care can be challenging due to diagnostic uncertainty. For example, the symptoms of RSV are non-specific and not all patients will have specimens collected and tested. Furthermore, some patients may acquire RSV during their inpatient stay rather than RSV being the cause of admission, although this is partly accounted for by using the primary diagnosis code.

The following sections provide an update to their corresponding paragraphs in the Rapid HTA in instances where newer evidence was identified.

Children (aged 0 to 4 years)

Updated findings from 2024 were reported by an Irish industry-funded analysis, which estimated the economic burden of RSV-related hospitalisations among children aged less than two years using data sourced from HIPE.[178] The analysis reported on the RSV burden in secondary care from 2017 to 2022, highlighting the substantial burden in this population. Excluding 2020 (due to the influence of COVID-19), the RSV-specific total annual inpatient costs were estimated to range from €4.8 million (2017) to €10.8 million (2022).[178] The analysis also included hospitalisations due to acute bronchiolitis as potentially attributable to RSV, to account for potential under-reporting. When considering both RSV-confirmed inpatient costs and bronchiolitis inpatient costs, estimated total inpatient hospitalisation costs ranged from €11.4 million (2017) to €16.5 million in 2022.[179]

A 2024 systematic review co-authored by Sanofi employees reported on the burden of RSV infection in Germany, identifying 42 relevant articles, 23 of which reported healthcare resource use associated with RSV infection.[180] The authors identified one study that reported costs associated with RSV-LRTI, focusing on children aged less than three years between 1999 and 2001. The estimated mean cost (including direct and indirect costs) was €163 per outpatient case and €2,700 per hospitalised RSV case.

A 2025 publication, led by Pfizer employees, reported a retrospective health claims analysis of RSV inpatient cases (with either a primary or a secondary RSV diagnosis) between 2014 and 2019 in Germany.[181] The authors assessed direct costs per RSV case and health resource use, for 4,909 infants (1-12 months old) RSV cases and 1,730 toddlers (13-24 months old) cases. Mean direct costs attributable to healthcare resource utilisation were found to be higher in infants than toddlers (RSV-specific costs of €4,021 and €3,641, respectively; RSV plus unspecified bronchiolitis or pneumonia costs of €3,775 and €3,062, respectively). For both cohorts, mean costs for RSV plus unspecified bronchiolitis or pneumonia cases were higher for cases that required ICU admission. Specifically, costs were 4.7 times higher in the

infant cohort (€17,273 versus €3,655) and 9.5 times higher in the toddler cohort (€27,605 versus €2,891). Mean excess costs relative to matched controls (patients who did not have an RSV or bronchiolitis diagnosis, matched for age, sex and preterm status) were also calculated. Mean excess costs for both cohorts were consistently higher for RSV patients than matched controls. For RSV and unspecified bronchiolitis or pneumonia cases occurring during the RSV season, the mean 30-day excess costs ranged from €2,953 for infants born full-term with no increased risk and hospitalised for five days, to €6,694 for infants born extremely premature (<29 weeks gestational age) and hospitalised for seven days. RSV-specific mean 30-day excess costs ranged from €3,183 to €8,337 for the same cohorts.

A 2025 systematic review co-authored by Sanofi employees identified 18 articles from Italy providing data on either economic costs or healthcare resource utilisation related to RSV infections in children aged less than five years old.[182] According to the review authors, one study provided comprehensive RSV disease cost data, reporting that the mean cost per inpatient for children testing positive for RSV was €5,753 (range: €3,711 to €7,795) compared with €5,395 (range: €3,354 to €7,436) for RSV-negative children.

A 2024 publication reported on the economic burden associated with RSV-associated hospitalisations in children less than five years of age in Austria, between 2015 and 2022.[183] Of the 976 cases of RSV-related hospitalisations, 41% occurred among infants aged less than three months of age, and 66% occurred among infants aged less than six months. For 2021, RSV-related hospitalisation costs among children less than five years (excluding productivity losses) were approximately €2 million and accounted for 3.3% of the overall all-cause hospitalisation costs of €60 million in this age group. Similarly, a 2025 Spanish study authored by Pfizer employees, estimated RSV hospitalisation costs in children less than 18 years of age between 2016 and 2019.[184] The highest incidence was seen in infants aged less than six months who accounted for 63% (€24.8 million) of all RSV hospitalisation costs. Over the study period, the total annual RSV-specific hospitalisation cost increased from €35 million in 2016 to €45 million in 2019. Over the same period, the total annual hospitalisation costs for unspecified bronchiolitis, bronchitis or pneumonia cases, decreased from €57 million in 2016 to €48 million in 2019. The authors partly attributed these trends to an increased awareness of RSV over time and or improved diagnostic testing practices, with an increase in specific-RSV cases consequently leading to fewer recorded cases of unspecified bronchiolitis, bronchitis or pneumonia.

Older adults (aged 65 years and older)

Using data sourced from HIPE for the period 2017 to 2021, an analysis by a commercial consultancy group estimated that the cost of RSV-related

hospitalisations for adults aged 65 years and older in Ireland ranged from €147,000 in 2017 to €870,000 in 2019.[179] To account for potential under-reporting of RSV cases in this age-group, the authors undertook an additional analysis in which they assumed that approximately 6.8% of hospitalisations in older adults for respiratory-related infections were due to RSV. In this, they estimated that total hospitalisation costs due to RSV in this age-group exceeded €8.1 million (€0.4 million in reported and €7.7 million in unreported RSV hospitalisation costs) in 2021.

An Italian study from 2025 led by GSK employees reported on economic outcomes of RSV-hospitalised patients aged 60 years and older in Italy, between 2010 and 2021.[185] The analysis was limited to data from six administrative databases covering approximately 20% of the population of Italy, and to those for whom at least 12 months of data availability was available in a single local health authority. Of the 201 included patients, 60% were aged 75 years or older. The total mean direct healthcare costs per patient during the 12-month follow up were €11,599 and €8,385 for adults aged 60 years and older and 75 years and older, respectively. The total mean direct healthcare costs were also stratified by risk status, with costs per high-risk patient estimated at €12,269. For certain comorbidities, the total mean direct healthcare costs per patient ranged from €9,920 among those with heart failure to €11,629 among COPD patients. The total mean direct healthcare costs per patient were higher for immunocompromised patients, estimated at €16,129.

The considerable economic and health resource burden associated with RSV was further documented in a 2024 study from Germany, reporting on health claims data between 2015 and 2018 among adults aged 18 years and older.[186] This study, co-authored by Pfizer employees, reported on RSV-related productivity loss from inpatient episodes by age group; productivity losses were considered to represent the time that patients could not participate in employment or pursue other "productive" activities (not specified) due to their illness. RSV-related inpatient episodes were reported to result in 9.79 (± 6.77) days, 10.29 (± 6.43) days, and 10.79 (± 6.35) days of productivity loss among adults aged 60 to 74 years, 75 to 84 years and 85 years and older, respectively. For each age group, the mean direct cost per inpatient episode was higher for severe cases than non-severe cases. For the 60 to 74 year cohort, the mean direct cost per inpatient episode for €12,168 (± €13,352) and €3,168 (± €3,672) for severe and non-severe cases, respectively.

Two publications were identified from 2025 reporting on the economic impact of RSV infections among Spanish adults.[187, 188] The first, authored by employees from Pfizer, estimated the costs associated with RSV and influenza hospitalisations in adults aged 18 years and older between 2016 and 2019, using the validated Minimum Basic Data Set, which covers 90% of all public and private hospital admissions in Spain.[187] Hospitalisation costs per episode were higher among those

with a higher risk profile, for all ages and infection types. No overall significant difference was detected in the cost per episode between RSV or influenza infections, after adjustment for age group, risk status and year of admission (RSV €3,870, 95% CI: €3,773 to €3,942; influenza €3,888, 95% CI: €3,836 to €3,931). Total annual hospitalisation costs increased with age for both RSV and influenza, with the greatest burden among those aged 80 years and older (RSV €145 million (76% of RSV costs among adults); influenza €29 million (35% of influenza costs among adults)). For adults aged 60-69 and 70-79, the total annual RSV-related hospitalisation costs were estimated at €19 million and €12 million, respectively. The second study reported the findings of an observational study of adults aged 60 years and older hospitalised with a confirmed RSV infection between October 2023 and March 2024 inclusive.[188] The authors compared directs costs between 1,952 ARI and 229 RSV cases. The mean total costs were estimated to be higher for RSV cases (€5,197, standard deviation (SD) €10,020) compared with ARI cases (€3,329, SD €7,176). The differences between the mean costs of RSV and ARI cases were statistically significant ($p < 0.001$) for the age groups 60 to 70 years (RSV €3,981, SD €4,237; ARI €2,976, SD €7,849) and 70 to 80 years (RSV €7,800, SD €17,474; ARI €3,371, SD €8,510). The large standard deviations in all instances indicate the data are likely right-skewed, with a small proportion of patients incurring very high costs.

3.10 Discussion

This chapter describes the epidemiology of RSV in Ireland, and the burden of disease in Ireland, EU/EEA countries and the UK among children aged 0 to 2 years, and adults aged 65 years and older. In summary, RSV surveillance data for Ireland, for the last seven seasons, excluding the 2020/21 season, show a considerable burden associated with RSV. Moreover, the data indicate seasonal variability in the burden associated RSV in those aged 0 to 2 years and in adults aged 65 years and older over the seven-year period since 2018/19.

In Ireland, considering all age groups, the highest reported burden has consistently been seen in those aged less than two years, followed by those aged 3 to 4 years. This reported burden is substantially higher than among the adult population, including among adults aged 65 years and older. For example, since 2018/19, (excluding the 2020/21 season due to the influence of COVID-19) the notified case rates among children aged less than two years ranged from 1,211.8 to 2,225.7 per 100,000, while they ranged from 47.1 to 283.5 per 100,000 among adults aged 65 years and above. Differences are also noted when considering RSV-related ED visits and hospitalisations among notified cases. For the same period, the notified RSV ED visit rates among children aged less than two years ranged from 286.6 to 990.6 per 100,000, while they ranged from 9.4 to 77.4 per 100,000 among adults aged 65

years and above. The notified RSV hospital admission rates among children aged less than two years ranged from 643.8 to 1,063.9 per 100,000, while they ranged from 18.3 to 93.4 among adults aged 65 years and older. While there has been a general trend of increasing notifications over time, possibly driven by changes in testing practices, notified case rates and rates of ED visits and hospital admissions among notified cases were substantially lower in those aged less than two years for the 2024/25 RSV season than in previous years, likely as a consequence of the introduction of the Pathfinder immunisation programme for those born during the RSV season, as discussed below.[189]

HPSC data in relation to ICU admissions among notified RSV cases were limited to the 2023/24 and 2024/25 RSV seasons. Such admissions were uncommon in those aged 65 years and older, with a total of seven and 13 admissions reported in the 2023/24 and 2024/25 RSV seasons, respectively. This can be compared with a total of 125 and 61 such admissions among children aged less than two years in the 2023/24 and 2024/25 RSV seasons, respectively.

While the overall burden of RSV measured via the rate of notified RSV cases, ED visits, hospitalisations and ICU admissions is lower among older adults as compared with infants, the reported rate of RSV-related mortality is comparatively higher among the older population. This is consistent with published literature on the topic of the RSV burden in different age groups. A 2024 systematic review reporting on the epidemiological or economic burden of RSV in Germany noted that RSV imposes substantial disease burden in infants, young children, and older adults in Germany, with infants being particularly affected. However it also noted that the reported mortality rate associated with RSV infection in hospitalised adult populations was higher than in children.[180] A comparative analysis of RSV-related hospitalisations in children and adults over a seven year-period before, during and after the COVID-19 pandemic found that overall, children were hospitalised more often for RSV, while older adults showed more severe outcomes.[190] A 2023 systematic analysis of the Global Burden of Disease 2019 study found that from 1990 to 2019, among specific age groups, deaths in children under five years decreased from 1990 to 2019, while deaths in adult age groups increased. Mortality rates differed by geographical region and were lower in developed countries.[1]

Among children aged less than two years, the RSV burden is not uniform, with the burden typically decreasing with increasing age. Specifically, the burden is disproportionately higher among infants less than six months, with the highest rates of notified cases, ED visits, hospitalisations, and hospitalisations that include ICU admission consistently reported in this youngest group and among those aged less than three months in particular up until the 2024/25 season, when the HSE's Pathfinder Programme was introduced. The Pathfinder Programme offered

immunisation with nirsevimab to all infants born during the six-month period between 1 September 2024 and 28 February 2025. Immunisation with nirsevimab was also extended to infants and children up to two years of age at high risk of severe disease who would previously have been eligible for palivizumab. The cumulative national uptake rate of the Pathfinder Programme was high at 83%. The HSE reported that among infants born during the period September to February, the total number of notified cases, cases presenting to EDs, RSV-related hospitalisations and RSV-related ICU admissions was 65%, 57%, 76% and 65% lower, respectively, in 2024/25 compared with the same period in 2023/24.[31]

HPSC data for the 2024/25 RSV season show that there was a reduction in the burden of RSV in those aged less than two years, driven largely by a reduction in the burden in those aged less than six months. Specifically, the notified case rate in those aged less than three months was the lowest reported since 2018/19, while the rate in those aged 3 to 6 months was 60 to 70% lower than that reported in the previous three years. Notably, there was a change in the distribution of cases in those aged less than two years. Between the 2018/19 and 2023/24 RSV seasons (excluding 2020/21), infants aged less than six months accounted for 55% of the total number of seasonal notified RSV cases in this cohort. In contrast, they accounted for 23% of reported cases in those aged less than two years for the 2024/25 season, with the largest reduction seen in infants aged less than three months (9% vs 30-39% of notified cases in previous years). A corresponding decline in RSV ED visit rates and hospitalisations among notified cases was seen for those aged less than six months, who accounted for 24% and 22% of RSV ED visits and hospitalisations, respectively, in 2024/25 compared with 53% and 57% of all such visits in those aged less than two years in the RSV seasons since 2018/19 and 2023/24. As the reported data on morbidity and mortality associated with RSV are not linked to immunisation uptake data or other patient risk-status data, it is not known what proportion of the observed morbidity and mortality in the 2024/25 season occurred in those at increased risk of severe RSV-related disease or in those who did not receive immunisation.

A study conducted in Ireland highlighted the burden of RSV on the healthcare system before the implementation of the Pathfinder Programme. The study reported a significant impact of RSV in two tertiary paediatric hospitals from October 2023 to January 2024, with bed occupancy levels in Paediatric Intensive Care units (PICUs) exceeding 100% and a high demand for invasive and non-invasive ventilation. The burden on PICUs also led to the cancellation of elective surgeries during this period.[191] The PICU data for the 2024/25 season indicated that total RSV-related admissions and case severity were lower compared with the previous season (70 vs

155), including specifically a lower burden in those aged less than six months (40 vs 118).[122]

The burden of RSV among those aged 65 years and older is also not homogenous. When data for this group were disaggregated by five-year age band, in general, the burden of RSV was found to increase with increasing age, with the highest burden observed among those aged 80 years and older. Chronic conditions associated with severe outcomes of RSV such as COPD, chronic kidney disease, diabetes mellitus are generally more common in older adults.[192-194] As highlighted in section 3.6.3, the population aged 65 years and older is expected to grow substantially, with CSO projected increases from 833,300 in 2024 to over a million by 2032. As such, healthcare utilisation due to RSV in older adults will likely also increase, contributing to demands on the healthcare system. Currently, there are no population-based RSV vaccination programmes targeted at older adults in Ireland. As noted in Chapter 2, a number of countries within the UK and Europe have recently implemented regional or national vaccination programmes targeting subsets of the population aged 65 years and older, specifically adults aged 75 years or older and or those at increased risk of severe disease due to specified chronic conditions. A comprehensive review of the safety, efficacy and effectiveness of RSV vaccination in older adults is described in Chapter 4.

The Pathfinder cohort aside, since 2022/23, RSV notification rates in all age groups are higher than in the pre-COVID-19 period. This is most notable among those aged 65 years and older, with corresponding increases also seen in rates of RSV-related ED visits and hospitalisations among notified cases. It is possible that this reflects improved case ascertainment rather than a true increase in the burden of RSV. The COVID-19 pandemic changed the landscape of respiratory virus testing in Ireland, with more laboratories conducting respiratory virus testing and increased use of multiplex PCR assays to test for respiratory viruses, including RSV. A 2023 HPSC survey (n=40 hospitals, 75% response rate) of respiratory virus testing capacity and practices reported a widespread availability of multiplex RT-PCR testing in acute hospital settings in Ireland.[195] In late 2024, the HSE issued guidance on ARI testing recommending the use of multiplex testing for a panel of viruses including RSV by a method that detects viral nucleic acid.[196] A 2024 systematic review reported RT-PCR test as the most sensitive paediatric RSV diagnostic test that is unlikely to miss RSV cases or only a relatively small proportion among the children presenting with LTRI.[197] Multiplex RT-PCR test is also the most sensitive diagnostic test for RSV among adults.[198] Despite anecdotal reports of variability in testing practices across hospitals, the increased laboratory capacity in hospital settings and the HSE recommendation to use a multiplex test that has high diagnostic performance, support an assumption that the most recent Irish data are likely a more accurate

reflection of the true burden of RSV on the healthcare system, especially at secondary care level. It is acknowledged, however, that the most recent data still underestimate the true burden, as not all cases are (or will likely ever be) notified. The 2023 HPSC survey showed that 93% of laboratories reported testing specimens from hospital inpatients and ICU patients, making these the most common source of specimens; only 30% of laboratories reported testing specimens submitted from primary care practices. It is noted that there are no specific antiviral treatments for RSV, while antiviral treatment for those with influenza and COVID-19 is indicated only for those at high risk of severe disease. With the exception of sentinel surveillance, multiplex testing in primary care is likely limited given that it typically will not influence patient management. As such, the true burden of RSV in primary care is likely much higher than that reported.

For immunisation programmes, achieving a high uptake rate is important to maximise health benefits. As discussed, uptake of nirsevimab in Ireland during the most recent RSV season was high at 83%. However this figure is slightly lower than the overall uptake of vaccines included in the childhood immunisation programme and this may reflect the fact that Pathfinder was a newly launched programme. Available data on uptake of nirsevimab for infants within other EU/EEA countries show a wide range from 69% to 95% in different regions. However, it is noted that uptake was typically higher for those born during the RSV season who were immunised prior to discharge from the maternity hospital (range: 80% to 95%) compared with uptake in the catch-up cohort (range: 65% to 90%). Looking at uptake of the RSV maternal vaccine, data from England and Wales (where it is nationally funded) show rates ranging from 33.6% to 47.6% and from 18.7% to 46.1%, respectively, with uptake noted to generally have increased over time among women who gave birth between September 2024 and February 2025. In Ireland, uptake of other maternal vaccines was previously reported as 49.9% for the pertussis vaccine, and ranged between 42.1% and 62% for the seasonal influenza vaccine and between 6% and 19.6% for COVID-19 vaccines in recent years. Data on the uptake of RSV vaccines for older adults is available from the UK where it is nationally funded. While noting differences in the reporting interval across the different countries, uptake for the catch-up programme (those aged 75-79 years) ranged from 44% to 69%. In Ireland, uptake of vaccines among older adults aged 65 years and over was previously reported as 36% for pneumococcal vaccination, and ranged between 54.5% and 76.5% for the seasonal influenza vaccine programme and between 46.4% and 61% for COVID-19 vaccination in recent years. In general the uptake of all adult vaccines in Ireland (both maternal and older adult vaccines) is lower as compared with uptake within the childhood immunisation programme.

Using HIPE data for the period 2018 to 2024, the total annual cost of inpatient stays for those with a primary diagnosis of RSV ranged from €2.2 million (in 2024) to 6.2 million (in 2023) for cases with an ICU stay, and from €3.2 million (in 2020) to 20.4 million (in 2022) for cases without an ICU stay. While annual costs associated with inpatient stays have varied, they are substantial. However, it is acknowledged that they are likely an underestimate as not all RSV cases are laboratory confirmed and some discharges may not be coded. In addition to the HIPE inpatient costs, it is noted that there may be additional costs associated with rehabilitation after discharge, particularly among frail older adults. Rehabilitation may involve additional professional support at home, community-based multidisciplinary services, or admission to a Level 2 specialist rehabilitation bed. A 2022 systematic review reported that the pooled prevalence of frailty among those aged 65 years and older inpatients was 65.8% (95% CI 25.7-100%) in Ireland.[199] Furthermore, the economic burden associated with RSV also includes direct costs resulting from providing care to the patient, such as primary care visits and medical costs, and indirect costs resulting from productivity loss due to illness, or premature death. Although limited research has been published on the total economic burden of RSV in Ireland, international estimates suggest that the burden, including both direct and indirect costs, is likely to be considerable. This will be explored further in the economic evaluation chapter.

In summary, RSV places a significant burden on young children, older adults and secondary healthcare services, with the highest burden seen in children less than two years. RSV poses a particular challenge for paediatric healthcare services, as a high proportion of hospital discharges occur in Q4 each year. While testing capacity has increased, the identified data are likely an underestimate of the total burden, and particularly the burden in primary care, as not all RSV cases are laboratory confirmed and some discharges may not be coded.

4 Clinical efficacy, effectiveness and safety

Key Points

- Systematic review evidence was used to address four research questions relating to the efficacy, effectiveness and safety of authorised interventions and approaches for the prevention of RSV and associated complications. These approaches comprised the:
  - active immunisation of adults aged 65 years and older through vaccination
  - passive immunisation of infants through maternal vaccination
  - passive immunisation of infants and young children through the use of extended half-life monoclonal antibodies (EHL-mAbs).

Active immunisation of older adults through vaccination

- Overall, three RCTs (n=97,547) and three observational studies (two test-negative case control studies (n=81,595) and one target trial emulation (n=146,852 vaccinated matched to 582,936 unvaccinated controls)) were included (search updated to 25 April 2025). The evidence identified relates to adults aged 60 years and older and included three authorised RSV vaccines (RSVPreF3 (Arexvy®), RSVpreF (Abrysvo®), and the mRNA vaccine mRESVIA®).
- Considering the estimated vaccine efficacy/effectiveness (VE) of RSV vaccination of older adults:
  - VE against RSV-related lower respiratory tract disease (LRTD) was 78% over one RSV season (high certainty of evidence based on pooled data from three RCTs). There was evidence of waning immunity based on two RCTs reporting cumulative and per season data for two (RSVpreF, RSVPreF3) and three (RSVPreF3) seasons. Cumulative vaccine efficacy against RSV-related LRTD was estimated at 67% over two seasons (pooled data from two RCTs) and 69% over three seasons (data from one RCT).
  - VE against medically attended RSV-related LRTD, reported by two RCTs, was 88% and 70%, respectively.
  - VE against RSV-related hospitalisation was 77% (moderate certainty of evidence based on pooled data from two test-negative case-control studies). A similar vaccine effectiveness estimate (80%) was reported by a trial emulation study. The RCTs were underpowered to detect differences in RSV-related hospitalisation between the vaccine and control groups.

- There were insufficient data to determine VE against RSV-related ICU admissions or RSV-related mortality.

- Considering the safety of RSV vaccination of older adults:
  - Local and systemic reactions were relatively common among vaccine recipients; however, these were mostly mild-to-moderate reactions; severe solicited adverse events were less common.
  - Overall, serious adverse events (SAEs) related to the intervention were rare. In the pooled analysis, there was no statistically significant difference in the risk between vaccine and placebo groups (low certainty of evidence based on three RCTs).
  - Post-marketing surveillance supports the safety of RSV vaccination in older adults. While there is some uncertainty over potential SAEs such as Guillain-Barré syndrome (GBS), the evidence suggests these events are rare, with estimates ranging from 16 to 25 and from 3 to 10 excess cases of GBS per million doses for RSVpreF and RSVPreF3, respectively.

Passive immunisation of infants through maternal vaccination

- Overall, one RCT (n=7,420) and one observational study (test-negative case control study (n=505)) were included (search updated to 25 April 2025). The evidence identified relates to infants aged six months and younger and included RSVpreF (Abrysvo®), the only RSV vaccine authorised in Europe for the passive immunisation of infants through maternal vaccination.

- Considering the efficacy and effectiveness of maternal RSV vaccination during pregnancy, estimated VE against:
  - Medically attended RSV-related LRTD and RSV-related hospitalisation in infants at 180 days follow-up was 49% and 55%, respectively (moderate certainty of evidence for both outcomes, based on one RCT).
  - RSV-related hospitalisation in infants was 73%, up to 180 days follow-up based on one observational study (low certainty of evidence).

- There was no statistically significant effect of maternal vaccination on RSV-related mortality (low certainty of evidence based on one event in one RCT).

- Considering the safety of maternal RSV vaccination during pregnancy:
  - In both pregnant women and infants, most adverse events reported in the period up to one month after vaccination were mild-to-moderate. Severe events represented approximately 10% of all adverse events among both vaccine and placebo groups.

- Overall, intervention-related SAEs were rare. There was no statistically significant difference in risk between vaccine and placebo groups (low certainty of evidence based on one RCT).
- Pharmacovigilance assessments support the overall safety of RSV maternal vaccination during pregnancy, although countries continue to closely monitor recipients due to some concerns regarding a potential safety signal associated with preterm births.

Passive immunisation of infants and young children through the use of extended half-life monoclonal antibodies

- Overall, four RCTs (n=16,121 for clinical efficacy estimates, n= 14,570 for safety estimates) (search updated to 23 April 2025; the CLEVER RCT was published after this date and included in a post-hoc update) and 15 observational studies (n=96,392) (search updated to 25 February 2025) were included. The RCT data relate to both nirsevimab (Beyfortus®) and clesrovimab (Enflonsia®), whereas the observational data relate exclusively to nirsevimab.
- Considering the impact of EHL-mAbs on the protection of infants and children less than two years of age at increased risk of RSV-related disease:
  - EHL-mAbs reduce medically attended RSV-associated LRTI over one season, with an estimated efficacy of 69% (pooled data from three RCTs; high certainty of evidence). Effectiveness of nirsevimab against RSV-related LRTI incidence in infants was estimated at 87% (pooled data from two observational studies; moderate certainty of evidence). However, EHL-mAbs probably do not reduce MA RSV-associated LRTI over two seasons (pooled data from two RCTs; moderate certainty of evidence).
  - EHL-mAbs probably reduce RSV-associated LRTI with hospitalisation over one season, with an estimated efficacy of 83% (pooled data from four RCTs; moderate certainty of evidence). Effectiveness of nirsevimab against RSV-related hospitalisation among infants was estimated at 87% (low certainty of evidence based on pooled data from nine observational studies). However, nirsevimab probably does not reduce RSV-associated LRTI with hospitalisation over two seasons (data from a single RCT; moderate certainty of evidence).
  - There were insufficient data to determine efficacy against RSV-related ICU admissions or efficacy and or effectiveness against RSV-related mortality. However, there was evidence that nirsevimab probably reduces the risk of RSV-related ICU admissions over one season (moderate certainty of evidence based on pooled data from four observational studies).

- Considering the safety of EHL-mAbs for infants and children less than two years of age at increased risk of RSV-related disease:
  - Adverse events (AEs) were common; however, these were typically mild to moderate in severity, with Grade 3+ AE occurring less frequently. The pooled result across the four RCTs indicated no significant difference in the incidence of any AEs between the EHL-mAb and control groups.
  - Across four RCTs, only two participants (out of 8,380) were reported to have had an SAE which was related to an EHL-mAb, while one participant (out of 6,190) had an SAE related to placebo. While rare, due to the low certainty of evidence, it is unclear if EHL-mAbs are associated with SAEs related to the study intervention.
  - To date, post-marketing surveillance supports the overall safety of nirsevimab administration to this cohort.

Risk of bias

- The risk of bias of the underpinning primary studies varied, but was generally assessed to be low, though some concerns were noted.
  - In relation to vaccination of older adults, outcomes relating to the first RSV season in all three of the included RCTs were considered to be at low risk of bias. However, some concerns were identified regarding outcomes relating to subsequent seasons from two RCTs. The three included observational studies were deemed to be at moderate (two studies) to serious (one study) risk of bias.
  - In relation to maternal vaccination, the single RCT was assessed as being at low risk of bias for all outcomes. Moderate risk of bias was identified in the single included observational study.
  - In relation to EHL-mAbs, three RCTs were considered at low risk of bias across all outcomes while one RCT was assessed as having 'some concerns' for both efficacy and safety outcomes. Of the 15 observational studies, 14 were assessed to be at low risk of bias, while one study was assessed to be at moderate risk of bias.

Conclusion

- There is consistent evidence that all currently authorised RSV immunisation products are safe and effective for the prevention of RSV and associated complications, over one season. While local and systemic events are common, these are mostly mild-to-moderate in severity; serious adverse events (SAEs) are rare. Continued monitoring and vigilance will be required given that these are new interventions. For older adults, there is evidence of waning immunity

over time, with data limited to a maximum of three years' follow-up. The potential harms that are associated with immunisation must be considered in the context of the potential for clinical benefit within the population.

4.1 Introduction

The aim of this chapter was to review the clinical efficacy, effectiveness and safety of authorised interventions and approaches for the immunisation against respiratory syncytial virus (RSV) infection. The interventions that were considered included the active immunisation of adults aged 65 years and older through vaccination, the passive immunisation of infants through maternal vaccination, and the passive immunisation of infants and young children through the use of extended half-life monoclonal antibodies (EHL-mAbs).

4.2 Methods

Research questions

Four research questions were formulated with respect to the efficacy, effectiveness and safety outcomes associated with the use of the authorised RSV immunisation strategies:

- What is the clinical efficacy and effectiveness of the currently authorised EHL-mAbs for the prevention of RSV and associated complications, in infants in the general population and in children aged less than two years at increased risk of severe disease?
- What is the safety profile of the currently authorised EHL-mAbs when used for the prevention of RSV and associated complications, in infants in the general population and children aged less than two years at increased risk of severe disease?
- What is the clinical efficacy and effectiveness of the currently authorised RSV vaccines for the prevention of RSV and associated complications in infants (through maternal vaccination) and in adults aged 65 years and older?
- What is the safety profile of the currently authorised RSV vaccines when used for the prevention of RSV and associated complications in infants (through maternal vaccination) and in adults aged 65 years and older?

While the scope was limited to currently authorised products, a decision was taken to also include published phase II and III randomised controlled trial (RCT) data for products for which an assessment of a marketing authorisation application was being considered by the European Medicines Agency (EMA), and where the study dose was in line with that submitted for authorisation.

The specific inclusion criteria, in terms of population, intervention, comparator, outcomes and study design (PICOS) for this HTA are presented in Table 4.1.

Table 4.1 PICOS for clinical efficacy, effectiveness and safety of authorised RSV immunisation strategies

Population	Infants, children (aged less than two years at increased risk of severe disease), pregnant women and older adults (aged 65 years and older)
Intervention	One of the following forms of authorised RSV immunisation: **RSV monoclonal antibodies (extended half-life):** – nirsevimab (Beyfortus®) – clesrovimab (Enflonsia®) **RSV vaccines**: ▪ Pregnant women – RSVpreF (Abrysvo®) ▪ Older adults – RSVpreF (Abrysvo®) – RSVPreF3 (Arexvy®) – RSV mRNA vaccine (mRESVIA®)
Comparator	▪ No immunisation ▪ Placebo ▪ Co-administration with another vaccine ▪ Another authorised form of RSV immunisation (head-to-head comparison with RSV vaccine or RSV monoclonal antibodies)
Outcomes	**Efficacy or effectiveness – main outcomes** ▪ RSV infection§ ▪ RSV-related outpatient medically attended (MA) lower respiratory tract infection§ (LRTI) ▪ RSV-related hospitalisation including duration of hospitalisation§ ▪ RSV-related ICU admission* ▪ RSV-related death* **Efficacy or effectiveness – additional outcomes** ▪ Duration of protection (against any main outcome) ▪ Duration of stay in ICU ▪ Duration of invasive ventilation

	▪ Patient-reported outcomes and quality of life ▪ Antibiotic use for LRTI ▪ Long-term outcomes: – development of asthma (children) – reduced functional capacity (adults) **Safety – main outcomes** ▪ Serious adverse events[+] related to vaccination or immunisation (including neurological disorders such as Guillain-Barré syndrome) **Safety – additional outcomes** ▪ All adverse events, including: – solicited adverse events (local and systematic reactions) – unsolicited adverse events (spontaneously reported/other adverse events) ▪ Adverse pregnancy outcomes after vaccination during pregnancy[‡] ▪ Adverse neonatal outcomes after vaccination during pregnancy[^]
Study design	▪ High-quality systematic reviews[¥] of randomised controlled trials (RCTS) and non-randomised studies with a control group ▪ RCTs and non-randomised studies with a control group

Key: ICU – intensive care unit; LRTI – lower respiratory tract infection; MA – medically attended; mRNA – messenger ribonucleic acid; RCT – randomised controlled trial; RSV – respiratory syncytial virus.

Notes: * Phase II & III RCTs involving clesrovimab were eligible for inclusion in this review given that an application for this product has been submitted to European Medicines Agency for authorisation; decision pending.

[§] A positive laboratory diagnosis by polymerase chain reaction (PCR), virus culture or antigen detection.

[+] An adverse reaction that results in death, is life-threatening, requires hospitalisation or prolongation of existing hospitalisation, results in persistent or significant disability or incapacity, or is a birth defect.

[‡] Spontaneous abortion, foetal death, stillbirth, preterm birth (less than 37 weeks), pre-eclampsia and eclampsia.

[^] Congenital malformations (minor and major), neonatal death, and small-for-gestational age.

[¥] As described in section 4.1.

In accordance with the protocol for this HTA, evidence from high-quality, recently published systematic reviews of the clinical effectiveness and safety of RSV immunisation strategies were used, where available, and updated as necessary, to address the above research questions. Details relating to the necessary characteristics that must be present for a systematic review to be considered high quality are outlined in the protocol.[12]

The HIQA evaluation team identified three potentially suitable systematic reviews that address the above research questions when considered collectively:

- a living systematic review of RSV vaccines commissioned by the European Centre for Disease Prevention and Control (ECDC) a draft of which had been provided to HIQA on a confidential basis[200]
- a 2024 review by Sevendal et al. of the clinical efficacy and safety of mAbs[201]
- a 2025 review by Sumsuzzman et al. of the effectiveness of nirsevimab (a mAb).[202]

A decision was taken to use these reviews to inform this HTA based on a combination of their relevance to the HIQA evaluation team's research questions, the recency of their literature searches, and their quality, as assessed using the AMSTAR (A MeaSurement Tool to Assess Systematic Reviews) 2 tool.[203] This section summarises the methodology used in these identified systematic reviews and describes the methodology adopted by the HIQA team for the updates, where applicable.

4.2.1 Summary of the methods used in the systematic reviews

Review protocols

Protocols for the identified systematic reviews (ECDC, Sevendal et al. and Sumsuzzman et al.) were prospectively registered with the international prospective register of systematic reviews (PROSPERO) with registration numbers CRD42023439128,[204] CRD42022376633,[201] and CRD42024628782[205], respectively.

Summary of review methods

The HIQA evaluation team received a confidential version of the ECDC systematic review in December 2024. As a living review, the primary ECDC review was completed in April 2024, with a search until 18 May 2023. The first update by the same authors was completed in October 2024, with the search extended to 8 April 2024, and published in September 2025.[206] Hereafter, the living review is referred to as the ECDC review, with this term encompassing the studies identified in the

primary review and the first update. In the context of a rapidly-changing evidence base, a decision was made by the HIQA evaluation team to update the ECDC review, as the cut-off date for the most recent literature search available was over six months old. Specifically, it was noted that the ECDC review had not identified any studies in real-world settings, while topic exploration by the HIQA evaluation team indicated that such studies were published following implementation of RSV immunisation programmes in some countries for the 2023-2024 RSV season. The review assessed the efficacy, effectiveness and safety of authorised and unauthorised RSV vaccines in all human population groups, in addition to different dosages and dosing schedules to those of the currently authorised vaccines. As such, its scope was broader than the HIQA review, which focused on authorised interventions for the immunisation of infants and adults aged 65 years and older. Studies included in the ECDC review that did not meet the inclusion criteria for this HTA were excluded in this update, and as such are not discussed in this chapter.

The systematic review by Sevendal et al. was published in August 2024, with a search spanning 1 January 2000 to 29 November 2023. As the literature search cut-off date was over six months old, a decision was taken to update the review given the rapidly evolving evidence base for the RSV-specific mAbs. Specifically, it was noted that the review had not identified any completed RCTs involving clesrovimab, while topic exploration by the HIQA evaluation team had indicated that such RCTs may now be available. The Sevendal et al. systematic review assessed the efficacy and safety of novel RSV mAbs or antiviral therapies in all human population groups. As such, its scope was broader than the HIQA review, which focused on the immunisation of infants and was limited to authorised interventions and those with published phase II or III RCT data for which an application for authorisation has been submitted to the EMA. Studies included in the review by Sevendal et al. that did not meet the inclusion criteria for this HTA were excluded in this update and are not discussed in this chapter.

The systematic review by Sumsuzzman et al. was published in May 2025, with a search spanning 1 January 2023 to 25 February 2025. The review assessed the real-world effectiveness of nirsevimab in children aged two years and younger based on observational studies conducted during the first season (2023-2024) of nirsevimab immunisation programmes. The quality of included studies were evaluated using the Joanna Briggs Institute (JBI) Critical Appraisal Checklist for Observational Studies. The primary outcomes reported were RSV-related hospitalisation, ICU admission, incidence of LRTI, and length of hospital stay. These outcomes were relevant to the research questions and PICOS for this HTA. Not all studies included in the Sumsuzzman review met the inclusion criteria for this HTA. The HIQA evaluation

team excluded such studies and instead synthesised outcome data from the remaining studies; these analyses are reported in this chapter.

4.2.2 Methods used by HIQA to update and report on the systematic reviews

Search strategy and information sources

The search strategies developed by the authors of the ECDC and Sevendal et al. reviews were incorporated and updated by a librarian and are provided in Tables A4.1 and A4.2 in the appendix, respectively. The ECDC search was updated by the HIQA evaluation team for the purpose of this report, from 9 April 2024 to 9 January 2025, in the first instance, and further updated on 25 April 2025. Similarly, the HIQA evaluation team updated the Sevendal et al. search on 23 April 2025. Forward and backward citation searching was conducted on studies included after full text screening. This was completed on 25 April and 2 May 2025 for the ECDC updated searches, and on 9 May 2025 for the Sevendal et al. updated search, using citationchaser.[207]

As part of the HTA process, the health technology developer of each authorised medicinal product included in this assessment was provided with an opportunity to submit a dossier that included a list of studies pertaining to their product. This list was subsequently cross-checked by the HIQA evaluation team to ensure all studies which met the PICOS were included. No additional studies were identified through this process.

For the review of RSV vaccines, one additional study that was eligible for inclusion was identified after searches were complete, having been published on 5 May 2025. A decision was made to include this study in the update, as it reported on maternal vaccination effectiveness, and was considered important given that no other observational studies reporting on such data had been identified for inclusion. Regarding the review of RSV-specific mAbs, one study reporting the results of the phase IIb-III CLEVER RCT of clesrovimab was included in a post-hoc update in September 2025. A decision was made to include this study as no other efficacy or safety data for clesrovimab had been identified for inclusion.

Study selection and data extraction

With regard to the two reviews that were updated,[200, 201] titles and abstracts of articles retrieved were screened independently by two reviewers. The full text of potentially eligible articles was retrieved and independently assessed for eligibility by two reviewers according to the pre-specified inclusion and exclusion criteria outlined in Table 4.2. Data extraction was conducted independently by two reviewers using a standardised, pre-piloted electronic data extraction form. Any disagreements were

resolved through discussion and with third-party arbitration, when required. In addition, outcome data were extracted from eligible studies included in the identified systematic reviews. Data were extracted by a single reviewer and cross-checked by a second reviewer. The extracted data were further cross-checked against the primary studies for a random sample of studies. When discrepancies were identified within a review, a decision was taken for two reviewers to independently re-extract the outcome data. Any disagreements were resolved by discussion or with third-party arbitration, when required.

Table 4.2 Inclusion and exclusion criteria for the updates and or reporting of the identified systematic reviews

Inclusion criteria	Exclusion criteria
ECDC review of efficacy, effectiveness and safety of RSV vaccines	
▪ RCTs or NRSIs of authorised RSV vaccines ▪ Reporting efficacy, effectiveness or safety data* ▪ Published between 9 April 2024 and 9 January 2025. Further updated until 25 April 2025+ ▪ Published in the English language ▪ RSV infection was diagnosed via positive laboratory diagnosis by PCR, virus culture or antigen detection.	▪ Animal or laboratory studies ▪ Case reports, case series, review articles, observational studies, results only presented in abstract form, editorials, letters, results, trial registries, non-peer reviewed articles ▪ Medicinal products that have been discontinued.
Sevendal et al. review of the efficacy and safety of RSV EHL-monoclonal antibodies	
▪ RCTs of either authorised RSV EHL-mAbs or Phase II or III RCTs of unauthorised RSV EHL-mAbs that target human RSV infection ▪ Reporting efficacy or safety data* ▪ Published between 30 Nov 2023 and 23 April 2025§ ▪ Published in the English language ▪ RSV infection was diagnosed via positive laboratory diagnosis by PCR, virus culture or antigen detection.	▪ Animal or laboratory studies ▪ Case reports, case series, review articles, observational studies, results only presented in abstract form, editorials, letters, trial registries, non-peer reviewed articles ▪ Medicinal products that have been discontinued.
Sumsuzzman review of the effectiveness of nirsevimab	
▪ NRSIs of nirsevimab ▪ Reporting effectiveness or safety data* ▪ RSV infection was diagnosed via positive laboratory diagnosis by PCR, virus culture or antigen detection.	▪ Case reports, case series, review articles, observational studies, results only presented in abstract form, editorials, letters, results, trial registries, non-peer reviewed articles ▪ Intervention and control groups were compared across two different RSV seasons.

Key: NRSIs – non-randomised studies of intervention; PCR – polymerase chain reaction; RCTs – randomised controlled trials; RSV – respiratory syncytial virus.
Notes: * Safety where evaluated and reported with efficacy and or effectiveness within a study.
+ Forward and backward citation searching was conducted on 25 April 2025 and 2 May 2025 using citationchaser.
§ Forward and backward citation searching was conducted on 9 May 2025 using citationchaser.

Quality assessment

Two reviewers independently assessed the quality of studies included in the updates to the ECDC and Sevendal et al. reviews. For RCTs, the revised Cochrane risk-of-bias tool for randomized trials (RoB 2) was used to assess the risk of bias.[208] For non-randomised studies, risk of bias was assessed using the Risk of Bias in Non-randomized Studies of Interventions (ROBINS-I) tool (version 2).[209] Disagreements were resolved through discussion, or if necessary, involvement of a third reviewer. In addition, critical appraisal of all three reviews (ECDC, Sevendal et al. and Sumsuzzman et al.) was performed using the AMSTAR 2 tool.

Data synthesis and analysis

Reporting in this chapter adhered to the PRISMA 2020 statement.[210] Where studies were sufficiently homogenous in terms of participants, interventions and outcomes, meta-analysis was used to generate a combined effect estimate. For binary outcomes, risk ratios (RR), odds ratios (OR) or incidence rate ratios (IRR) were calculated, as appropriate, with these effect ratios then converted to efficacy or effectiveness, expressed as a percentage, to facilitate interpretation of the results. Percentage efficacy or effectiveness of immunisation products (vaccines or EHL-mAbs) was defined as 1 minus the effect ratio multiplied by 100. For continuous outcomes, the standardised mean difference was calculated as the measure of effect.

Meta-analysis was conducted using the *meta* package in R version 4.4.2. Fixed or random effects models were used, as appropriate. The fixed-effects model was used when a small number of studies were available for individual comparisons, as it was considered that there were insufficient data to support a reliable estimate of between-study variance using a random-effects model. For random-effects models, the Knapp-Hartung adjustment was used to control for the uncertainty in estimates of the between-study heterogeneity. The metabin function was used for binary outcomes, and the metacont function was used for continuous outcomes. The metainc function was used for the analysis of incidence rate ratios. Statistical heterogeneity was quantified using the I^2 statistic, and categorised according to the potential level of heterogeneity in line with Cochrane methodology.[211] The results are presented as forest plots, showing effect sizes and corresponding 95%

confidence intervals (CIs). Subgroup analyses (for example, based on age group, product, immune status and so on) were not performed due to limited data.

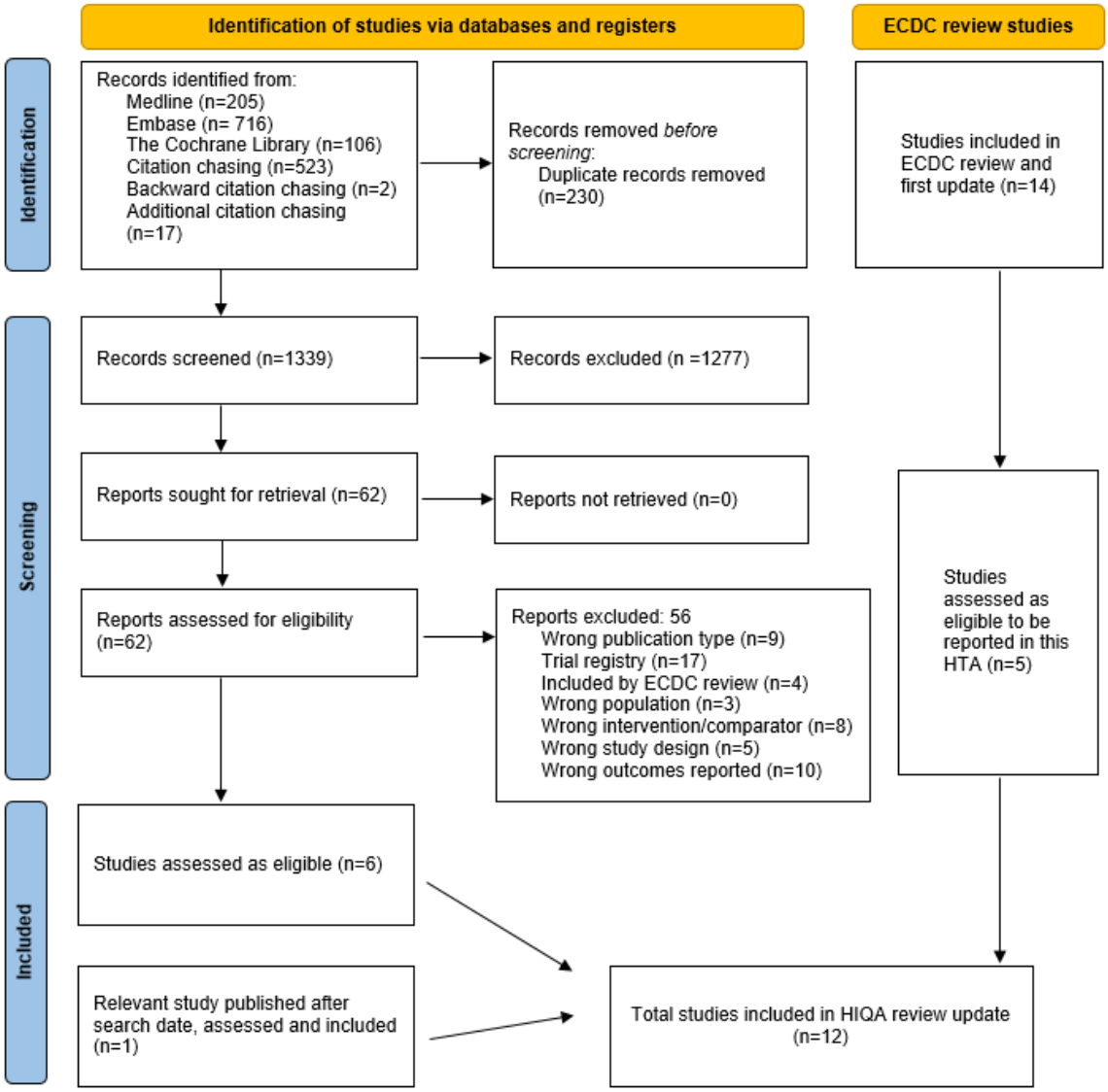
Data relating to efficacy or effectiveness were analysed on both an intention-to-treat (ITT) and a per protocol (PP) basis. Safety data were derived from the specified solicited safety cohort of trial participants for solicited safety outcomes, and from the exposed population (that is, those who received a vaccine or placebo injection) for other safety outcomes.

The certainty of evidence of the primary outcomes were assessed following the GRADE (Grading of Recommendations, Assessment, Development and Evaluation) approach,[212] using the GRADEpro tool.[213]

4.3 Results: efficacy, effectiveness and safety of RSV vaccines

In the first search (9 April 2024 to 9 January 2025), after removal of duplicates, 609 title and abstracts were assessed for eligibility. A total of 54 studies required full-text review, with two studies fulfilling the inclusion criteria.[214, 215] In the second search (to 25 April 2025), 730 title and abstracts were screened; eight new studies required full-text review, with four studies meeting the inclusion criteria.[216-219] After the completion of the second search, a relevant study fulfilling the inclusion criteria was published.[220] In addition, 5 of 14 studies from the ECDC review were assessed as meeting the inclusion criteria for this HTA.[221-225] As a result, a total of 12 studies were included in the data synthesis. An overall overview of the study selection process for both searches is presented in Figure 4.1.

Figure 4.1 PRISMA flow diagram of study selection process



4.3.1 Characteristics of included studies

Twelve unique records comprising eight studies reporting on four RCTs, three test-negative case control studies and one target trial emulation were included in this review. All studies were published between 2023 and 2025. All four RCTs were conducted across multiple study centres in multiple countries worldwide. Two of the test-negative case control studies and the target trial emulation were conducted in the USA. The remaining test-negative case control study was conducted in Argentina. A summary of the characteristics of each included study is provided in Table 4.3 while the characteristics of the participants and the interventions are outlined in Table 4.4.

The clinical efficacy of RSV vaccines in the older adult population was informed by RCT data relating to 97,547 unique individuals. These studies comprised six studies reporting on three RCTs: three studies reporting on RSVPreF3 (one interim analysis and two updated analyses from the same RCT),[219, 221, 224] two studies reporting on RSVpreF (one interim analysis and one updated analysis from the same RCT),[218, 222] and one study reporting on the RSV mRNA vaccine.[223] All six studies included adults aged 60 years and older, each was industry funded, all reported safety outcomes in addition to efficacy, and all reported some measure of frailty and or comorbidity status for the included participants (Tables 4.3 and 4.4). Median follow-up times reported for each RCT were 112 days (range: 1 to 379) during one RSV season,[223] 514 days (range: 15 to 762) across two RSV seasons,[218] and 30.6 months (interquartile range: 26.2 to 32.0) across three RSV seasons (Table 4.3).[219] Two of the three studies on RSVPreF3 reported on the efficacy and safety of seasonal revaccination,[219, 224] which are outside the scope of the current review. These outcomes are therefore not reported in this chapter.

The clinical effectiveness of RSV vaccines in the older adult population was informed by three US-based studies, which included adults aged 60 years and older and were conducted during the 2023/2024 RSV season: two test-negative case control studies that reported on a total of 81,595 laboratory confirmed RSV-related hospitalisations or emergency department encounters,[215, 216] and one target trial emulation that matched 146,852 vaccinated older adults to 582,936 unvaccinated controls.[217] Two of these studies examined effectiveness of vaccination with either RSVpreF or RSVPreF3,[216, 217] while one study examined RSVpreF vaccination only (Table 4.4).[215]

The clinical efficacy and safety of maternal vaccination with the RSVpreF vaccine for the passive immunisation of newborns and infants against RSV was informed by RCT evidence relating to 7,420 unique pregnant women and 7,307 infants born. Specifically, the evidence included two studies (one interim analysis[225] and one updated analysis)[214] reporting on a single RCT, the industry-funded Maternal Immunization Study for Safety and Efficacy (MATISSE) trial, which was limited to pregnant women with no known increased risk of pregnancy complications. Reported efficacy outcomes in this trial related to infants only, while safety outcomes were reported for both infants and pregnant women. Median follow-up times were 398 days (range: 1 to 939) and 392 days (range: 1 to 1,004) for children in the vaccinated and placebo groups, respectively (Table 4.3).

One industry-funded test-negative case control study reported on the clinical effectiveness of maternal RSVpreF vaccination.[220] The study included 505 infants aged six months or younger who were hospitalised with lower respiratory tract disease (LRTD) across 12 hospitals in Argentina during the 2024 RSV season. The

study predominantly included full-term infants who were otherwise healthy, with at least 85% of infants born at 37 weeks of gestation or later, and at least 96% having no known comorbidities (Table 4.4).

Case definitions and terminology used to describe efficacy outcomes were noted to differ between studies that reported on vaccine efficacy in the older adult population (Table A4.6 in the appendix).[218, 219, 221-224] All studies required confirmation of RSV infection by reverse transcriptase-polymerase chain reaction (RT-PCR). However, the number and nature of clinical signs and symptoms used to define cases of RSV-related acute respiratory illness (ARI) and lower respiratory tract disease (LRTD) differed to some extent between studies. The types of healthcare visits considered to be 'medically attended' also differed somewhat between studies that reported on medically attended (MA) RSV-related LRTD.[218, 219, 224] Despite these differences, it was considered reasonable to combine these outcomes for summary estimates, as outlined in Table A4.6 in the appendix and reported in Section 4.3.2.

Table 4.3 Characteristics of included studies

Author, year	Source	Population Sample size (n)	Design Funding	Study period	Geographic setting	Outcomes reported
Vaccination of adults aged ≥65 years						
RCT of RSVPreF3 - NCT04886596						
Papi et al.,[221] 2023	ECDC primary review	Adults aged ≥60 years Randomised overall: 25,040 ▪ RSVPreF3 group: 12,503 ▪ Placebo group: 12,537 (group ITT values obtained from Ison et al., 2024 as not reported in Papi et al., 2023)	Phase 3 RCT (interim analysis) Industry-funded: GSK	Enrolment between 25 May 2021 and 31 January 2022 with data reported up to 11 April 2022. Median follow-up: 6.7 months	278 locations across 17 countries	Vaccine efficacy:* ▪ RSV-related LRTD Secondary efficacy: ▪ RSV-related LRTD by subtype, age, comorbidities, and frailty status ▪ severe RSV-related LRTD ▪ RSV-confirmed ARI Safety: ▪ Reactogenicity of RSVPreF3 including solicited local and systemic events within four days of injection Safety of RSVPreF3 in terms of unsolicited AEs within 30 days of injection, all SAEs or pIMDs within 6 months of injection, related SAEs or pIMDs from day one until study end, and any fatal SAEs from day one until study end.
Ison et al.,[224] 2024	ECDC 1st update	Adults aged ≥60 years Overall: 25,040	Phase 3 RCT (update of	Enrolment between 25 May 2021 and 31 January 2022 and data	278 locations across 17 countries	Primary outcomes reported in Papi et al., 2023 Secondary efficacy outcomes*:

Author, year	Source	Population Sample size (n)	Design Funding	Study period	Geographic setting	Outcomes reported
		Season 1 ▪ RSVPreF3 group: 12,470 ▪ Placebo group: 12,503 Season 2 ▪ Dose 1 only group: 4,991 ▪ Placebo group: 10,033 Note: Season 1 RSVPreF3 group re-randomised in Season 2 into a Dose 1 only group (as above) and a Revaccinated group (n=4,966). Dose 1 only group reported in the current review.	Papi et al., 2023) Industry funded: GSK	collected until 31 March 2023. Median follow-up: 1. 6.7 months (season 1) 17.8 months (season 2)		▪ Efficacy of one RSVPreF3 dose and of revaccination one year later in preventing RSV-related LRTD over two seasons post-dose one ▪ Efficacy of the above in preventing severe RSV-related LRTD and RSV-related ARI ▪ Efficacy of the above in preventing RSV-related LRTD by RSV subtype, season, year, participant age at dose one, co-existing medical conditions, and frailty status Safety of one dose of RSVPreF3, and revaccination, one year later.
Ison et al.,[219] 2025	HIQA update	Adults aged ≥60 years Overall: 25,040 Season 1 (randomised)	Phase 3 RCT (update of Ison et al., 2024 and Papi et al., 2023)	Enrolment between 25 May 2021 and 31 January 2022. Trial ended on 31 May 2024.	275 locations across 17 countries	Efficacy and safety outcomes, as reported in Ison et al., 2024 and Papi et al., 2023: ▪ for season 3

Author, year	Source	Population Sample size (n)	Design Funding	Study period	Geographic setting	Outcomes reported
		▪ RSVPreF3 group: 12,503 ▪ Placebo group: 12,537 Seasons 2 and 3 (exposed) ▪ Dose 1 only group: 4,988 ▪ Placebo group: 10,033	Industry funded: GSK	Median follow-up: ▪ season 1: 6.7 months (IQR 5.7-7.8) ▪ season 2: 6.3 months (IQR 5.7-6.8) ▪ season 3: 7.0 months (IQR 7.0-7.0) ▪ from day 15 post-dose 1 to the end of season 3: 30.6 months (IQR 26.2-32.0).		▪ cumulatively, from dose 1 until the end of season 3. Secondary efficacy outcome: ▪ Hospitalisations due to RSV-related respiratory disease over 3 seasons. Additional efficacy outcomes (post-hoc analyses) by season, and cumulatively over 2 and 3 seasons: ▪ RSV-LRTD with medically attended visits ▪ RSV-related acute respiratory illness with medically attended visits.
RCT of RSVpreF - NCT05035212						
Walsh et al.,[(222)] 2023	ECDC primary review	Adults aged ≥60 years Randomised overall: 34,284 ▪ RSVpreF group: 17,215 Placebo group: 17,069	Phase 3 RCT Industry funded: Pfizer	From 31 August 2021 through 14 July 2022. Median follow-up: not reported.	240 locations across seven countries	Vaccine efficacy:* ▪ RSV-related LRTI with ≥2 signs or symptoms (cough, sputum production, wheezing, shortness of breath, tachypnoea) ▪ RSV-related LTRI with ≥3 signs or symptoms (cough, sputum production, wheezing, shortness of breath, tachypnoea)

Author, year	Source	Population Sample size (n)	Design Funding	Study period	Geographic setting	Outcomes reported
						▪ RSV-associated acute respiratory illness ▪ Frequency of RSV infection. Safety: ▪ SAEs related to vaccination ▪ Local reactions ▪ Systemic reactions.
Walsh et al.,[218] 2025	HIQA update	Adults aged ≥60 years Randomised overall: n=36,966 ▪ RSVpreF group: 18,487 Placebo group: 18,479	Phase 3 RCT (update of Walsh et al. 2023) Industry funded: Pfizer	From 31 August 2021 to 18 December 2023	241 locations across 7 countries	Efficacy and safety outcomes, as reported in Walsh et al., 2023: ▪ for season 2 ▪ cumulatively, from vaccination until the end of season 2. Additional efficacy outcomes (exploratory analyses): ▪ MA RSV-LRTI in season 1, season 2, and across two seasons. Final safety outcomes: ▪ unsolicited AEs from enrolment through 1 month post-vaccination ▪ all SAEs, and SAEs related to vaccination, throughout the study ▪ newly diagnosed chronic medical conditions throughout the study.

Author, year	Source	Population Sample size (n)	Design Funding	Study period	Geographic setting	Outcomes reported
RCT of RSV mRNA - NCT05127434						
Wilson et al.,[223] 2023	ECDC 1st update	Adults aged ≥60 years Randomised overall: n=35,541 ▪ mRNA-1345 group: 17,793 ▪ placebo group: 17,748	Phase 3 RCT (interim analysis) Industry funded: Moderna	Randomisation from 17 November 2021 to 31 October 2022. Data cut-off point reported of 30 November 2022. Median follow-up: 112 days (range: 1 to 379)	269 locations across 23 countries	Vaccine efficacy:+ ▪ RSV-related lower respiratory tract disease with ≥2 signs or symptoms ▪ RSV-related lower respiratory tract disease with ≥3 signs or symptoms ▪ RSV-related acute respiratory disease ▪ Efficacy according to RSV subtype ▪ All-cause mortality Safety: ▪ SAEs related to vaccination ▪ Unsolicited adverse events ▪ Adverse events of special interest (AESI) ▪ Local reactions ▪ Systemic reactions.
Non-randomised studies of RSVpreF and RSVPreF3						
Payne et al.,[216] 2024	HIQA update	Adults aged ≥60 years attending sites in the VISION network, an electronic health record-based health systems collaboration	Test-negative case control study Publicly funded: CDC	From 1 October 2023 to 31 March 2024.	6 sites across the USA, representing 230 hospitals and 245 emergency departments	Vaccine effectiveness: ▪ RSV-associated hospitalisation lasting more than 24 hours – critical illness (as a subset of hospitalisations), defined as ICU admission, in-hospital death, or both ▪ RSV-associated ED encounters.

Author, year	Source	Population Sample size (n)	Design Funding	Study period	Geographic setting	Outcomes reported
		Hospitalisations: n=36,706 ED encounters: n=37,842				Outcomes reported overall and for subgroups by age and immunocompromised status.
Bajema et al.,[217] 2025	HIQA update	Adults aged ≥60 years enrolled with the US Veterans Health Administration Total: n=729,788 ▪ Vaccinated: n=146,852 Matched unvaccinated controls: 582,936	Target trial emulation Publicly funded: US federal departments and FDA	Enrolment from 1 September 2023 until 31 December 2023. Follow-up until 31 March 2024. Median follow-up: 124 days (IQR 102-150) from day 14 post-index date.	USA	Vaccine effectiveness: ▪ Documented RSV infection, overall and for subgroups by age, immunocompromised status, and vaccine (RSVpreF or RSVPreF3) ▪ RSV-associated ED or urgent care visit ▪ RSV-associated hospitalisation ▪ RSV-associated ICU admission RSV-associated death.
Non-randomised study of RSVpreF						
Tartof et al.,[215] 2024	HIQA update	Adults aged ≥60 years Total: n=7,047 ▪ Cases: 623 ▪ Controls (Strict): 804	Retrospective test-negative case control study Industry funded: Pfizer	Laboratory confirmed RSV-related hospitalisation or ED encounter between 24 November 2023 and 9 April 2024	Southern California, USA	Vaccine effectiveness: ▪ RSV-related hospitalisation or ED visit Additional effectiveness outcomes: ▪ RSV-related hospitalisation ▪ RSV-related hospitalisation among those with chronic conditions ▪ RSV-related ED visits ▪ severe RSV-related hospitalisation and ED visits.

Author, year	Source	Population Sample size (n)	Design Funding	Study period	Geographic setting	Outcomes reported
						Outcomes were defined based on the results of laboratory testing ≤ 14 days before an LRTD encounter through to ≤3 days after an LRTD encounter.
Passive immunisation of newborns and infants through maternal vaccination						
RCT of RSVpreF - NCT04424316						
Kampmann et al.,[225] 2023	ECDC primary review	Pregnant women aged ≤49 years at 24-36 weeks of gestation Randomised pregnant women: ▪ Total: 7,392 ▪ RSVpreF group: 3,695 ▪ Placebo group: 3,697 Children born: ▪ Total: 7,128 ▪ Vaccine group: 3,570 Placebo group: 3,558	Phase 3 RCT (MATISSE) (interim analysis) Industry funded: Pfizer	From 17 June 2020 through 2 October 2022. Data cut-off date for efficacy: 30 September 2022 Data cut-off date for safety: 2 September 2022 Median follow-up: not reported	464 locations across 18 countries	Efficacy outcomes: ▪ MA RSV-related LRTI (within 90, 120, 150 and 180 days after birth) ▪ MA severe RSV-related LRTI (within 90, 120, 150 and 180 days after birth) Additional efficacy outcomes: ▪ MA RSV-related LRTI within 360 days after birth ▪ MA RSV-related hospitalisation within 360 days after birth ▪ MA LRTI of any causes within 360 days after birth ▪ MA RSV-related ARI ▪ MA RSV-related LRTI by RSV subtype Safety:

Author, year	Source	Population Sample size (n)	Design Funding	Study period	Geographic setting	Outcomes reported
						▪ Reactogenicity and adverse events in the maternal participants: – local and systemic events monitored for 7 days after injection – unsolicited events collection until 1 month after injection – SAEs collected through 6 months after delivery – Adverse events and newly diagnosed chronic medical conditions in the infant cohort – adverse events collected from birth to month of age. SAEs and newly diagnosed chronic medical conditions monitored from birth through 12 months of age.
Simoes et al.,[214] 2025	HIQA update	Pregnant women aged ≤49 years vaccinated at 24-36 weeks of gestation Randomised pregnant women: ▪ Total: 7,420 ▪ Vaccine group: 3,711	Phase 3 RCT (MATISSE) (update of Kampmann et al., 2023) Industry funded: Pfizer	17 June 2020 to 27 October 2023 Median follow-up: ▪ Vaccinated: 398 days (range: 1 to 939) ▪ Placebo: 392 days (range: 1 to 1,004)	464 locations across 18 countries	Vaccine efficacy: ▪ Severe RSV-related MA-LRTI within 180 days of birth ▪ RSV-related LRTI within 180 days of birth Safety: ▪ RSVpreF safety and tolerability in pregnant participants: – Adverse event collection through 1 month after injection

Author, year	Source	Population Sample size (n)	Design Funding	Study period	Geographic setting	Outcomes reported
		▪ Placebo group: 3,709 Children born: ▪ Total: 7,307 ▪ Vaccine group: 3,660 ▪ Placebo group: 3,647				– SAE collection through 6 months after delivery – AESI collected throughout entire study duration – Safety and tolerability in newborns and infants – Adverse events collected from birth through 1 month of age – SAEs and newly diagnosed chronic medical conditions collected from birth until age 12 or 24 months – AESI collected throughout the study. Additional efficacy outcomes ▪ RSV-related hospitalisation ▪ All-cause MA-LRTI within 360 days of birth. Exploratory efficacy outcomes ▪ RSV-related MA respiratory tract illness ▪ RSV-related hospitalisations within 730 days of birth.
Non-randomised study of RSVpreF						

Author, year	Source	Population Sample size (n)	Design Funding	Study period	Geographic setting	Outcomes reported
Pérez Marc et al.,[220] 2025	HIQA update	Infants hospitalised with RSV-associated LRTD from birth until 6 months (≤180 days) N= 505 infants included: ▪ 286 cases ▪ 219 controls	Test-negative case-control study Industry funded: Pfizer	Hospitalisations from 1 April 2024 to 30 September 2024.	12 hospitals across Argentina	Vaccine effectiveness: ▪ Hospitalisation due to RSV-LRTD from: – 0 to ≤180 days – 0 to ≤90 days – Hospitalisation due to severe RSV-LRTD from: – 0 to ≤180 days – 0 to ≤90 days (post-hoc analysis).

Key: AE – adverse event; AESI – adverse events of special interest; ARI – acute respiratory illness; CDC – Centers for Disease Control and Prevention (USA); ECDC – European Centre for Disease Prevention and Control; ED – emergency department; FDA – Food and Drug Administration (USA); HIQA – Health Information and Quality Authority; ICU – intensive care unit; IQR – interquartile range; LRTD – lower respiratory tract disease; LRTI – lower respiratory tract infection; MA – medically attended; pIMD – potential immune-mediated disease; RCT – randomised controlled trial; RSV – respiratory syncytial virus; SAE – serious adverse event; SD – standard deviation; VISION – Virtual SARS-CoV-2, Influenza, and Other respiratory viruses Network.

Note: *Efficacy outcomes were based on RSV-related LRTD cases occurring after Day 15 following injection and confirmed by qRT-PCR

⁺Efficacy outcomes were based on RSV-related LRTD cases occurring between 14 days and 12 months after injection.

Table 4.4 Characteristics of the participants and interventions

Author, year	Age and Sex	Comorbidities	Number of participants (ITT)	Intervention	Comparator
Vaccination of adults aged ≥65 years					
RCT of RSVPreF3 - NCT04886596					
Papi et al.,[221] 2023	Mean age (SD): ▪ RSVPreF3: 69.5 (6.5) ▪ Placebo: 69.6 (6.4) 60-69 years: ▪ Dose 1 only: 55.9% ▪ Placebo: 55.8% 70-79 years: ▪ Dose 1 only: 36.0% ▪ Placebo: 35.9% ≥80 years: ▪ Dose 1 only: 8.2% ▪ Placebo: 8.2% Female: ▪ RSVPreF3:52% ▪ Placebo: 51.4%	RSVPreF3, ▪ Frail: 1.5% ▪ Any pre-existing condition of interest: 39.6% Placebo, ▪ Frail: 1.4% ▪ Any pre-existing condition of interest: 38.9 %	Randomised overall: 25,040 ▪ RSVPreF3 group: 12,503 ▪ Placebo group: 12,537 (group ITT values obtained from Ison et al., 2024 as not reported in Papi et al., 2023)	RSVPreF3 vaccine	Placebo
Ison et al.,[224] 2024	Mean age (SD): ▪ RSVPreF3 overall: 69.5 (6.5)	RSVPreF3 overall, ▪ Frail: 1.5% ▪ ≥1 condition of interest: 40%	Overall: 25,040 Season 1 ▪ RSVPreF3: 12,503	RSVPreF3 vaccine, single	Placebo

Author, year	Age and Sex	Comorbidities	Number of participants (ITT)	Intervention	Comparator
	▪ Dose 1 only: 69.5 (6.4) ▪ Placebo: 69.6 (6.4) 60-69 years: ▪ RSVPreF3 overall: 55.8% ▪ Dose 1 only: 55.9% ▪ Placebo: 55.8% 70-79 years: ▪ RSVPreF3 overall: 36.0% ▪ Dose 1 only: 36.0% ▪ Placebo: 35.9% ≥80 years: ▪ RSVPreF3 overall: 8.2% ▪ Dose 1 only: 8.1% ▪ Placebo: 8.2% Female: ▪ RSVPreF3 overall: 52% ▪ Dose 1 only: 52.7% ▪ Placebo: 51.4%	Dose 1 only, ▪ Frail: 1.7%) ▪ ≥1 condition of interest: 39.8% Placebo, ▪ Frail: 1.4% ▪ ≥1 condition of interest: 39.4%	▪ Placebo: 12,537 Season 2 ▪ Dose 1 only: 4,991 ▪ Placebo: 10,033 Note: Season 1 RSVPreF3 group re-randomised in Season 2 into a Dose 1 only group (as above) and a Revaccinated group (n=4,966). Dose 1 only group reported in the current review.	dose administered season 1	
Ison et al.,[219] 2025	As per Ison et al., 2024	RSVPreF3 overall, ▪ Frail: 1.5% ▪ ≥1 condition of interest: 40.2% Dose 1 only, ▪ Frail: 1.7% ▪ ≥1 condition of interest: 40.2% Placebo,	Overall: 25,040 Season 1: ▪ RSVPreF3: 12,503 ▪ Placebo: 12,537 Seasons 2 and 3: ▪ Dose 1 only: 6,225	RSVPreF3 vaccine, single dose administered season 1	Placebo

Author, year	Age and Sex	Comorbidities	Number of participants (ITT)	Intervention	Comparator
		▪ Frail: 1.4% ▪ ≥1 condition of interest: 39.6%	(exposed~ population: 4,988) ▪ Placebo: 12,537 (exposed^ population: 10,033)		
RCT of RSVpreF - NCT05035212					
Walsh et al.,[222] 2023	Mean age (SD): 68.3 years (6.16) Overall: ▪ 60-69 years: 62.5% ▪ 70-79 years: 31.8% ▪ ≥80 years: 5.6% Female: 49.2%	▪ ≥1 pre-specified high-risk condition: 51.6% ▪ Current tobacco use: 15.2% ▪ Diabetes: 19.0% ▪ Lung disease: 11.7% ▪ Heart disease: 13.0% ▪ Liver disease: 1.9% ▪ Renal disease: 2.8% ▪ ≥1 chronic cardiopulmonary condition: 15.3% ▪ Asthma: 8.9% ▪ COPD: 6.1% ▪ Congestive heart failure: 1.8%	Randomised overall: 34,284 ▪ RSVpreF group: 17,215 Placebo group: 17,069	RSVpreF vaccine	Placebo
Walsh et al.,[218] 2025	Mean age: (SD): 68.2 years (6.13) Overall: ▪ 60-69 years: 62.6% ▪ 70-79 years: 31.9% ▪ ≥80 years: 5.5%	≥1 pre-specified high-risk condition: ▪ RSVpreF: 52.3% ▪ Placebo: 52.3%	Overall: 36,966 ▪ RSVpreF: 18,487 Placebo: 18,479	RSVpreF vaccine, single dose administered season 1	Placebo

Author, year	Age and Sex	Comorbidities	Number of participants (ITT)	Intervention	Comparator
	Male: 50.6%				
RCT of RSV mRNA - NCT05127434					
Wilson et al.,[223] 2023	Mean age (SD): 68.1 years (6.2) ▪ 60-69 years: 63.5% ▪ 70-79 years: 30.9% ▪ ≥80 years: 5.6% Female: 49%	▪ Frailty: 5.7% ▪ ≥1 coexisting condition of interest: 29.3% ▪ Congestive heart failure: 1.1% ▪ COPD: 5.5% ▪ Congestive heart failure and COPD: 0.3%	Randomised overall: 35,541 ▪ mRNA-1345 group: 17,793 placebo group: 17,748	mRNA-1345 RSV vaccine	Placebo
Non-randomised studies of RSVpreF and RSVPreF3					
Payne et al.,[216] 2024	Hospitalisations, median (IQR) ▪ Cases: 76 years (69-84) ▪ Controls: 76 years (69-83) ▪ Unvaccinated: 76 years (69-83) ▪ Vaccinated: 78 years (72-84) ED encounters, median (IQR) ▪ Cases: 75 years (68-83) ▪ Controls: 75 years (67-82)	Hospitalisations, underlying conditions present ▪ Respiratory: 48% ▪ Non-respiratory: 90% ▪ Cardiovascular: 79% ▪ Cerebrovascular: 6% ▪ Neuromuscular: 38% ▪ Haematological: 9% ▪ Endocrine or metabolic: 64% ▪ Renal: 38% ▪ Gastrointestinal: 8% ▪ Immunocompromising condition: 23%	Hospitalisations: 36,706 ▪ Cases: 1,926 ▪ Controls: 34,780 ED encounters: 37,842 ▪ Cases: 2,760 Controls: 35,082	RSV vaccine (RSVpreF or RSVPreF3)	No vaccination

Author, year	Age and Sex	Comorbidities	Number of participants (ITT)	Intervention	Comparator
	▪ Unvaccinated: 74 years (67-82) ▪ Vaccinated: 77 years (71-83) % ≥75 years: ▪ Hospitalisations: 56% % Female: ▪ Hospitalisations: 53% ▪ ED encounters: 55%	ED encounters, underlying conditions present: ▪ Respiratory: 24% ▪ Non-respiratory: 32% ▪ Cardiovascular: 23% ▪ Cerebrovascular: 1% ▪ Neuromuscular: 6% ▪ Haematological: 1% ▪ Endocrine or metabolic: 11% ▪ Renal: 6% ▪ Gastrointestinal: 1% ▪ Immunocompromising condition: 3%			
Bajema et al.,[217] 2025	Median age (IQR): ▪ Vaccinated: 76.0 years (71.7-79.7) ▪ Unvaccinated: 75.9 years (71.6-79.7) Vaccinated and unvaccinated groups matched by age: ▪ 60-69 years: 19.3% ▪ 70-79 years: 56.4% ▪ ≥80 years: 24.4% % Female: ▪ Vaccinated: 6%	Vaccinated: ▪ Obesity (BMI ≥30 kg/m²): 40.2% ▪ Cardiovascular disease: 41.6% ▪ Heart failure: 11.2% ▪ Hypertension: 78.6% ▪ Chronic kidney disease: 19.9% ▪ Chronic liver disease: 6.8% ▪ Chronic lung disease: 30.2% ▪ Diabetes: 41.1% ▪ Immunocompromised (including steroid use): 11.2%	Total: 729,788 ▪ Vaccinated: 146,852 ▪ Matched unvaccinated controls: 582,936	RSV vaccine (RSVpreF or RSVPreF3)	No vaccination

Author, year	Age and Sex	Comorbidities	Number of participants (ITT)	Intervention	Comparator
	▪ Unvaccinated: 6.1%	▪ Neurological or neuromuscular conditions: 6.2% ▪ Dementia: 3.9% Note: Unvaccinated group matched to within ±0.1% for all conditions			
Non-randomised study of RSVpreF					
Tartof et al.,[215] 2024	Mean age (SD): 76.8 years (9.6) Aged ≥75 years: 57.4% Female: 54.2%	▪ Immunocompromised: 14.2% ▪ Myocardial infarction: 16.0% ▪ Congestive heart failure: 36.9% ▪ Cerebrovascular disease: 14.4% ▪ Peripheral vascular disease: 68.4% ▪ Moderate or severe liver disease: 1.7% ▪ Malignant neoplasm: 17.3% ▪ Kidney disease: 42.4% ▪ COPD: 49.9% ▪ Dementia: 12.1% ▪ HIV/AIDS: 0.3% ▪ Diabetes HbA1c ≥7.5: 15.6% ▪ Diabetes HbA1c <7.5: 34.0%	Total: 7,047 ▪ Cases: 623 Controls (Strict): 804	Case group includes participants who test positive for RSV-related LRTD events (Intervention received by vaccinated cohort was RSVpreF)	Strict control: Test-negative controls with LRTD events who test negative for vaccine preventable disease (VPD)* and positive for non-VPD+
Passive immunisation of newborns and infants through maternal vaccination					
RCT of RSVpreF - NCT04424316					

Author, year	Age and Sex	Comorbidities	Number of participants (ITT)	Intervention	Comparator
Kampmann et al., 2023	Mean age (SD): 29.0 years (5.7)	Participants were limited to those with no known increased pregnancy risk	Randomised pregnant women: ▪ Total: 7,392 ▪ RSVpreF group: 3,695 ▪ Placebo group: 3,697 Children born: ▪ Total: 7,128 ▪ Vaccine group: 3,570 Placebo group: 3,558	RSVpreF administered between 24 and 36 weeks of gestation	Placebo
Simoes et al.,[214] 2025	Mean age of pregnant women (SD): 29.0 years (5.7) Gestational age at birth (children born): ▪ 24–<28 weeks: <0.1% ▪ 28–<34 weeks: 0.4% ▪ 34–<37 weeks: 4.7% ▪ 37–<42 weeks: 93.9% ▪ ≥42 weeks: 0.8%	Participants were limited to those with no known increased pregnancy risk	Randomised pregnant women: ▪ Total: 7,420 ▪ Vaccine group: 3,711 ▪ Placebo group: 3,709 Children born: ▪ Total: 7,307 ▪ Vaccine group: 3,660 Placebo group: 3,647	RSVpreF administered between 24 and 36 weeks of gestation	Placebo

Author, year	Age and Sex	Comorbidities	Number of participants (ITT)	Intervention	Comparator
Non-randomised study of RSVpreF					
Pérez Marc et al.,[220] 2025	Mean age at hospitalisation (SD): ▪ Cases: 73.6 days (33.1) ▪ Controls: 76.7 days (44.2) Gestational age at birth (cases; controls): ▪ <34 weeks: 2%; 2% ▪ 34 to <37 weeks: 13%; 11% ▪ ≥37 weeks: 85%; 87% Female: ▪ Cases: 46% ▪ Controls: 40%	Any comorbidity (no; yes; unknown): ▪ Cases: 96%; 3%; 1% ▪ Controls: 97%; 3%; 0%	Overall: 505 ▪ Cases: 286 ▪ Controls: 219	RSVpreF vaccine administered between 32 and $36^{+6/7}$ weeks of gestation and ≥14 days before delivery	No vaccination

Key: AIDS – acquired immunodeficiency syndrome; BMI – body mass index; COPD – chronic obstructive pulmonary disease; ECDC – European Centre for Disease Prevention and Control; ED – emergency department; HIQA – Health Information and Quality Authority; HIV – human immunodeficiency virus; IQR – interquartile range; ITT – intention to treat; LRTD – lower respiratory tract disease; RSV – respiratory syncytial virus; SD – standard deviation; VPD – vaccine-preventable disease.

Note: *VPDs include infections caused by RSV, human metapneumovirus, influenza, SARS-CoV-2.
+Non-VPDs include infections caused by adenovirus, coronavirus (229E, HKU1, NL63, OC43), human rhinovirus/enterovirus, parainfluenza 1-4, *Chlamydia pneumonia*, *Myoplasma pneumonia.*
~Participants who received RSVPreF3 before the first RSV season and placebo before the second RSV season.
^Participants who received placebo before the first RSV season and a second dose of placebo before the second RSV season.

4.3.2 Clinical efficacy/effectiveness outcomes of RSV vaccination against RSV in older adults

Six studies reported on the clinical efficacy and or effectiveness of RSV vaccines in adults aged 60 years and older comprising nine records presenting the results of three unique RCTs and three non-randomised studies of intervention (NRSI). The NRSIs included two test-negative case control studies and one target trial emulation study. For all three RCTs, the primary analyses were reported for a modified vaccinated cohort, typically restricted to only those participants who received the vaccine or placebo injection as randomly assigned, had no major protocol deviations, and did not report RSV-related acute respiratory infection (ARI) before day 15 after injection. This approach to reporting could also be described as the "per-protocol" effect of the intervention. Results based on an intention-to-treat analysis are presented in appendix A4 (Figures A4.8 to A4.11), where such calculations were possible.

For all three RCTs, the intervention (an RSV vaccine) was compared with a placebo injection. Event data and follow-up time were extracted for each outcome and reported as the relative incidence rate of the event in the intervention arm compared with the control arm. Outcome data were summarised by meta-analysis, where appropriate. This pooled incidence rate ratio (IRR) was then converted to an average vaccine efficacy estimate, expressed as a percentage. In one of the three RCTs, the intervention group was re-randomised following the first RSV season into two groups – one that received placebo prior to season two, and another group that received a second vaccine dose prior to season two.[224] The results relating to the single-dose group are reported in the main analyses in this chapter.

For the test-negative case-control study, the odds of having received an RSV vaccine among cases of RSV-related LRTD were compared with the odds among test-negative controls with LRTD events who tested negative for vaccine preventable disease (VPD) and positive for non-VPD (as presented in Table 4.4). Outcome data were summarised by meta-analysis, where appropriate, with the odds ratio or pooled odds ratio for each outcome converted to a vaccine effectiveness estimate, expressed as a percentage. RCTs and NRSI studies were combined separately. An overview of the certainty of evidence for the primary outcomes reported in the subsequent sections is presented in the GRADE summary of findings tables, in appendix A4 (Tables A4.3 to A4.5).

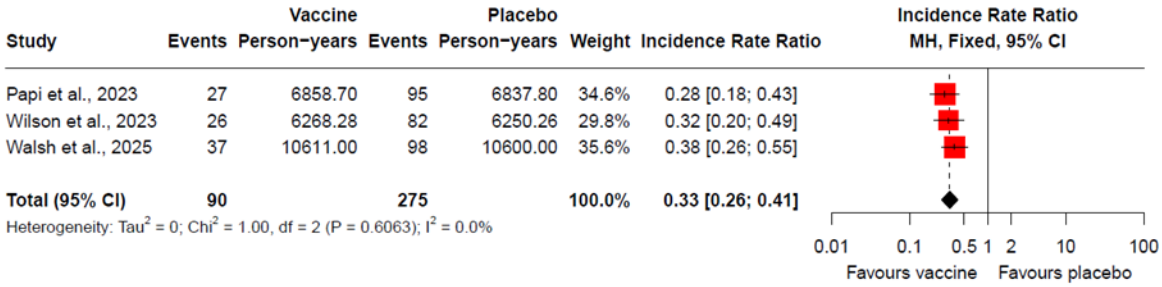
RSV-related infection

Six studies reporting on three RCTs examined the efficacy of an RSV vaccine against RSV-related acute respiratory infection (ARI) in adults aged 60 years and older.[221-224] [218, 219] The results are presented separately for one, two and three RSV

seasons. Where studies reported on the same season, the most up-to-data were used; as such, the results from five studies were included in the analysis. All studies showed a statistically significant reduction in RSV-related infection following vaccination for all time intervals.

Three studies reported on this outcome over one RSV season,[218, 221, 223] with the pooled vaccine efficacy (RSVPreF3, RSVpreF, RSV mRNA) estimated at 67% (95% CI: 59% to 74%) (Figure 4.2). There was no heterogeneity observed in this estimate.

Figure 4.2 Efficacy of RSV F protein-based vaccines compared with placebo against RSV-related ARI over one RSV season in adults aged 60 years and older

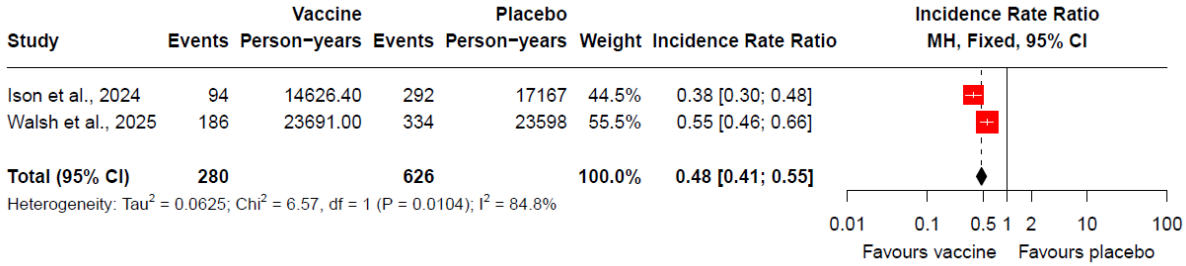


Note: The interventions in Papi et al. 2023, Walsh et al. 2025, and Wilson et al. 2023 were RSVPreF3, RSVpreF, and RSV mRNA, respectively.

Two RCTs reported on this outcome over two RSV seasons. The pooled cumulative vaccine efficacy (RSVPreF3, RSVpreF) was estimated at 52% (95% CI: 45% to 59%) (Figure 4.3).[218, 224] There was considerable heterogeneity in this estimate (I^2 = 84.9%).

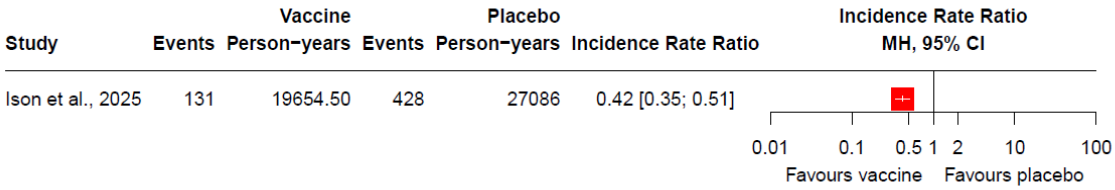
One RCT reported on the cumulative vaccine efficacy against RSV-related ARI over three seasons, with vaccine efficacy (RSVPreF3) estimated at 58% (95% CI: 49% to 65%) as depicted in Figure 4.4.[219]

Figure 4.3 Cumulative efficacy of RSV F protein-based vaccines compared with placebo against RSV-related ARI over two RSV seasons in adults aged 60 years and older



Note: The interventions in Ison et al. 2024 and Walsh et al. 2025 were RSVPreF3 and RSVpreF, respectively.

Figure 4.4 Cumulative efficacy of RSV F protein-based vaccines compared with placebo against RSV-related ARI over three RSV seasons in adults aged 60 years and older



Note: The intervention in Ison et al. 2025 was RSVPreF3.

Considering specifically within-season rather than cumulative vaccine efficacy against RSV-related ARI, this was estimated at 72% (57% to 82%) in season one (Figure 4.2),[221] 41% (95% CI: 19% to 57%) within season two[224] and 47% (95% CI 21% to 66%) within season three[219] for RSVPreF3 based on a single RCT. Similarly, for RSVpreF, it was estimated at 62% (95% CI: 45% to 74%) in season one (Figure 4.2)[222] and 37% (95% CI: 22% to 49%) within season two.[218]

Two studies reporting results from the same RCT over multiple seasons reported the vaccine efficacy, adjusting for seasonal variation.[219, 224] The cumulative VE (RSVPreF3) decreased when seasonal variation was considered. The reported cumulative VE against ARI over two RSV seasons was 53% (95% CI: 40% to 63%) with season as a covariate, compared with 62% (95% CI: 52% to 70%) without season as covariate. Over three RSV seasons, the reported cumulative VE against ARI was 51% (95% CI: 40% to 60%) with season as a covariate, compared with 58% (95% CI: 49% to 66%) without season as a covariate.

RSV-related medically attended ARI

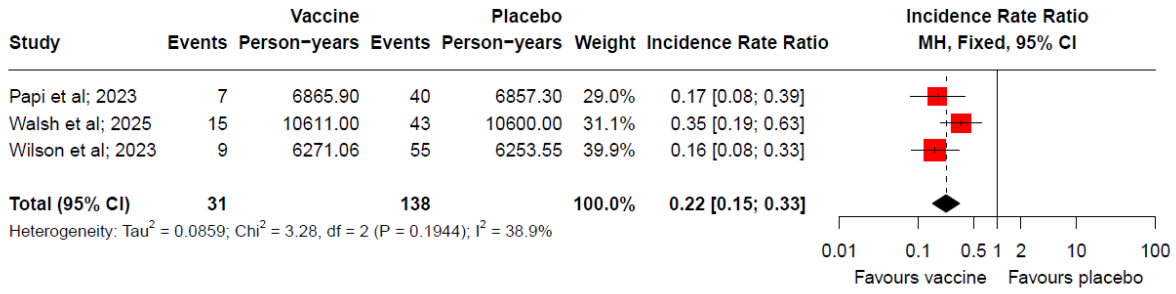
Two studies reported on the efficacy of RSV vaccine against medically attended (MA) ARI in adults aged 60 years and older. The results were not combined, as the follow-up times for this outcome were not consistently reported by the studies. Both studies reported a statistically significant reduction in events in the vaccine arm. Ison et al. reported vaccine efficacy (RSVPreF3) against MA ARI as 79% (95% CI: 54% to 92%) in the first season, with cumulative vaccine efficacy of 52% (95% CI: 27% to 69%) and 59% (95% CI: 40% to 72%) over two and three seasons, respectively.[219] Walsh et al. reported the vaccine efficacy (RSVpreF) against MA ARI as 65% (95% CI: 36% to 82%) in the first season and the cumulative vaccine efficacy over two seasons as 53% (95% CI: 36% to 66%), based on the modified exposed population.[218]

RSV-related LRTD

Six studies reporting on the results of three RCTs examined the efficacy of an RSV vaccine against laboratory-confirmed RSV-related LRTD in adults aged 60 years and older, with a maximum follow up of three RSV seasons.[218, 219, 221-224] All studies reported a statistically significant reduction in LTRD cases following vaccination at all time intervals. The pooled vaccine efficacy (RSVPreF3, RSVpreF, RSV mRNA) against RSV-related LRTD over one season was estimated at 78% (95% CI: 67% to 85%) (Figure 4.5).[218, 221, 223] There was a low degree of heterogeneity (I^2 = 39%) in this estimate.

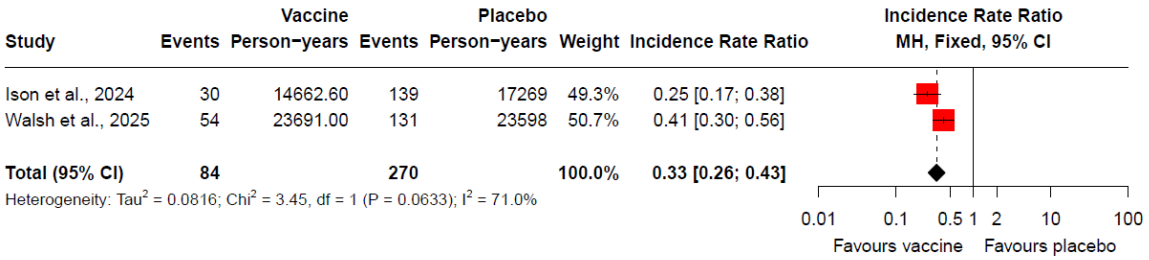
Two RCTs reported on the efficacy of RSV vaccines against RSV-related LRTD in adults aged 60 years and older over two RSV seasons (Figure 4.6).[218, 224] The cumulative vaccine efficacy (RSVPreF3, RSVpreF) was estimated at 67% (95% CI: 57% to 74%) with high heterogeneity (I^2 = 71%).

Figure 4.5 Efficacy of RSV F protein-based vaccines compared with placebo against RSV-related LRTD over one RSV season in adults aged 60 years and older



Note: The interventions in Papi et al. 2023, Walsh et al. 2025, and Wilson et al. 2023 were RSVPreF3, RSVpreF, and RSV mRNA, respectively.

Figure 4.6 Cumulative efficacy of RSV F protein-based vaccines compared with placebo against RSV-related LRTD over two RSV seasons in adults aged 60 years and older

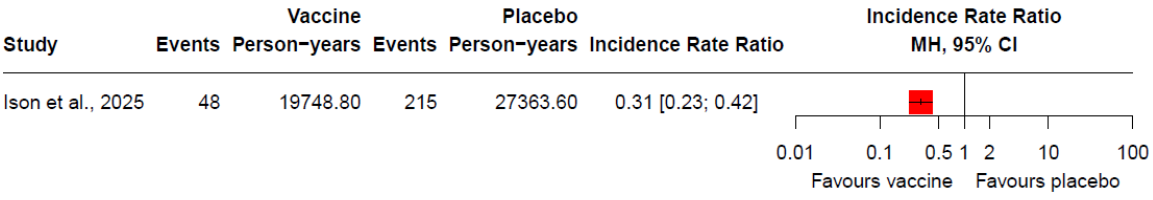


Note: The interventions in Ison et al. 2024 and Walsh et al. 2025 were RSVPreF3 and RSVpreF, respectively.

One RCT reported the cumulative vaccine efficacy against RSV-related LRTD (RSVPreF3) over three seasons.[219] This was estimated at 83% (95% CI: 61% to 92%)[221] over one season (Figure 4.5), 75% (95% CI: 62% to 83%)[224] over two seasons (Figure 4.6) and 69% (95% CI: 58% to 77%)[219] over three seasons (Figure 4.7).[219] This RCT indicated that the efficacy of RSV vaccination against RSV-related LRTD decreased over time and reported single season efficacy estimates for each of the three RSV seasons, with vaccine efficacy (RSVPreF3) decreasing from 83% (97% CI: 58% to 94%) within season one to 56% (95% CI: 28% to 74%) within season two to 48% (95% CI: 9% to 72%) in season three.[219]

Another RCT reporting results over two RSV seasons also reported decreasing vaccine efficacy against LRTD over time with vaccine efficacy (RSVpreF) reported at 65% (95% CI: 36% to 82%) in season one compared with 59% (95% CI: 43% to 71%) in season two.[218]

Figure 4.7 Cumulative efficacy of RSV F protein-based vaccines compared with placebo against RSV-related LRTD over three RSV seasons in adults aged 60 years and older



Note: The intervention in Ison et al. 2025 was RSVPreF3.

RSV-related medically attended LRTD

Three studies reporting on two RCTs examined the efficacy of an RSV vaccine against RSV-related MA LRTD in adults aged 60 years and older, with a maximum follow-up of three RSV seasons.

Two studies reported data for the first season; these were not combined, as the follow-up times were not reported. Both studies observed a statistically significant reduction in MA LRTD in the first season after vaccination, but the magnitude of the effect differed, ranging from an estimated VE (RSVPreF3) of 88% (95% CI 59% to 98%)[219] to VE (RSVpreF) of 70% (95% CI 33% to 88%).[218]

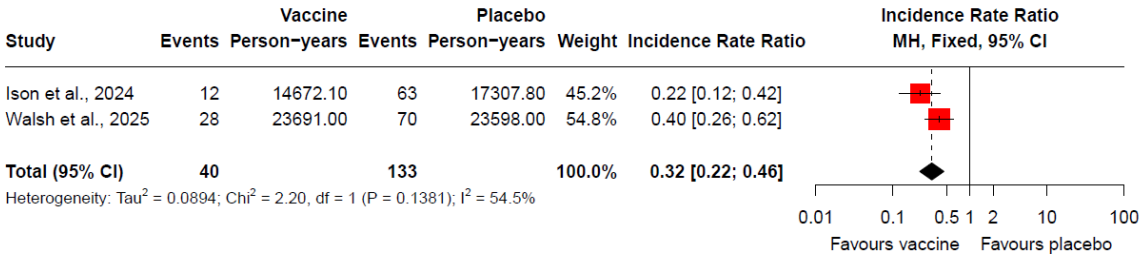
The studies also reported the cumulative vaccine efficacy (RSVPreF3, RSVpreF) over two RSV seasons (Figure 4.8). The pooled cumulative vaccine efficacy estimate over two seasons was 68% (95% CI: 54% to 78%), with moderate heterogeneity (I^2 = 54.6%).

One RCT (RSVPreF3) further reported cumulative vaccine efficacy against MA LRTD over three RSV seasons, estimated at 74% (95% CI: 56% to 84%) as depicted in Figure 4.9.[219] This compares with an estimated cumulative vaccine efficacy of 78% (95% CI: 58% to 88%) over two seasons (Figure 4.8)[224] and 88% (95% CI: 59% to 98%) over one season.[219]

Considering specifically within season efficacy data against MA LRTD, for RSVPreF3 this was estimated based on a single RCT at 88% (95% CI 59% to 98%) in season one as compared with 53% (95% CI: -4% to 81%) and 54% (95% CI: -14% to 85%) within season two and season three, respectively; these latter estimates were not statistically significant.[219]

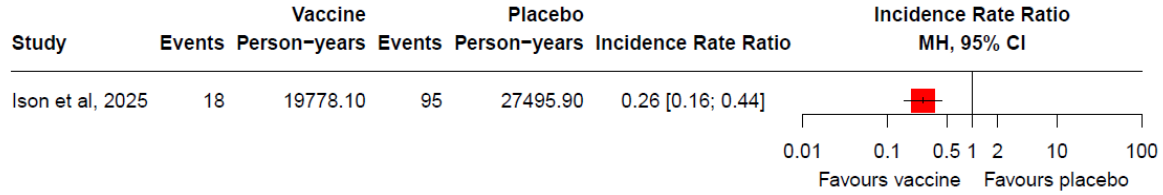
For RSVpreF, vaccine efficacy was estimated at 70% (95% CI: 33% to 88%) in season one compared with 54% (95% CI: 19% to 74%) in season two based on a single RCT.[218]

Figure 4.8 Cumulative efficacy of RSV F protein-based vaccines compared with placebo against medically attended RSV-related LTRD over two RSV seasons in adults aged 60 years and older



Note: The interventions in Ison et al. 2024 and Walsh et al. 2025 were RSVPreF3 and RSVpreF, respectively.

Figure 4.9 Cumulative efficacy of RSV F protein-based vaccines compared with placebo against medically attended RSV-related LTRD over three RSV seasons in adults aged 60 years and older



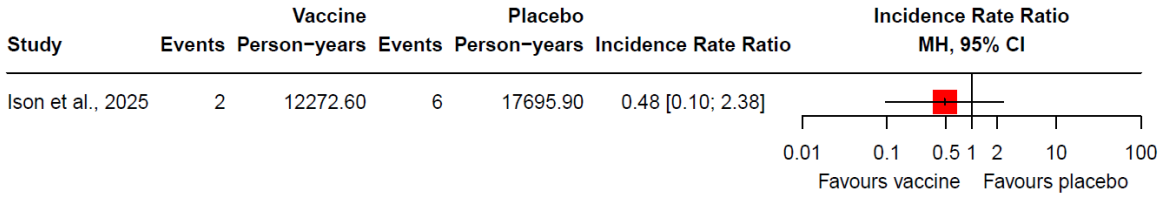
Note: The intervention in Ison et al. 2025 was RSVPreF3.

The three RCTs reported additional RSV-related LRTD outcomes.[218, 219, 223] The first RCT examined vaccine efficacy (RSVPreF3) against severe RSV-related LRTD and reported cumulative vaccine efficacy of 94% (95% CI: 62% to 100%) over one RSV season,[221] 83% (95% CI: 62% to 93%) over two RSV seasons[224] and 72% (95% CI: 51% to 85%) over three RSV seasons.[219] It also reported within season vaccine efficacy and reported the estimate during the second RSV season as 64% (95% CI: 6% to 89%)[224] and (the non-statistically significant estimate) during the third RSV season as 43% (-45% to 81.3%).[219] The second RCT examined vaccine efficacy (RSVpreF) against RSV-related LRTD described as having a more severe symptom profile (three or more symptoms) and reported cumulative vaccine efficacy of 89% (95% CI: 54% to 99%) over one RSV season and 82% (95% CI: 63% to 92%) over two RSV seasons.[218] It also reported the within season vaccine efficacy during the second RSV season as 78% (95% CI: 51% to 91%). The third RCT examined vaccine efficacy (RSV mRNA) against RSV-related LRTD with three or more signs or symptoms and reported cumulative vaccine efficacy of 82% (96.36% CI: 35% to 95%) over one RSV season.[223]

RSV-related hospitalisation

Two studies reporting on the results from the same RCT examined the cumulative efficacy of RSV vaccines against RSV-related hospitalisation over two[224] and three seasons,[219] respectively among adults aged 60 years and older. In the vaccine arm (RSVPreF3), there was a total of one hospitalisation due to RSV disease over two seasons and two hospitalisations over three seasons. In the placebo arm, there were a total of five hospitalisations over two seasons and six over three seasons. Efficacy could not be evaluated against RSV-related hospitalisations over two seasons due to the low event rates.[224] The overall event rate was also low when the follow up was extended over three seasons (Figure 4.10). This corresponded to a non-statistically significant vaccine efficacy of 52% (95% CI: -138% to 90%) over three seasons.[219]

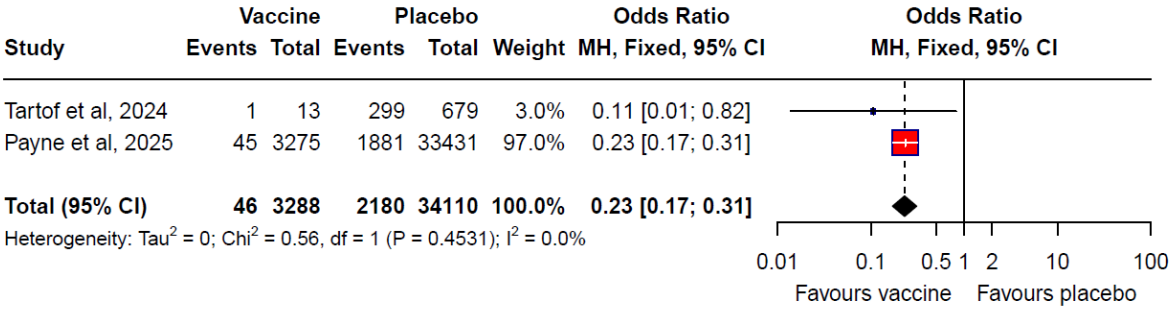
Figure 4.10 Efficacy of RSV F protein-based vaccines compared with placebo against RSV-related hospitalisation over three RSV seasons in adults aged 60 years and older



Note: The intervention in Ison et al. 2025 was RSVPreF3.

Three NRSIs reported on the effectiveness of RSV vaccines against RSV-related hospitalisation over one season among adults aged 60 years and older.[215-217] All three reported a statistically significant reduction in hospitalisations associated with vaccination. The results from two test-negative case control studies were combined. The pooled vaccine effectiveness was estimated as 77% (95% CI: 69% to 83%) (Figure 4.11). The heterogeneity of this estimate was low (I^2=0%).The third NSRI, a trial emulation study, estimated the vaccine effectiveness against RSV-associated hospitalisation as 80% (66% to 90%).[217]

Figure 4.11 Effectiveness of RSV F protein-based vaccines against RSV-related hospitalisation over one RSV season in adults aged 60 years and older



Note: Event and total numbers for the Payne study were calculated by summing the reported data for the immunocompetent and immunocompromised subgroups. The intervention in Tartof et al. 2024 was RSVpreF and in Payne et al. 2025 was either RSVPreF3 or RSVpreF.

RSV-related ICU admission

One NSRI reported the cumulative incidence rate of RSV-related ICU admission. The reported cumulative incidence was 0.01 (95% CI: 0.00 to 0.08) per 1,000 in the vaccinated group compared with 0.09 (95% CI: 0.07 to 0.13) per 1,000 in the unvaccinated group.[217] However, it was not possible to calculate the vaccine effectiveness against ICU admission due to the suppression of the total person-years data in the study.

RSV-related mortality

One RCT explicitly stated that no RSV-related deaths were reported during the study period,[221] while the remaining RCTs did not report RSV-related mortality.

Additional outcomes

In terms of duration of protection, all included studies reported results relating to a single RSV season. As outlined above, two RCTs reported findings for a second RSV season after vaccination, as well as overall outcomes over two RSV seasons.[224] One of these RCTs reported outcomes for a third RSV season, and cumulative outcomes across three RSV seasons.[219] This RCT also included a group of vaccinated participants who were randomised to be revaccinated prior to the second RSV season. Vaccine efficacy against RSV-related LRTD in this revaccinated group was reported to be similar to that of the single dose group for RSV season two (56%, 95% CI: 28% to 74% and 56%, 95% CI: 28% to 74%, respectively) and RSV season three (68%, 95% CI: 25% to 89% and 48%, 95% CI: 9% to 72%, respectively).

The included studies did not report on the other additional efficacy or effectiveness outcomes of interest outlined in Table 4.1.

Subgroup analysis

Two RCTs and two NSRIs reported the vaccine efficacy by different subgroups. It was not possible to combine the findings of subgroups across studies because of differing study designs and follow-up periods. The reported vaccine efficacy and or effectiveness against outcomes of interest, where reported by subgroup of interest, are presented in appendix A2 (Tables A4.12 to A4.17). Overall, results of subgroup analyses reported within each study indicated no clear differences in vaccine efficacy and effectiveness between subgroups based on age, immunocompromised status, frailty, or the presence or absence of certain co-morbidities.

4.3.3 Safety outcomes of RSV vaccination in older adults

As outlined in Table 4.1, the primary safety outcome of interest in this update was serious adverse events (SAEs) related to immunisation (including neurological disorders such as Guillain-Barré syndrome (GBS)). SAEs refer to reactions that result in death, are life-threatening, require hospitalisation or prolong existing hospitalisation, result in persistent or significant disability or incapacity, or in a birth defect.[226] Safety outcomes relating to adverse events of special interest (AESI) and potential immune mediated disease (pIMD) as defined by the individual trials were also extracted. AESIs and pIMDs events may also be categorised as SAEs depending on their level of severity. Additional safety outcomes of interest for older adults

included solicited local (for example, injection site pain or redness) and systemic (such as fever or fatigue) events, and unsolicited adverse events (that is, adverse events that were not specifically asked about by study investigators, but were spontaneously reported by the participants).[227]

Six studies reporting on safety outcomes from three RCTs were identified. Three of these studies reported on safety outcomes after vaccination with an authorised RSV vaccine or placebo over one RSV season.[221-223] Two studies, provided updated safety findings for participants through a second RSV season[218, 224] and one study provided data through a third RSV season.[219] The results are reported separately for the three studies reporting on outcomes over a single RSV season and data over multiple seasons. A summary of safety outcomes of interest across the three RCTs is provided in Table 4.5.

Table 4.5 Adverse event reporting with RSV vaccines compared with placebo in adults aged 60 years and older

Study, author	Serious adverse events related to intervention n (%)		AESI including pIMDS related to intervention n (%)		Solicited adverse events n (%)				Unsolicited adverse events n (%)	
					Local events		Systemic events			
	RSV	Placebo	RSV	Placebo	RSV	Placebo	RSV	Placebo	RSV	Placebo
Season 1										
Papi, et al.,[221] 2023	10 (0.08%)	7 (0.06%)	7 (0.1%)~	5 (<0.1%)~	Overall local or systemic reactions not reported				4,117 (33.02%)	2,229 (17.83%)
Walsh, et al.,[222] 2023	3 (0.02%)	0	2 (0.01%)‡	0	435 (12.01%)	248 (7.01%)	978 (27.01%)	920 (26.00)	1,544 (8.97%)	1,453 (8.51%)
Wilson, et al.,[223] 2024	4 (0.02%)	3 (0.02%)	1 (<0.01%)§	1 (<0.01%)§	10,367 (58.69%)	2,845 (16.17%)	8,432 (47.74%)	5,798 (32.95%)	3,624 (20.43%)	3,331 (18.84%)
Season 2*										
Ison, et al., 2024[224]	2 (0.04%)	4 (0.4%)	1 (0.02%)	2 (0.02%)	33 (9.57%)	51 (7.65%)	74 (21.45%)	121 (18.14%)	791 (15.85%)	1,495 (14.90%)
Season 3*										
Ison, et al., 2025	1 (0.07%)	2 (0.07%)	3 (0.2%)~	0	4 (6.78%)	7 (6.54%)	13 (22.03%)	21 (19.63%)	233 (15.88%)	422 (14.72%)
Over 2 seasons+										
Walsh et al., 2025[218]	3 (0.02%)	0	0	0	NR	NR	NR	NR	2,012^ (10.8%)	1,917^(10.5)

Key: AESI – adverse event of special interest; pIMD – potential immune mediated disease; RSV – respiratory syncytial virus

Note: ~These events relate to pIMDs considered related to the study intervention.

‡ These events relate to one case of Miller-Fisher syndrome (a subset of Guillain-Barré syndrome (GBS)) and one case consistent with GBS.

§ These events relate to any (AESI up to 28 days after vaccination related to the study intervention (as per supplement Table S13 of Wilson et al., 2023)
* Safety results limited to single season of follow-up for the single-dose vaccination group.
+ For Walsh et al., 2025, results related to a follow-up duration of the whole trial period (two seasons).
^ Reported in publication as any adverse event through one month post-vaccination based on total safety population.

Serious adverse events related to the intervention

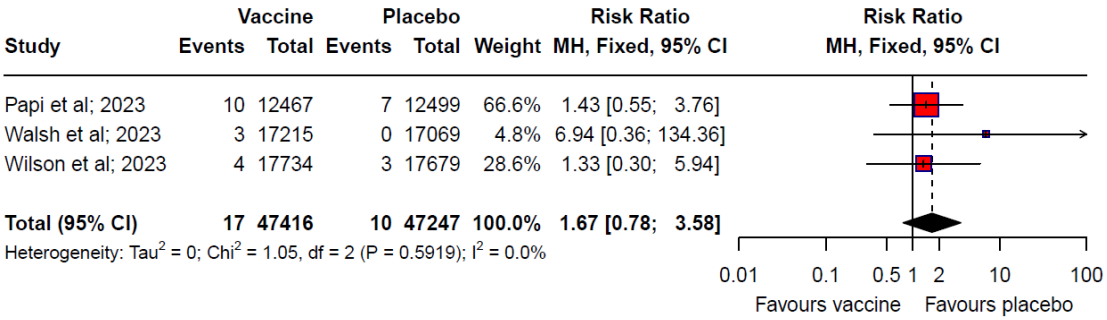
Three studies reporting on three different placebo-controlled RCTs reported on SAEs related to the intervention in adults aged 60 years and older over one RSV season (Figure 4.12). For each of the RCTs, data on intervention-related SAEs were collected from the day of injection until the end of the trials. While a higher frequency of intervention-related SAEs were observed in the vaccine groups, overall event rates were low (≤ 0.08%). In the pooled analysis, there was no statistically significant difference in the risk (risk ratio (RR): 1.67 (95% CI: 0.78 to 3.58))[221-223]

The study by Papi et al. (RSVPreF3) reported a slightly higher frequency of intervention-related SAEs in the vaccine group (0.08%) compared with the placebo group (0.06%), while the frequency of pIMDs that were considered related to the intervention were similar in both groups.[221]

The study by Walsh et al. noted three (0.02%) intervention-related SAEs in the vaccine (RSVpreF) group and none in the placebo group.[222] The three SAEs, considered by investigators to be related to vaccination, comprised one allergic reaction seven hours after injection, with recovery within the same day; one case consistent with Miller-Fisher syndrome, a subset of Guillain-Barré syndrome (GBS); and one case of myocardial infarction that developed six days after injection, and subsequent acute inflammatory demyelinating polyradiculoneuropathy, consistent with GBS, that began seven days after infection. No trial intervention-related deaths or adverse events leading to withdrawal from the study were reported. In terms of overall deaths, there were 52 (0.30%) in the vaccine group and 49 (0.29%) in the placebo group. None of the deaths were considered by the investigator to be related to the vaccine or placebo.

Wilson et al. reported the same percentage of intervention-related SAEs (0.02%) in the vaccine (RSV mRNA) and placebo groups; no breakdown of these events was provided.[223] No fatal adverse events related to the study intervention were reported in either group. There was one case of an adverse event in the intervention group leading to study discontinuation, and no such cases in the placebo group. Up until the data cut-off of this current analysis, no cases of acute disseminated encephalomyelitis or GBS were reported in either group. In terms of overall deaths from any cause within 28 days of vaccination, there was one (<0.01%) in the vaccine group and four (0.02%) in the placebo group.

Figure 4.12 Serious adverse events (SAEs) related to the intervention in older adults in the first season

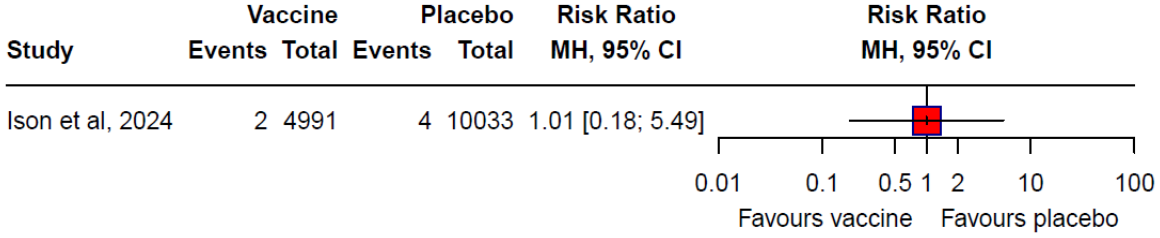


Note: The interventions in Papi et al. 2023, Walsh et al. 2023, and Wilson et al. 2023 were RSVPreF3, RSVpreF, and RSV mRNA, respectively.

Two studies reporting on second season and third season follow up of the same RCT provided results on SAEs related to vaccination at these time points.[219, 224] Event rates were low in both groups in the second and third seasons, with no difference reported between the groups (Figure 4.13). [219, 224] A total of 496 (2%) participants died throughout the trial period. Five deaths were considered by investigators during a blinded assessment to be related to the vaccine or placebo. Three of these deaths occurred in vaccine recipients (cardiopulmonary failure, left ventricular failure, and cardiac arrest) and two in placebo recipients (pulmonary embolism, and unknown cause of death). In addition, nine (<0.1%) recipients of a single dose of RSVPreF3 vaccine and nine (<0.1%) placebo recipients had a pIMD that was considered related to the intervention.

The other study (RSVpreF) providing follow-up through a second RSV season reported no additional related-SAEs through the end of season two.[218]

Figure 4.13 Serious adverse events (SAEs) related to the intervention in older adults in the second season



Note: The intervention in Ison et al. 2024 was RSVPreF3.

Local and systemic adverse events

Among the three RCTs (RSVPreF3, RSVpreF, RSV mRNA) reporting on outcomes after one RSV season,[221-223] the frequency of any spontaneous unsolicited adverse event ranged from 9.0% to 33.0% in the vaccine groups and 8.5% to 18.8% in the

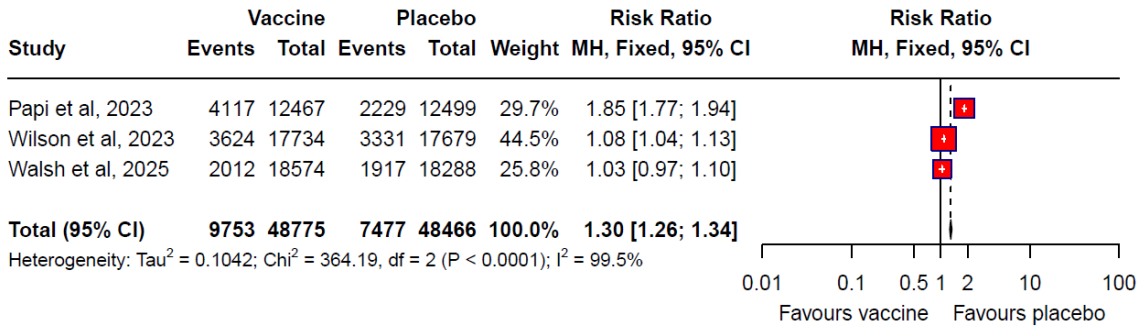
placebo groups. In the pooled analysis, the risk of experiencing any unsolicited adverse event was significantly higher in the vaccine arm (RR: 1.30 (95% CI: 1.26 to 1.34) (Figure 4.14). When considering each vaccine separately, a significantly increased risk was only observed for RSVPreF3 (RR: 1.85 (95% CI: 1.77 to 1.94).

In terms of solicited adverse events, combined results from two studies (RSVPreF3, RSV mRNA) indicated a significant higher risk in vaccinated participants compared with those who received placebo (RR: 1.81; 95% CI: 1.77 to 1.85) as shown in Figure 4.15.[221, 223]

Two studies (RSVpreF, RSV mRNA) reported on the frequency of solicited local reactions, for example, pain, redness or swelling at the injection site, between intervention and placebo groups. These ranged from 12.0% (RSVpreF) to 58.7% (RSV mRNA) in the vaccine group and from 7.0% (RSVpreF) to 16.2% (RSV mRNA) in the placebo group.[222, 223] Overall local and systemic reactions were not reported for the third RCT,[221] but the frequency of any solicited adverse reaction in this study (RSVPreF3) was 71.9% among vaccine recipients and 27.9% among placebo recipients. The frequencies of severe solicited adverse reactions (Grade 3 or 4 reactions) among vaccine recipients compared with placebo recipients were ≤0.7% vs ≤0.7% (RSV mRNA), 4.1% vs 0.9% (RSVPreF3) and 6.2% vs 4.1% (RSVpreF).[221-223]

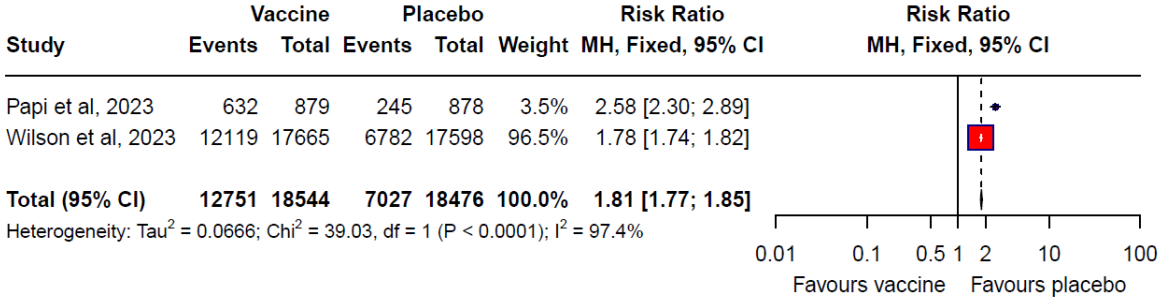
Two studies reported on the overall frequency of solicited systemic events, such as, myalgia, fatigue or fever.[222, 223] These ranged from 27.0% (RSVpreF) to 47.7% (RSV mRNA) among vaccine recipients and 26.0% (RSVpreF) to 33.0% (RSV mRNA) among placebo recipients. One of these studies (RSV mRNA) provided the frequency of severe (grade 3 or 4) solicited systemic events, with 4.0% occurring among vaccine recipients and 2.9% among placebo recipients.[223]

Figure 4.14 Any unsolicited adverse events within one month following RSV prefusion vaccine vs placebo in older adults



Note: The interventions in Papi et al. 2023, Wilson et al. 2023, and Walsh et al. 2025 were RSVPreF3, RSV mRNA, and RSVpreF, respectively.

Figure 4.15 Solicited adverse events following RSV prefusion vaccine vs placebo administration in older adults



Note: The interventions in Papi et al. 2023 and Wilson et al. 2023 were RSVPreF3 and RSV mRNA, respectively. Reporting periods – Papi et al., 2023: ≤4 days post-vaccination; Wilson et al., 2023: ≤7 days post-vaccination.

4.3.4 Clinical efficacy/effectiveness outcomes of maternal vaccination against RSV in infants

Two studies reporting on the results of a single RCT and one NRSI (a test-negative case control study) were included in this update.[214, 225] The reported RCT outcomes in this section relate to the results from the final updated analysis of the MATISSE trial, published by Simoes et al. in 2025.[214]

Vaccine efficacy was reported at 90 days, 120 days, 150 days, and 180 days of follow-up in the RCT and less than or equal to 90 days and 180 days in the NRSI. As a typical RSV season is usually six months in duration, and the duration of protection of the maternal vaccine is approximately six months, the estimates included in the following section relate to the 180 days follow-up period.

RSV-related infection

The included studies did not report on RSV-related ARI in infants.

RSV-related LRTD

One RCT (RSVpreF) reported on RSV-related LRTD in infants, showing a statistically significant reduction in events following vaccination compared with placebo. Vaccine efficacy against MA RSV LRTD was estimated at 49% (95% CI: 32% to 62%) at 180 days follow-up (Figure 4.16).[214] In terms of severe MA RSV-related LRTD, vaccine efficacy was estimated at 70% (95% CI: 51% to 82%) over the same follow-up period (Figure 4.17).[214]

Figure 4.16 Efficacy of RSVpreF against medically attended RSV-related LRTD in infants at 180 days

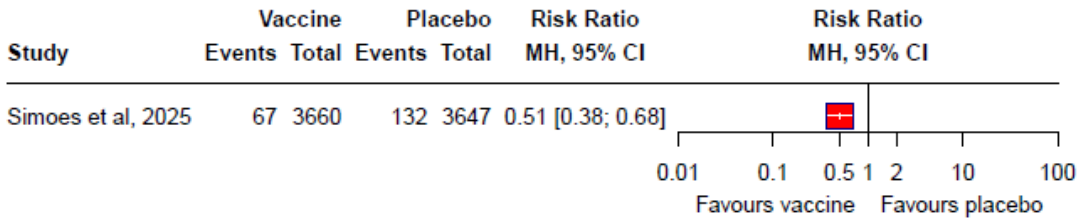
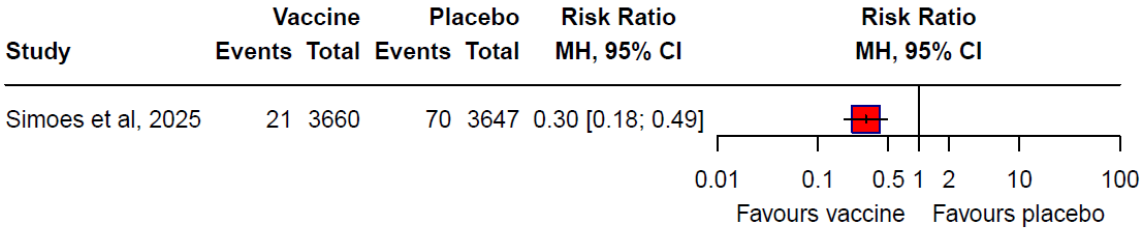


Figure 4.17 Efficacy of RSVpreF against severe medically attended RSV-related LRTD in infants at 180 days

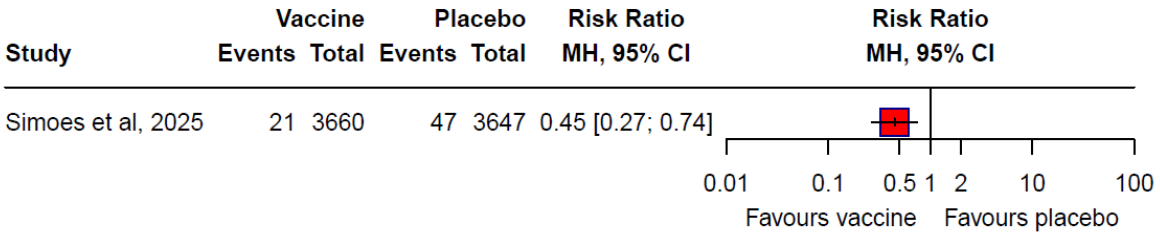


The included NRSI did not report on this outcome.

RSV-related hospitalisation

One RCT (RSVpreF) reported on RSV-related hospitalisation in infants, showing a statistically significant reduction in events associated with vaccination. Vaccine efficacy was estimated at 55% (95% CI: 26% to 73%) at 180 days follow-up (Figure 4.18).[214] Results were also reported for RSV-related hospitalisations at 360 days follow-up, with no significant difference noted between the vaccine and placebo arms (VE: 24% (95% CI: -11% to 49%)).

Figure 4.18 Efficacy of RSVpreF against RSV hospitalisation in infants at 180 days



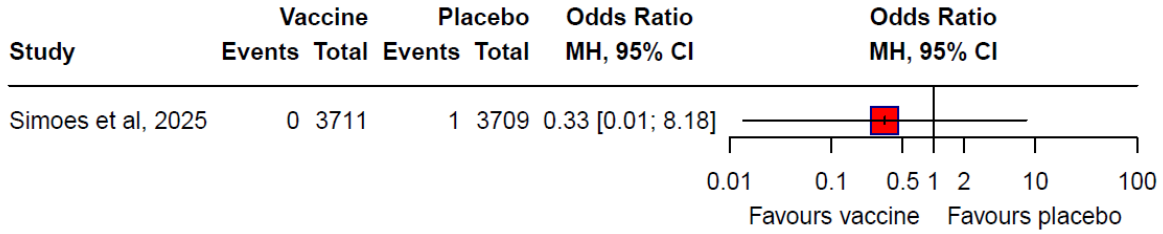
The included NRSI (n=505) reported on RSV-related LRTD leading to hospitalisation up to 180 days after birth, noting a statistically significant reduction in hospitalisations with vaccination (RSVpreF) compared with no vaccination.[220] Vaccine effectiveness for this outcome was reported as 71% (95% CI: 53% to

82%). A sensitivity analysis was conducted excluding 36 RSV positive case infants tested by non-PCR methods and reported a similar vaccine effectiveness estimate of 71% (95% CI: 52% to 83%).

RSV-related mortality

There were no reported deaths due to RSV in the vaccine group for the duration of follow-up in the RCT. One death in a 120-day-old full-term infant in the placebo group was later classified as caused by RSV-related ARI (Figure 4.19).[214]

Figure 4.19 Efficacy of RSVpreF against mortality related to RSV in infants



The NRSI reported that there were no deaths among the 160 hospitalised infants who were born to an RSVpreF-vaccinated pregnant woman.[220] However, there were three RSV-related deaths among 345 hospitalised infants whose mothers had not received RSVpreF during pregnancy. No deaths were reported among 219 RSV-negative infants in the control group.

Additional outcomes

The included RCT reported on a number of additional efficacy outcomes of interest outlined in Table 4.1. Specifically, a number of outcomes relating to healthcare utilisation were reported, with no differences observed between the trial arms within 180 days after birth, as confirmed by an independent Endpoint Adjudication Committee. These outcomes included ICU admissions greater than four hours' duration (OR: 1.69 (95% CI: 0.45 to 6.12), asthma-related illness (OR: 1.38 (95% CI: 0.33 to 5.29), bronchodilator use (OR: 0.79 (95% CI: 0.41 to 1.50), and antibiotic use (OR: 1.17 (95% CI: 0.60 to 2.26).

The included NRSI did not report on vaccine effectiveness against these outcomes. Proportions of the total number of vaccinated and unvaccinated case infants (that is, infants who were both hospitalised and RSV positive) who experienced certain similar outcomes relating to healthcare utilisation were reported. For example, ICU admission for more than four hours was reported for 20% of vaccinated case infants and 25% of unvaccinated case infants. Any antibiotic use during hospitalisation was reported for 49% of vaccinated case infants and 47% of unvaccinated case infants.

The included RCT did not specifically report on requirement for or duration of invasive ventilation, which was also an additional outcome of interest (Table 4.1). However, the RCT reported on RSV-related LRTD requiring oxygen support in infants, showing a statistically significant reduction in events associated with vaccination. At 180 days follow-up, there were 13 and 25 cases in the vaccine and placebo groups, respectively, of MA RSV-related LRTD with oxygen saturation less than 90% or requiring supplemental oxygen (VE: 77% (95% CI: 31% to 92%)).[214] Separating out these outcomes, there were nine and 20 cases with oxygen saturation less than 90%, in the vaccine and placebo groups, respectively, corresponding to a statistically significant vaccine efficacy estimate of 55% (95% CI: 2% to 80%). Estimated vaccine efficacy against RSV-related LRTD requiring supplemental oxygen was not significant (VE: 42% (95% CI: -47% to 77%)), with seven and 12 cases reported in the vaccine and placebo groups, respectively.

Vaccine effectiveness against these outcomes was not reported in the included NRSI. Among hospitalised RSV positive cases, similar proportions of vaccinated and unvaccinated infants had a documented oxygen saturation less than 90% (22% and 24%, respectively), or required high-flow oxygen (41% and 43%, respectively) at any time.[220]

4.3.5 Safety outcomes of maternal vaccination against RSV in infants

The included NRSI[220] did not report on safety outcomes, hence, all safety outcomes reported below are based on the RCT data.[214] A summary of the safety outcomes of interest is provided in Table 4.6.

Table 4.6 Summary of adverse events, serious adverse events, and adverse events of special interest among pregnant women and newborns/infants

Outcome	Pregnant women		Newborns/infants	
	RSVpreF n (%)*	Placebo n (%)*	RSVpreF n (%)*	Placebo n (%)*
Adverse events (AEs)				
Any AEs	14%	13.2%	38%	35.4%
Severe AEs	1.8%	1.4%	4.6%	3.9%
Serious adverse events (SAEs)				
Any SAEs	4.3%	3.8%	16.3%	16.1%
SAEs related to intervention	3 (0.08%)	1 (0.03%)	0 (0%)	0 (0%)
Adverse events of special interest				
Preterm delivery/birth (<37 weeks)	207 (5.7%)	172 (4.7%)	207 (5.7%)	172 (4.7%)
Low birthweight (≤2,500g)	N/A	N/A	5.1%	4.3%

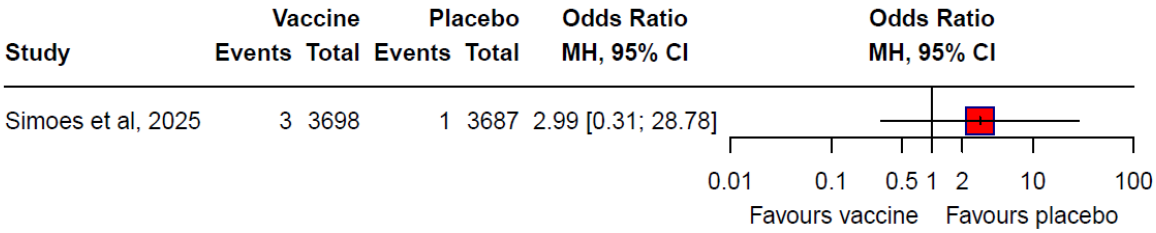
Key: AE – adverse event; RSV – respiratory syncytial virus; SAE – serious adverse event

Note: *Number of events and or percentages, as per data reported by study authors.

Serious adverse events related to vaccination

The only RCT included reported on SAEs related to the intervention in pregnant women from the time of consenting to participate until six months after delivery. No significant difference in SAEs was noted between the vaccine and placebo arms (OR: 2.99, 95% CI: 0.31 to 28.78) (Figure 4.20). Three reported SAEs (severe extremity pain which resolved in six days with uncomplicated delivery at 41 weeks' gestational age; premature labour the day after vaccination which resolved that day after fluids and rest with uncomplicated delivery at 39 weeks' gestational age; eclampsia 15 days after vaccination followed by a caesarean section delivery of a live newborn at 38 weeks) were considered related to the intervention in the vaccine group and one (moderate premature placenta separation) in the placebo group.[214] The study authors reported that each of these related SAEs resolved. Overall, the frequency of any SAE was 4.3% in the vaccine group and 3.8% in the placebo group (Table 4.6), while the frequency of life-threatening adverse events in these groups was 0.5% and 0.3%, respectively.

Figure 4.20 Serious adverse events (SAEs) in pregnant women related to RSVpreF vaccination and placebo



Among newborns and or infants, no SAEs were considered related to maternal vaccination in either the vaccine (n=3,659) or placebo (n=3,646) groups. Overall, the frequency of any SAE was 16.3% among the vaccine group and 16.1% among the placebo group (Table 4.6).

Adverse maternal/perinatal outcomes

Aside from the SAEs related to vaccination noted above, a range of other adverse maternal or perinatal outcomes were reported in the RCT. Preterm delivery (that is, delivery at less than 37 weeks' gestation) was considered to be an adverse event of special interest (AESI) by the study investigators.[214] Preterm delivery was reported in 5.7% of vaccine recipients compared with 4.7% of placebo recipients; these figures are inclusive of the relevant SAEs (Table 4.6).

Overall, there were 19 still births reported in pregnant participants (vaccine group: n=10, placebo group: n=9). There was one maternal death due to postpartum haemorrhage and hypovolemic shock, which was reported in the vaccine group. Three cases of spontaneous abortion were reported in total (vaccine group: n=1, placebo group: n=2).

Adverse newborn/infant outcomes

Adverse neonatal outcomes were reported in the RCT across several categories of adverse events, including SAEs as noted previously. Congenital abnormalities were also reported as SAEs and were observed with similar frequencies in the vaccine (5.6%) and placebo (6.7%) groups. Preterm birth (that is, less than 37 weeks' gestation), low birthweight (that is, ≤2,500g) and developmental delay were considered AESIs by the study investigators.[214] Preterm birth was reported in 5.7% of the vaccine group and 4.7% of the placebo group. Low birthweight was reported in 5.1% and 4.3% of the vaccine and placebo groups, respectively (Table 4.6).

Overall, there were 22 deaths reported among newborns and or infants over a 24 month follow-up period (vaccine group: n=8, placebo group: n=14). One death in a 120-day-old full-term infant in the placebo group was classified as caused by RSV-related ARI.

The authors also reported on asthma-related events in newborns and infants, as a composite of safety and efficacy outcomes. These included asthma as a newly diagnosed chronic medical condition (defined as a disease or medical condition, not previously identified, that was expected to be persistent or otherwise long-lasting in its effects), asthma-related diagnoses, asthma-like symptoms reported during MA respiratory tract illness visits, or as adverse events. The authors noted that diagnoses of asthma-like respiratory symptoms reported during MA LRTI visits or as AEs occurred at similar frequencies for the RSVpreF (6.8%) and placebo (6.3%) groups. There were 478 events overall (vaccine group: n=247, placebo group: n=231), with a total of 281 events related to bronchitis (vaccine group: n=147, placebo group: n=134) and a total of 241 categorised as respiratory, thoracic and mediastinal disorders (vaccine group: n=118, placebo group: n=125).

Local and systemic adverse events

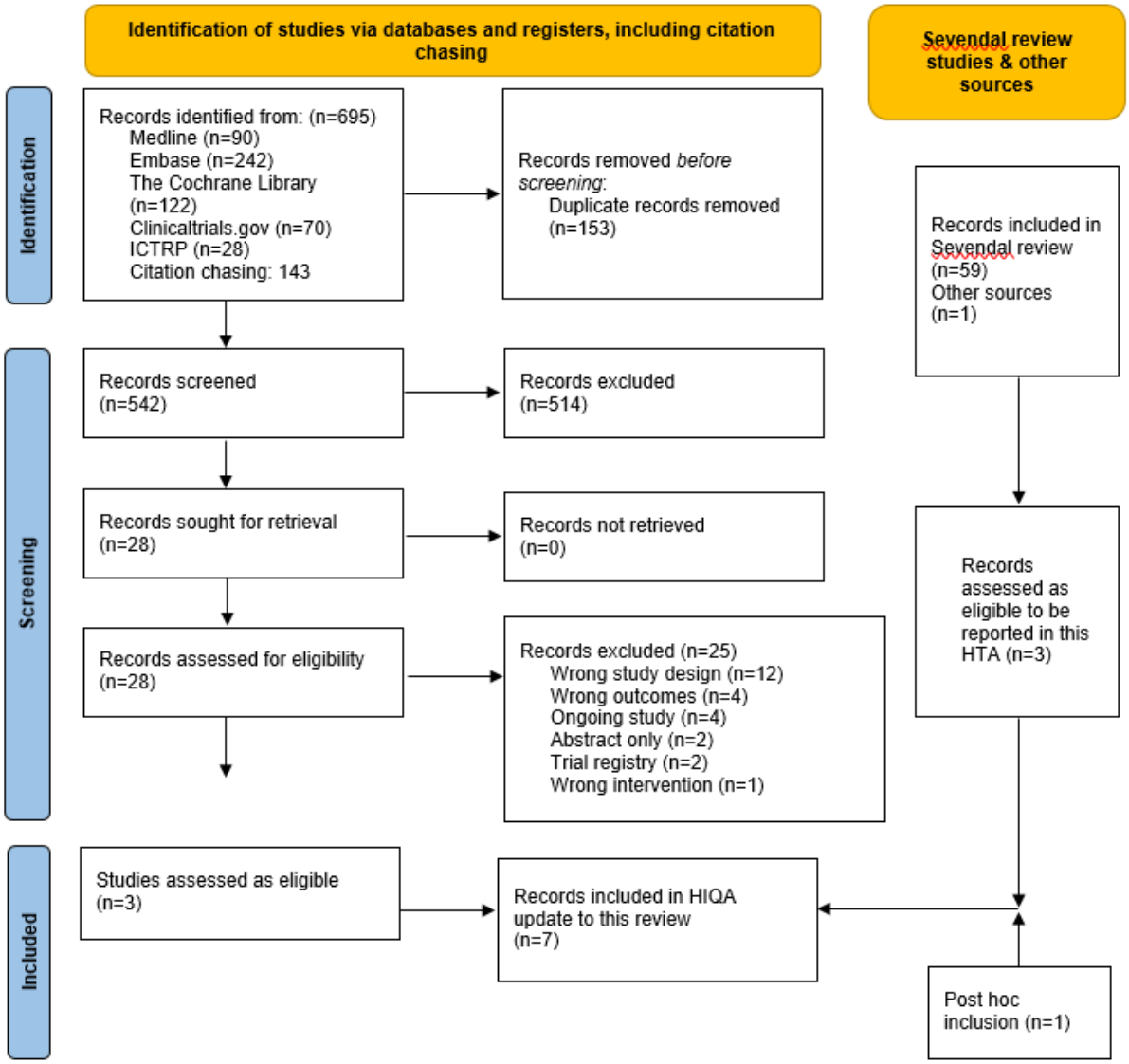
The included RCT reported on all adverse events occurring up to one month after vaccination for pregnant women and from birth up to one month of age for newborn participants. A summary of these outcomes is presented in Table 4.6. For both pregnant women and newborns, the proportions of participants experiencing any adverse event were similar in the vaccine and placebo groups. However, for pregnant women, local reactions occurring within seven days after vaccination were

reported more frequently in the vaccine group than in the placebo group. The most commonly reported local reaction was injection-site pain (vaccine group: 41%; placebo group: 10%). The most common systemic reactions after vaccination were fatigue (vaccine: 46%; placebo: 44%), headache (vaccine: 31%; placebo: 28%) and muscle pain (vaccine: 27%; placebo 17%). The study authors reported that most adverse events were considered mild to moderate.

4.4 Results: efficacy and safety of extended-half life monoclonal antibodies against RSV in infants

From the search of the databases and registers (30 November 2023 to 23 April 2025), after removal of duplicates, 399 title and abstracts were assessed for eligibility. A total of 21 records required full-text review, with three records fulfilling the inclusion criteria.[228-231] In addition, 2 of 59 records from the Sevendal et al. review[201] were assessed as meeting the inclusion criteria for this HTA.[232-234] A total of 143 records were screened as part of forward and backward citation chasing, including four records which required full-text review, but no additional records met the inclusion criteria for this HTA. A further eligible record, published after the database search had been carried out, was identified during data extraction.[235] Therefore, a total of six records, reporting results from three RCTs were included in the data synthesis on the clinical efficacy and safety of extended half-life monoclonal antibodies (EHL-mAbs).[229-231, 233-235] One additional RCT that was eligible for inclusion was published on 17 September 2025. A decision was made to include the study in the update as no other efficacy data for this agent (clesrovimab) had been identified for inclusion.[236] An overview of the study selection process is presented in Figure 4.21.

Figure 4.21 PRISMA flow diagram of study selection process (clinical efficacy and safety of nirsevimab against RSV in infants)



4.4.1 Characteristics of included RCTs (EHL-mAbs)

Seven unique records[229-231, 233-236] reporting on four RCTs were included in this review. Six records reporting on three RCTs related to the EHL-mAb nirsevimab, while one record reported on the results of the phase 2b-3 CLEVER RCT with clesrovimab.[236] Regarding nirsevimab, the three RCTs included a Phase I/II study reported by Griffin et al.,[233] along with two Phase III studies, known as the MELODY and HARMONIE RCTs. Three publications were included in this review relating to the MELODY study[229, 231, 234] and two for the HARMONIE study.[230, 235] All RCTs were published between 2020 and 2025, were conducted across multiple study centres in multiple countries worldwide, and were industry funded. A summary of the characteristics of each included study is provided in Table 4.7 while the characteristics of the participants and the interventions are outlined in Table 4.8. All

four included RCTs recruited healthy or predominantly healthy infants; one study recruited preterm infants only,[233] while three studies (reported in six publications) recruited both preterm and term infants (Table 4.7).[228, 230, 235, 236] All four RCTs excluded those eligible for palivizumab. All included infants entering their first RSV season, with studies specifying that they were immunised during a two month period immediately before the RSV season[230, 234] or at the start of or during the RSV season.[230, 236]

Each of the four RCTs included in this review reported both clinical efficacy and safety outcomes. Specifically, the clinical efficacy of EHL-mAbs was informed by RCT evidence relating to 12,522 and 3,599 unique individuals for nirsevimab and clesrovimab, respectively, while the safety review was informed by RCT evidence relating to 10,959 and 3,611 unique individuals for nirsevimab and clesrovimab, respectively. All studies required confirmation of RSV infection by RT-PCR. However, the number and nature of clinical signs and symptoms used to define cases of RSV-related ARI and MA LRTI, where reported, differed slightly between studies (see Table A4.7 in the Appendix). Despite these differences, it was considered reasonable to combine these outcomes for summary estimates, as reported in section 4.4.2.

Table 4.7 Summary of characteristics of included RCTs: efficacy and safety of EHL-mAbs

Author, year Trial name Trial number	Source	Population Sample size (n)	Design Funding	Study period	Geographic location	Outcomes reported*
Nirsevimab studies						
Griffin et al.[233] 2020 NCT02878330	Sevendal SR	Healthy preterm infants (GA 29-35 weeks, aged <12 months) entering their 1st RSV season. Not eligible for palivizumab. Total: n=1,453 ▪ nirsevimab: n=969 ▪ placebo: n=484	Phase IIb, randomised, double-blind, placebo-controlled trial AstraZeneca (formerly MedImmune LLC) & Sanofi Pasteur	Enrolment: Nov 2016-Nov 2017 Follow-up: Dec 2018	Argentina, Australia, Belgium, Brazil, Bulgaria, Canada, Chile, Czechia, Estonia, Finland, France, Hungary, Italy, Latvia, Lithuania, New Zealand, Poland, South Africa, Spain, Sweden, Turkey, UK, US	Efficacy & safety outcomes: ▪ Incidence of MA RSV-confirmed LRTI through Day 150 ▪ Incidence of hospitalisation due to RSV-confirmed LRTI though through Day 150 ▪ Incidence of AEs, SAEs, AESI & NOCDs through Day 361
Hammitt et al.,[234] 2022 Dagan et al.,[231] 2024 Arbetter et al.[229] 2024	Sevendal SR & HIQA update	Predominantly healthy late preterm (≥35 weeks GA) & term infants, aged<12 months entering their 1st RSV season. Not eligible for palivizumab.	Phase III, double blind RCT Astra Zeneca (formerly MedImmune	Enrolment: Northern hemisphere –July 2019-Nov 2019 Southern hemisphere – Jan 2020-Mar 2020	Austria, Belgium, Bulgaria, Canada, Czechia, Estonia, Finland, France, Germany, Israel,	Efficacy & safety outcomes: ▪ Incidence of medically attended RSV-confirmed LRTI through Day 150 post dose (primary cohort & all participants) ▪ Incidence of hospitalisation due to RSV-confirmed LRTI

Author, year Trial name Trial number	Source	Population Sample size (n)	Design Funding	Study period	Geographic location	Outcomes reported*
MELODY NCT03979313 EudraCT 2019-000114-11		Total from primary cohort (paused enrolment during COVID): n=1,490 ▪ nirsevimab: n=994 ▪ placebo: n=496 Total from final cohort (primary cohort + cohort post-COVID peak): n=3,012 ▪ nirsevimab: n=2,009 ▪ placebo: n=1,003 Total number that completed through Day 361 & were followed up through 2nd RSV season without re-dosing: n=2,911 (97%) ▪ nirsevimab: n=1,944 ▪ placebo: n=967	LLC) & Sanofi Pasteur	Follow-up: Mar 2023 Season 1: Day 1 - Day 151 Season 2: Day 362 - Day 511	Japan, Korea, Latvia, Lithuania, Poland, Russian Federation, South Africa, Spain, UK, US	(primary cohort & all participants) ▪ Incidence of AEs, related AEs, SAEs, related SAEs, AESI through Day 360 ▪ Number of participants with medically attended LRTI of any cause from the 2nd RSV season ▪ Incidence of hospitalisation for any respiratory illness of any cause from the 2nd RSV season
Drysdale et al.,[230] 2023 Munro et al.,[235] 2025 **HARMONIE**	HIQA update	Healthy preterm & term infants (GA ≥29 weeks), aged ≤12 months, entering their 1st RSV	Phase IIIb pragmatic, randomised, open-label trial; nirsevimab	Enrolment: Sep 2022-Feb 2023 Follow-up: 12 months	France, Germany, UK	Efficacy & safety outcomes: ▪ Incidence of hospitalisation due to RSV-confirmed LRTI through Day 180

Author, year Trial name Trial number	Source	Population Sample size (n)	Design Funding	Study period	Geographic location	Outcomes reported*
NCT05437510 ICTRPU1111-1272-2514 Eudra-CT2022-000099-20-FR		season. Not eligible for palivizumab. Total: n=8,057 ▪ nirsevimab: n=4,038 ▪ No intervention: n=4,019	versus no intervention Sanofi & AstraZeneca			▪ Incidence of very severe RSV-confirmed LRTI through Day 180 ▪ Incidence of RSV-confirmed LRTI hospitalisation through Day 180 ▪ Incidence of hospitalisation for all-cause RTI through Day 180 ▪ Incidence of TEAEs, TESAEs, medically attended TEAEs
Clesrovimab study						
Zar et al., 2025[236] **CLEVER** NCT04767373	HIQA update	Health preterm & term infants (GA ≥29 weeks), aged ≤12 months and entering their 1st RSV season. Not eligible for palivizumab. Total randomised: n=3,632 ▪ clesrovimab: n=2,421	Phase IIb-III double blind RCT Merck Sharp and Dohme	Enrolment: not specified Follow-up: Season 1: 0 to 180 days after administration Season 2: 365 to 515 days after administration	Argentina, Belgium, Canada, Chile, China, Colombia, Denmark, Finland, France, Italy, Japan, Korea, Malaysia, Mexico, Peru, Philippines, Poland, South Africa, Thailand, Turkey, United	Efficacy & safety outcomes: ▪ Incidence of MA RSV-related LRTI* with ≥1 indicator of disease severity (through 150 days and 180 days) ▪ Incidence RSV-related hospitalisation (through 150 days and 180 days) ▪ Incidence of MA RSV-related LRTI with ≥2 indicators of disease severity (through 150 days and 180 days)

Author, year Trial name Trial number	Source	Population Sample size (n)	Design Funding	Study period	Geographic location	Outcomes reported*
		▪ placebo: n=1,211			Kingdom, United States.	▪ Incidence of severe MA RSV-related LRTI (through 150 days and 180 days) ▪ Incidence of RSV-related hospitalisation for LRTI (through 150 days and 180 days) ▪ Incidence RSV-related ARI (through 150 days and 180 days) ▪ Incidence of AEs, solicited AEs, Serious AEs, AESI, and death.

Key: AE – adverse events; AESI – adverse events of special interest; ARI – acute respiratory infection; GA – gestational age; HIQA – Health Information and Quality Authority; LLC – limited liability company; LRTI – lower respiratory tract infections; MA – medically attended; NOCD – new onset chronic disease; RSV – respiratory syncytial virus; RT-PCR - reverse transcriptase-polymerase chain reaction; SR – systematic review; TEAE – treatment emergent adverse event; TESAE – treatment-emergent serious adverse events; UK – United Kingdom; US – United States

Note: *Study refers to LRI in publication. Here referred to as LRTI throughout for consistency.

Table 4.8 Characteristics of the participants and interventions: efficacy and safety of EHL-mAbs

Author, year Trial name Trial number	Age and sex	Comorbidities	Number of participants & type of analysis	Intervention	Comparator
Nirsevimab (MEDI8897)					
Griffin et al.,[233] 2020 NCT02878330	Mean age (SD): ▪ nirsevimab: 3.29 months (2.22); GA 32.7 weeks (1.4) ▪ placebo: 3.28 months (2.31); GA 32.7 weeks (1.5) Female: ▪ nirsevimab: n=468 (48.3%) ▪ placebo: n=224 (46.3%)	None reported	Overall: n=1453 Analysis based on ITT population for efficacy outcomes: ▪ nirsevimab n=969 ▪ placebo n=484 Analysis based on as treated population for safety outcomes: ▪ nirsevimab n=968 ▪ placebo n=479	Single IM dose of nirsevimab 50mg on Day 1 administered during a 2-month period immediately before the RSV season	Single IM dose of placebo matched to nirsevimab on Day 1
Hammit et al.,[234] 2022 Dagan et al.,[231] 2024 Arbetter et al.,[229] 2025 NCT03979313 **MELODY**	Mean age (SD): ▪ nirsevimab: 2.91 months (2.22) ▪ placebo: 3.01 months (2.25) Female: ▪ nirsevimab: n=464 (46.8%) ▪ placebo: n=257 (51.8%)	n=4 (0.3%) had serious & stable underlying disease (n=1: cystic fibrosis; n=3: Down's syndrome)	Overall n=3,012 Analysis based on ITT population for efficacy outcomes: ▪ nirsevimab n=994 ▪ placebo n=496 Analysis based on as treated population for safety outcomes: ▪ nirsevimab n=987 ▪ placebo n=491	Single IM dose of nirsevimab (50 mg if <5 kg; 100 mg if ≥5 kg) on Day 1	Single IM dose of placebo on Day 1

Author, year Trial name Trial number	Age and sex	Comorbidities	Number of participants & type of analysis	Intervention	Comparator
Drysdale et al.,[230] 2023 Munro et al.,[235] 2025 **HARMONIE**	Median age, months: ▪ nirsevimab: 4 months (2.0 – 7.0) ▪ no intervention: 4 months (1.0 – 7.0) Female: ▪ nirsevimab: n=1,950 (48.3%) ▪ no intervention: n=3,862 (47.9%)	None reported	Overall: n=8,057 Analysis based on ITT for efficacy outcomes: ▪ nirsevimab n=4,038 ▪ placebo n=4,019 Analysis based on as treated population for safety outcomes. ▪ nirsevimab n=4,016 ▪ control n=4,018	Single IM dose of nirsevimab (50 mg for infants weighing <5 kg; 100 mg for those weighing ≥5 kg) administered during their first RSV season.	Standard care (no intervention)
Clesrovimab (MK-1654)					
Zar et al., 2025[236] **CLEVER** NCT04767373	Mean age, months: ▪ clesrovimab: 3.7 months (±2.6) ▪ placebo: 3.7 months (±2.6)	None reported	Overall randomised: n=3,632 Analysis based on full analysis population⁺ for efficacy outcomes: ▪ clesrovimab n=2,398 ▪ placebo n=1,201 Analysis based on as treated population for safety outcomes: ▪ clesrovimab n=2,409 ▪ placebo n=1,202	Single IM dose of clesrovimab (105 mg) administered on Day 1 before or during their first RSV season	Single IM dose of placebo on Day 1

Key: GA – gestational age; IM – intramuscular; ITT – intention to treat; SD – standard deviation

Note: Full analysis population was defined as all the participants who underwent randomisation and received an injection of clesrovimab or placebo and were not excluded for certain protocol deviations.

4.4.2 Clinical efficacy outcomes of EHL-mABs against RSV in infants

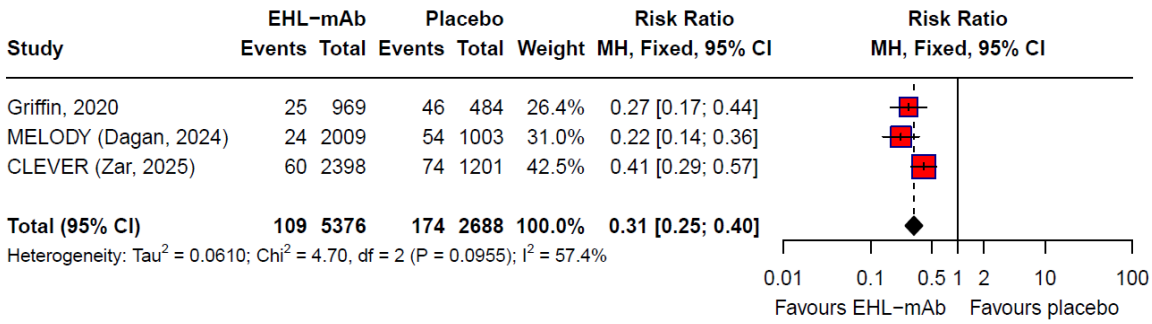
An overview of the certainty of evidence for the primary outcomes reported in the subsequent sections is presented in the GRADE summary of findings table – Table A.2.2. ICU admissions are not presented in the GRADE table as this particular outcome was only reported in a single study and had a very low number of events. Similarly, mortality was not included in the GRADE table as an outcome because no treatment-related deaths were reported.

RSV-associated medically attended LRTI

Of the included trials, two reported (within four publications) on the efficacy of nirsevimab against RSV-associated MA LRTI.[228, 231-234] Both trials were placebo-controlled; one reported on this outcome over a single RSV season (150 days),[233] while one study (MELODY) also reported over a second RSV season (362-511 days).[231, 234] One trial reported on the efficacy of clesrovimab against RSV-associated MA lower respiratory infection (LRI) with at least one indicator of disease severity over 150 days.[236] As noted in Table A2.5, for consistency in reporting, this outcome is referred to as LRTI in the remaining sections. Combining the outcome data from these three trials, EHL-mAbs were associated with a statistically significant reduction in events, with the pooled efficacy of EHL-mAbs compared with placebo for this outcome over one RSV season estimated at 69% (95% CI: 60% to 75%) (Figure 4.22).

The GRADE certainty of evidence of nirsevimab for this outcome was assessed to be high (Table A.2.3).

Figure 4.22 RSV-associated medically attended LRTI in infants – one RSV season



Key: CI – confidence interval; LRTI – lower respiratory tract infection; MH – Mantel-Haenszel; RSV – respiratory syncytial virus.
Note: The intervention in Griffin, 2020 and MELODY was nirsevimab, and in CLEVER was clesrovimab.

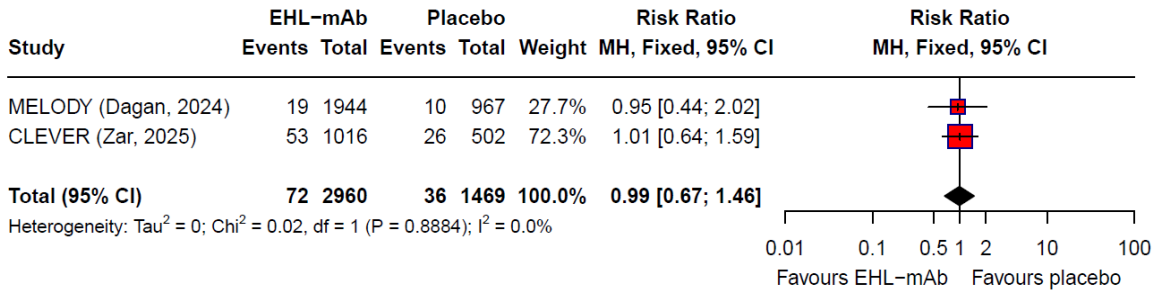
The CLEVER trial also reported post-hoc on the efficacy of clesrovimab against RSV-associated MA LRTI with two or more indicators of disease severity over 150 days,

with an estimated efficacy of 88% (95% CI: 76% to 94%). Additionally, the trial reported on this and other outcomes over 180 days (Table A2.12).

The MELODY and CLEVER trials reported the efficacy of EHL-mAbs for MA LRTI over a second season (MELODY: days 362-511 post-dose; CLEVER: days 365 to 515 post-dose) without re-dosing.[231] There was no statistical difference in the incidence of MA LRTI between the EHL-mAb group and placebo at this time point for either study; pooled efficacy 1% (95% CI: -46% to 33%) as indicated in Figure 4.23.

The GRADE certainty of evidence indicates that EHL-mAbs probably do not reduce MA RSV-associated LRTI over two seasons. The certainty of evidence was assessed as moderate due to the inclusion of only two studies with relatively few events and wide confidence intervals. (Table A.2.3).

Figure 4.23 RSV-associated medically attended LRTI in infants – two RSV seasons



Key: CI – confidence interval; LRTI – lower respiratory tract infection; MH – Mantel-Haenszel; RSV – respiratory syncytial virus
Note: The interventions in MELODY and CLEVER were nirsevimab and clesrovimab, respectively.

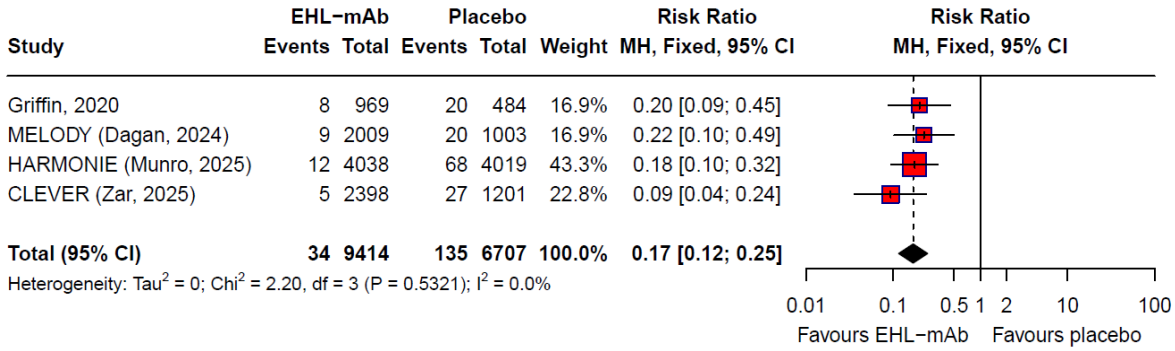
RSV-associated LRTI with hospitalisation

In total, four RCTs reported on efficacy against RSV-associated LRTI with hospitalisation. These included three nirsevimab-related RCTs (within five publications),[228, 231-235] one of which, the MELODY study, reported on this outcome over two RSV seasons.[228] Two RCTs (reported within three publications) were placebo controlled,[231-234] while HARMONIE included standard care (no intervention) as a comparator.[235] The placebo-controlled CLEVER trial reported on the efficacy of clesrovimab against RSV-associated hospitalisation and RSV-associated hospitalisation for LRTI, over 150 and 180 days (see Table A2.12 for outcomes over 180 days).[236]

EHL-mAbs were associated with a statistically significant reduction in events in a single RSV season (through 150 days), with a pooled efficacy against RSV-associated LRTI with hospitalisation estimated as 83% (95% CI: 75% to 88%) (Figure 4.24).

The GRADE certainty of evidence for the use of EHL-mAbs for this outcome, was assessed to be moderate (Table A.2.3).

Figure 4.24 RSV-associated LRTI with hospitalisation – one RSV season

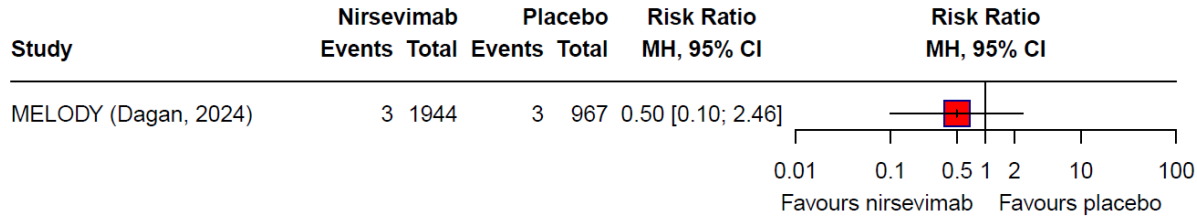


Key: CI – confidence interval; LRTI – lower respiratory tract infection; MH – Mantel-Haenszel; RSV – respiratory syncytial virus; SC – standard care.
Note: The intervention in Griffin, 2020, MELODY and HARMONIE was nirsevimab, and in CLEVER was clesrovimab.

As noted, the MELODY trial reported the efficacy of nirsevimab for preventing RSV-associated LRTI hospitalisation over a second RSV season (days 361-510 post dose) without re-dosing,[231] with no significant difference observed between the two arms (efficacy 50%, 95% CI: -146% to 90%) as indicated in Figure 4.25.

The GRADE certainty of evidence indicates that nirsevimab probably does not reduce RSV-associated LRTI with hospitalisation over two seasons. The certainty of evidence was assessed as moderate due to the inclusion of only a single study with few events and wide confidence intervals (Table A.2.3).

Figure 4.25 RSV-associated LRTI with hospitalisation – two RSV seasons



Key: CI – confidence interval; LRTI – lower respiratory tract infection; MH – Mantel-Haenszel; RSV – respiratory syncytial virus

Additionally, the efficacy of clesrovimab compared with placebo against RSV-associated hospitalisation (not specifically related to LRTI) over 150 days was 84% (95% CI: 67% to 93%). The incidence of RSV-associated hospitalisation events through the second RSV season (from days 365 to 515 post-dose) was low in both the clesrovimab (3/1,016, 0.3%) and placebo (2/502, 0.4%) groups.

RSV-associated severe LRTI, use of ventilation, supplementary oxygen and ICU admission

RSV-associated LRTI requiring supplemental oxygen or ventilation and very severe illness was defined differently depending on the study and therefore the studies were not pooled in a meta-analysis.

Griffin et al. reported that among participants with MA RSV-associated LRTI, a lower proportion of those in the nirsevimab arm required either assisted ventilation (0/25 (0%) vs 4/46 (8.7%)) or supplemental oxygen (4/25 (16%) vs 15/46 (32.6%)) compared with the placebo arm.[233] This corresponded to an estimated efficacy of 80% (95% CI: -262% to 99%) and 51% (95% CI: -32% to 82%) for these outcomes, respectively in this subgroup.

In the MELODY trial, very severe MA RSV-associated LRTI was defined as children requiring supplemental oxygen or IV fluids for the management of the condition.[231] For the first season of RSV (0-151 days), nirsevimab protected against very severe cases with an efficacy of 79% (95% CI: 51% to 91%) with an incidence of in 0.3% in participants who had received nirsevimab compared to 1.7% in participants who had received placebo. Over the second RSV season (days 362 to 511), without re-dosing, there was no difference in the incidence of severe cases between groups, with severe cases reported for 0.2% of participants who had received nirsevimab and 0.3% of participants who had received placebo (efficacy 50%, (95% CI: -146% to 90%).[231]

In the HARMONIE trial, very severe RSV-related LRTI was defined as the need for hospitalisation with oxygen saturation less than 90% and oxygen supplementation.[235] In the group of infants who received nirsevimab, 0.1% (n=6/4,038) were classified as having very severe RSV-related LRTI compared with 0.6% (n=24/4,019) in the standard care group up to 180 days post randomisation. The efficacy of nirsevimab compared to standard care for protecting against this outcome was 75% (95% CI: 39% to 90%).

In the CLEVER trial, the definition of severe MA LRTI included a requirement of severe hypoxemia (defined as an SpO_2 <90% on room air at sea level or <87% at >1800 meters or the need for high flow nasal cannula or mechanical ventilator support).[236] The cumulative incidence over 150 days was 0.01% and 1.0% in the clesrovimab and placebo groups, respectively, corresponding to an efficacy of 92% (95% CI: 63% to 98%) for this outcome. Outcomes over 180 days are presented in Table A2.12. This trial did not report on ICU admissions.

Overall, there is evidence that compared with placebo or standard care, EHL-mAbs are associated with a lower incidence of very severe RSV-associated LRTI, and

specifically the requirement for oxygen supplementation and or mechanical ventilation in the first RSV season. Based on findings from a single study, this protection does not last into a second RSV season.

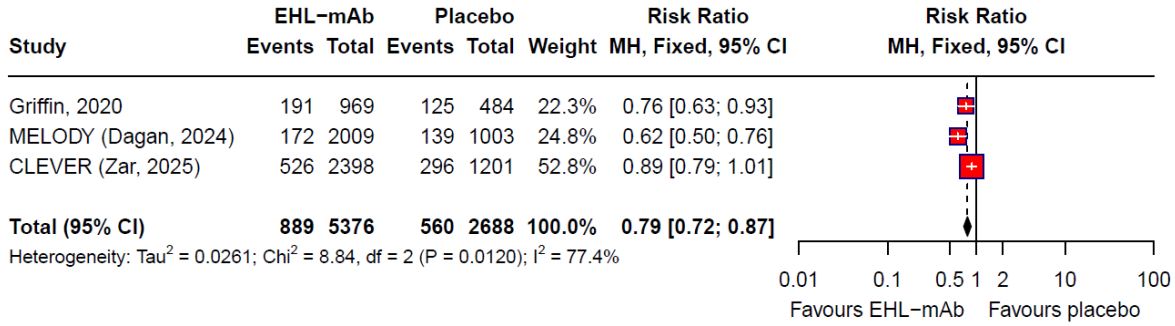
Only one EHL-mAb study reported in relation to RSV-related ICU admission.[233] Griffin et al. reported that among participants with MA RSV-associated LRTI, a lower proportion of those in the nirsevimab arm were admitted to ICU (0/25 [0%]) compared with the placebo arm (5/46 [10.9%]) in the period through 150 days post dose. This corresponds to an estimated efficacy of 83% (95% CI: -188% to 99.0%). No data were identified with respect to clesrovimab for this outcome.

All-cause medically attended LRTI

Two of the nirsevimab placebo-controlled RCTs reported the incidence of 'all-cause' MA LRTI,[231-233] of which one, the MELODY trial reported on this outcome over two RSV seasons.[231] The placebo-controlled clesrovimab RCT, CLEVER, reported MA LRTI of any cause through 150 days after administration.[236] Over one RSV season, the pooled efficacy of EHL-mAbs against MA LRTI of any cause was estimated to be 21% (95% CI: 13% to 28%) see Figure 4.26.

The GRADE certainty of evidence of nirsevimab for this outcome was assessed to be high for this outcome (Table A.2.3).

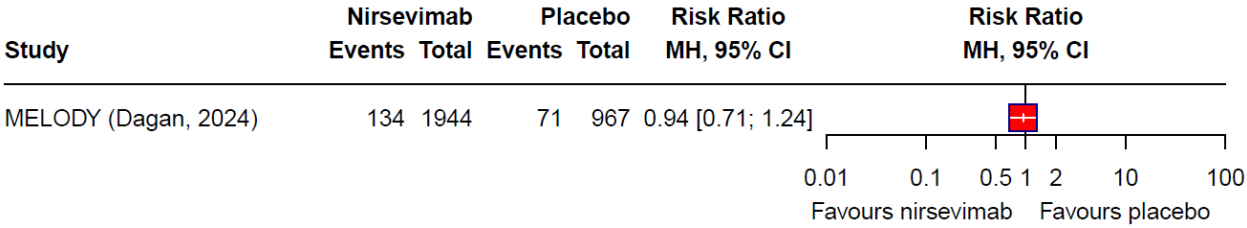
Figure 4.26 All-cause medically attended LRTI – one RSV season



Key: CI – confidence interval; LRTI – lower respiratory tract infection; MH – Mantel-Haenszel; RSV – respiratory syncytial virus.
Note: The intervention in Griffin, 2020 and MELODY was nirsevimab, and in CLEVER was clesrovimab.

Over the second RSV season, the MELODY RCT reported no significant difference between the nirsevimab and the placebo arms (efficacy 6%, 95% CI: -24% to 29%) as indicated in Figure 4.27.

Figure 4.27 All-cause medically attended LRTI – two seasons

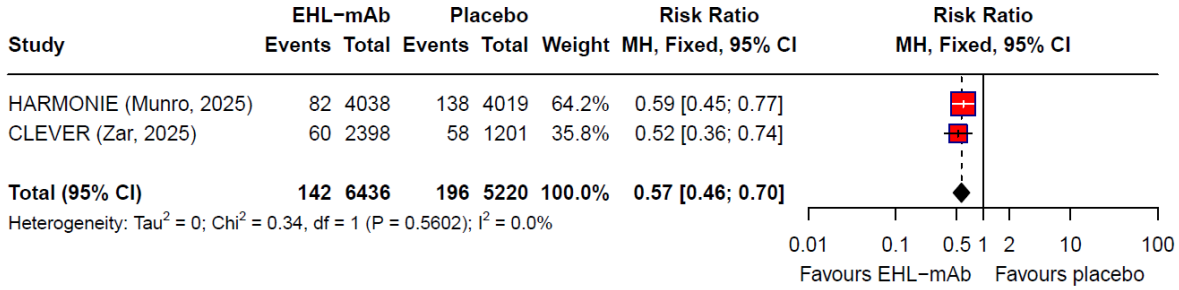


Key: CI – confidence interval; LRTI – lower respiratory tract infection; MH – Mantel-Haenszel

All-cause LRTI with hospitalisation

Two RCTs, the HARMONIE and CLEVER trials, reported on 'all-cause' LRTI with hospitalisation through 180 days post randomisation and 150 days post administration, respectively.[235, 236] Both trials reported a higher incidence of events among the standard care group compared with the EHL-mAb group (HARMONIE: 3.4% versus 2.0%; CLEVER: 4.8% versus 2.5%).[235, 236] The estimated pooled efficacy of EHL-mAbs for this outcome was 43% (95% CI: 30% to 54%) as indicated in Figure 4.28.

Figure 4.28 Hospitalisation for all-cause LRTI

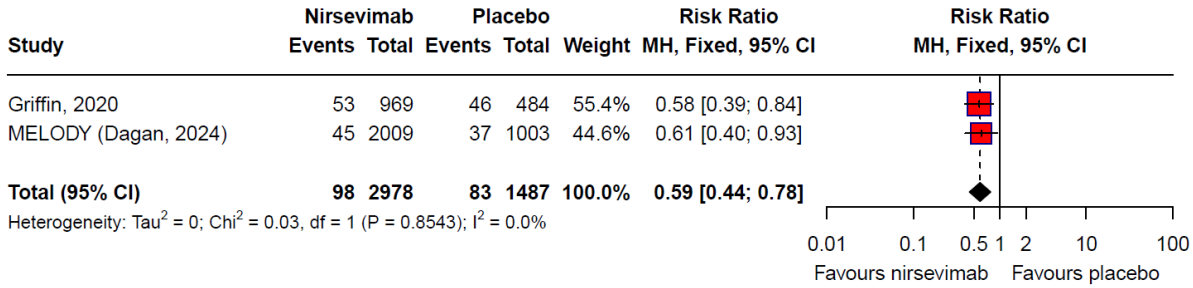


Key: CI – confidence interval; LRTI – lower respiratory tract infection; MH – Mantel-Haenszel; RSV – respiratory syncytial virus
Note: The interventions in HARMONIE and CLEVER were nirsevimab and clesrovimab, respectively.

All-cause ARI with hospitalisation

Based on two studies,[231, 233] the pooled efficacy of nirsevimab for preventing all-cause ARI with hospitalisation over one season is 41% (95% CI: 22% to 56%) as indicated in Figure 4.29.

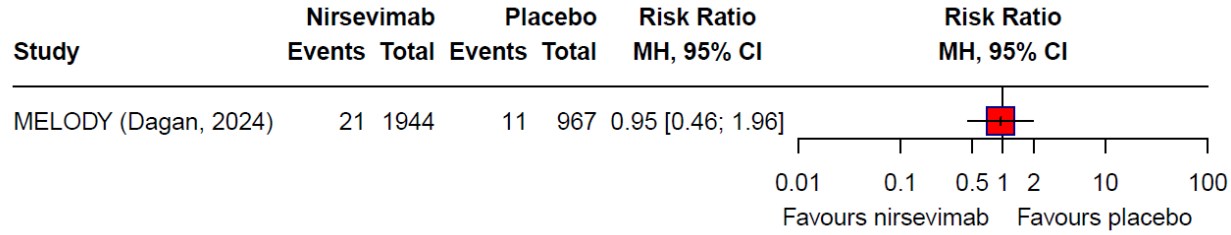
Figure 4.29 Hospitalisation for all-cause ARI – one RSV season



Key: ARI – acute respiratory illness; CI – confidence interval; MH – Mantel-Haenszel; RSV – respiratory syncytial virus

The MELODY trial reported on the incidence of hospitalisation for 'all-cause' respiratory illness over a second RSV season; the incidence was reported to be the same in both groups (1.1% placebo versus 1.1% for nirsevimab group; efficacy 5%, 95% CI: -96% to 54%) as indicated in Figure 4.30.[231]

Figure 4.30 Hospitalisation for all-cause ARI – two RSV seasons



Key: ARI – acute respiratory illness; CI – confidence interval; MH – Mantel-Haenszel; RSV – respiratory syncytial virus

Other efficacy outcomes of interest

None of the included studies reported on new onset of chronic diseases, patient-reported outcomes, quality of life measures or antibiotic use.

For the MELODY trial, Arbetter et al. reported lower RSV infection rates through Day 151 for those infants who received nirsevimab compared with placebo (1.2% and 5.4%, respectively) and noted that rates of other viral infections were similar between the two groups (87% and 88%, respectively).[229]

The CLEVER trial reported on RSV-associated ARI over 150 and 180 days.[236] The efficacy of clesrovimab compared with placebo for this outcome was 52% (95% CI: 40% to 62%) and 50% (95% CI: 37% to 60%) over 150 and 180 days, respectively.

Duration of protection

The MELODY RCT evaluated the incidence of RSV-associated respiratory disease between RSV seasons one and two (152 to 361 days post-dose) and reported similar

incidence rates of disease in both the nirsevimab and placebo groups.[231] The incidence of MA LRTI was 0.8% (16/1977) in the nirsevimab group and 1.3% (13/985) in the placebo group. The incidence of RSV-associated MA LRTI with hospitalisation was 0.1% (2/1977) in the nirsevimab group and 0.2% (2/985) in the placebo group.

The CLEVER RCT reported incidence and efficacy outcomes over 150 and 180 days after administration of clesrovimab or placebo.[236] For each outcome, the values were similar over 150 and 180 days (Table A2.12). Over a second season, the five-month incidence of RSV-associated MA LRTI was similar for the clesrovimab (6%; 95% CI: 4 to 7) and placebo groups (5%; 95% CI: 4 to 8).

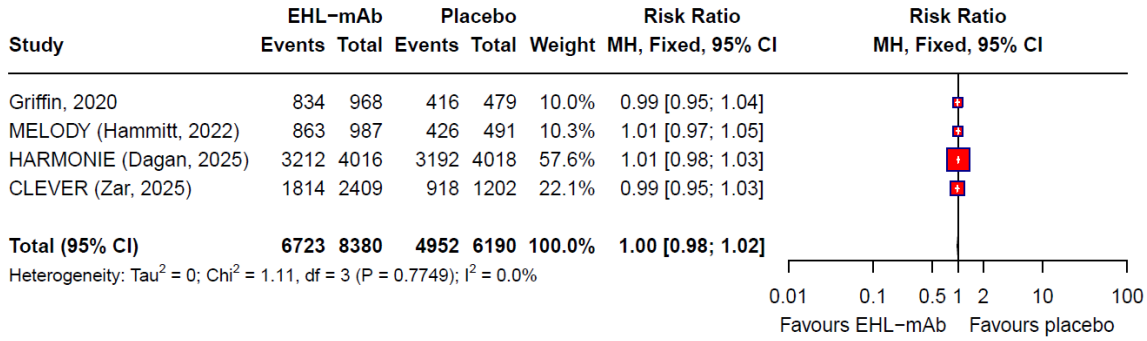
4.4.3 Safety outcomes of nirsevimab against RSV in infants

Overall incidence of adverse events

All four RCTs reported on the incidence of adverse events (AEs) with EHL-mAbs,[232-236] of which three (MELODY, Griffin et al. and MELODY) related to nirsevimab. There were slight differences between the RCTs in terms of the AEs considered and the reporting periods. The MELODY trial reported safety outcomes based on a smaller cohort (not the full cohort which was used for efficacy outcomes). This outcome was evaluated up to 361 days post immunisation for the MELODY RCT and Griffin et al., while the HARMONIE RCT evaluated non-serious AEs up to day 31, and adverse events of special interest (AESI), MA AEs, and serious adverse events (SAEs) up to 365 days post randomisation. The CLEVER trial reported on safety outcomes for the as-treated population, which included participants who were randomised and received a dose of either clesrovimab or placebo.[236] Participants were followed through 365 days after administration for any adverse events (AEs, SAEs, death), solicited adverse events on days one to five after administration, and AESI on days 1 to 42 after injection.

The incidence of any AE was similar between the nirsevimab group and the placebo or standard care group for each of the three RCTs and ranged from 80% to 87.4% in the nirsevimab group and 79.4% to 86.8% in the placebo group. The most frequent AEs reported across these three trials included gastrointestinal disorders, upper RTIs, respiratory, thoracic and mediastinal disorders, skin and subcutaneous tissue disorders.[233, 235] In the CLEVER RCT, the incidence of any AE was similar between groups (clesrovimab 75.4%; placebo 76.4%).[236] Combining the evidence for both EHL-mAbs, the pooled RR was 1.00 (95% CI: 0.98 to 1.02), showing no statistical difference between the EHL-mAb and control groups across studies for this outcome (Figure 4.31).

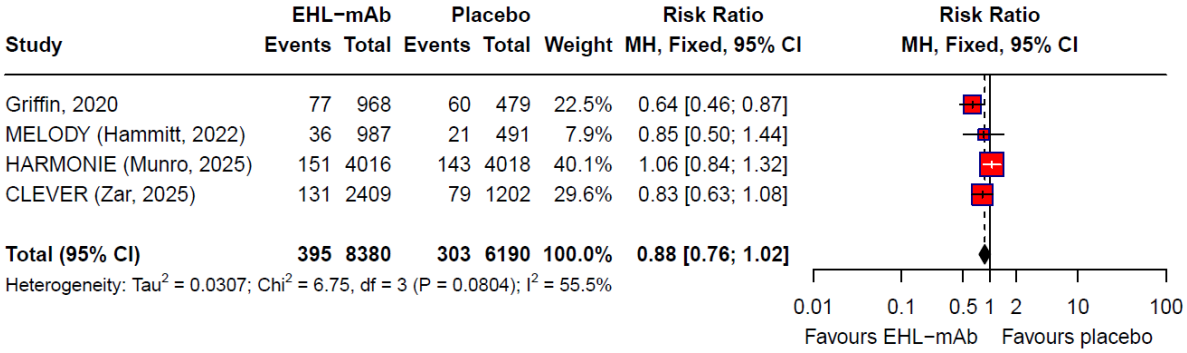
Figure 4.31 Any adverse events



Key: CI – confidence interval; MH – Mantel-Haenszel; RCT – randomised controlled trial.
Note: The intervention in Griffin, 2020, MELODY and HARMONIE was nirsevimab, and in CLEVER was clesrovimab.

Four RCTs reported in relation to ≥Grade 3 AEs. Three RCTs related to nirsevimab, with the incidence of ≥Grade 3 AEs noted to be much lower overall, ranging from 3.6% to 8% in the nirsevimab group and 3.6% to 12.5% in the placebo or standard care group. One study found a lower incidence of Grade 3 AEs in the nirsevimab group (Griffin et al., 8% versus 12.5%), while the other two studies found no statistically significant difference between the groups. For clesrovimab, the CLEVER RCT reported the incidence of ≥Grade 3 AEs by organ class,[236] which when combined gave an overall incidence of ≥Grade 3 AEs of 5.4% (n=131) for the clesrovimab group and 6.6% (n=79) in the placebo group. The majority of these severe AEs were in the infections and infestations class (clesrovimab: n=116/131; placebo: 70/79). The pooled result across these four RCTs suggested there was no statistically significant difference between the EHL-mAbs and control groups in terms of the incidence of ≥Grade 3 AEs, however this result should be interpreted with caution due to substantial heterogeneity between studies (RR 0.88, 95% CI:0.76% to 1.02%; I^2 55.5%) as indicated in Figure 4.32.

Figure 4.32 Any ≥Grade 3 adverse events



Key: CI – confidence interval; MH – Mantel-Haenszel; RCT – randomised controlled trial
Note: The intervention in Griffin, 2020, MELODY and HARMONIE was nirsevimab, and in CLEVER was clesrovimab.

Adverse events related to intervention

Four RCTs reported the incidence of AEs related to the intervention, three of which related to nirsevimab and one to clesrovimab.[233-236] As one of the RCTs (HARMONIE) was open-label and had standard care as a comparator, no meta-analysis was performed for this outcome.[235] Considering the three comparative studies, all reported no significant difference in the incidence of intervention-related AEs between the EHL-mAB and the control arm.

Griffin et al. reported a similar incidence of intervention-related AEs which were considered by the investigator to be related to the intervention in the nirsevimab and placebo groups, (2.3%, 22/968 in nirsevimab group versus 2.1%, 10/479 in placebo group, RR 1.09, 95% CI: 0.52 to 2.28). Similarly, in the MELODY trial there was no statistically significant difference in the incidence of intervention-related AEs reported in the nirsevimab and control groups (1.0%, 10/987 versus 1.4%, 7/491; RR 0.71, 95% CI: 0.27 to 1.86). In the HARMONIE trial, treatment-related AEs were reported at an incidence of 2.5% (102/4016) in the nirsevimab group; most were reported to be Grade 1 (2.0%) or Grade 2 severity (0.6%), only one (<0.1%) was reported to be Grade 3 severity. As this was an open label trial and the control group received no placebo or intervention, no treatment-related AEs were reported in the standard care group.[235] In the CLEVER trial there was a similar proportion of adverse events related to the intervention in each group (24.4%, 587/2,409 in the clesrovimab group vs 24.6%, 296/1,202 in the placebo group, estimated difference -0.3%, 95% CI: -3.3% to 2.7%).[236]

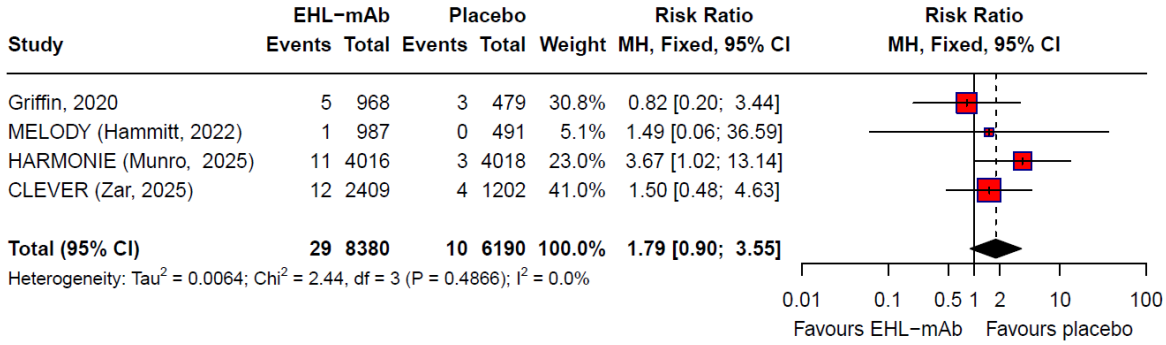
Adverse events of special interest

Four RCTs reported on AESIs.[233-236] Three trials identified hypersensitivity, immune complex disease and thrombocytopenia as AESIs, while one RCT identified anaphylaxis or hypersensitivity and rash as AESIs.[236] The pooled RR for this outcome suggests no significant difference in AESIs between the EHL-mAbs and the control groups (Figure 4.33).

Griffin 2020[233] reported eight Grade 1 AESI events in total; these included four participants with a rash and one with petechiae in the nirsevimab group, and three with a rash in the placebo group (RR 0.82, 95% CI 0.20 to 3.44). In the MELODY trial, one infant in the nirsevimab group (0.1%) was reported to develop an AESI, with no events in the placebo group. In the HARMONIE trial, 14 AESIs were reported in total, with a significant difference noted between the nirsevimab and standard care groups (RR 3.67, 95% CI: 1.02 to 13.14). Of the 11 AESIs in the nirsevimab group (0.3%, 11/4016), five were Grade 1 and six were Grade 2, while the three AESIs reported in the standard care group (<0.1%, 3/4019) included one Grade 1 and two Grade 3 AESIs. The CLEVER trial reported 16 AESIs, of which 12 occurred in

the clesrovimab group (anaphylaxis or hypersensitivity n=1; rash n=11) and four occurred in the placebo group (rash n=4) (RR 1.50, 95% CI: 0.48 to 4.63).[236] The study authors reported that all AESI events were Grade 1 or Grade 2 except for one Grade 3 event of urticaria on day nine after administration, which resolved after four days.

Figure 4.33 Any adverse events of special interest

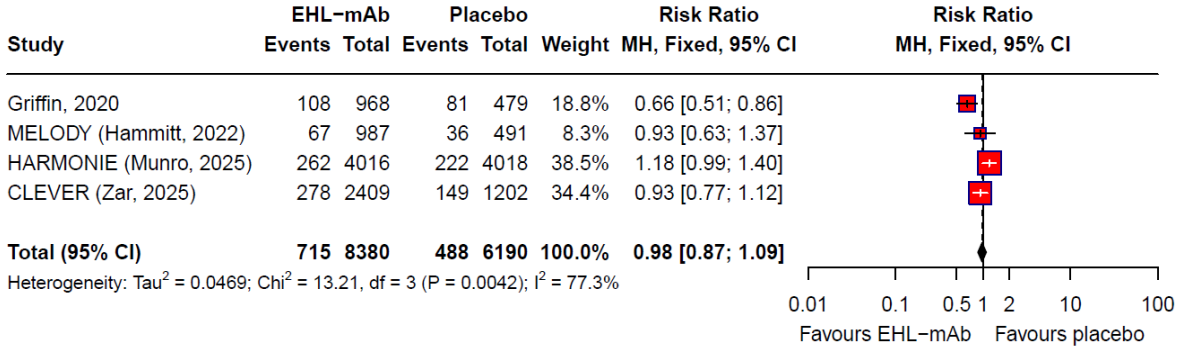


Key: CI – confidence interval; MH – Mantel-Haenszel; SC – standard care
Note: The intervention in Griffin, 2020, MELODY and HARMONIE was nirsevimab, and in CLEVER was clesrovimab.

Serious adverse events

All four of the RCTs reported on SAEs and whether these SAEs were related to the intervention.[233-235] Griffin 2020 reported a lower incidence of SAEs in the nirsevimab group compared with placebo (11.2% versus 16.9%, respectively), while MELODY, HARMONIE, CLEVER and the pooled result found no statistical difference in SAEs between the nirsevimab and control groups. However, due to substantial heterogeneity the pooled result should be interpreted with caution (RR 0.98, 95% CI: 0.87 to 1.09; I^2 77.3%) as indicated in Figure 4.34.

Figure 4.34 Serious adverse events



Key: CI – confidence interval; MH – Mantel-Haenszel; SC – standard care
Note: The intervention in Griffin, 2020, MELODY and HARMONIE was nirsevimab, and in CLEVER was clesrovimab.

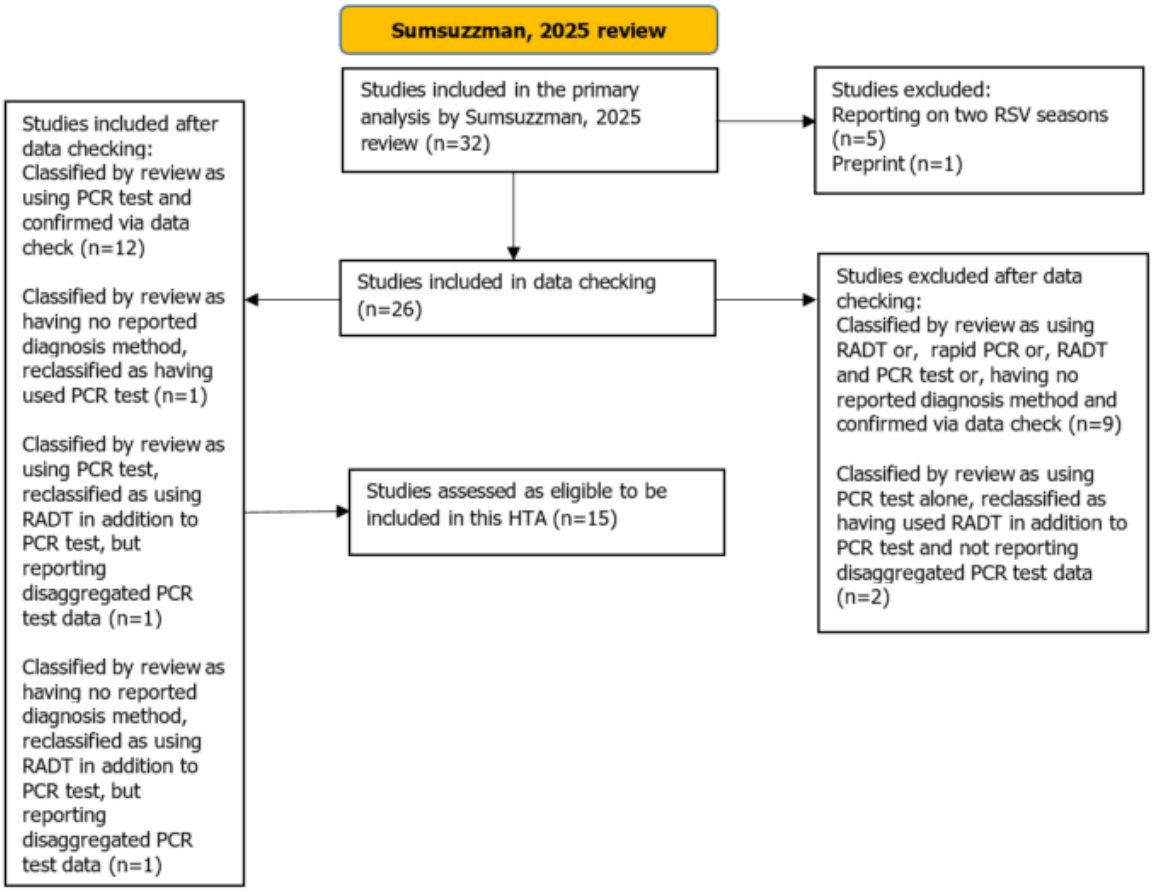
Two of these studies reported that none of the SAEs were related to immunisation,[233, 234] while the HARMONIE trial reported one intervention-related SAE in the nirsevimab group (0.03%),[235] and the CLEVER trial reported one-intervention related SAE in each of the clesrovimab (0.04%) and placebo (0.1%) groups.[236] The GRADE certainty of evidence for this outcome was assessed to be low (Table A.2.3).

Mortality was reported in four of the studies.[233-235] No study reported deaths related to the intervention. One study recorded no deaths.[235] Griffin et al.[233] reported five deaths, three in the nirsevimab group and two in the placebo group — none were known to be due to RSV or considered to be related to the intervention. In the MELODY trial five deaths were reported (out of 2,009 participants), all in the nirsevimab group; these were not considered to be related to the intervention.[231] The CLEVER trial reported seven deaths (7/2,409, 0.3%) in the clesrovimab group and three deaths (3/1,202, 0.2%) in the placebo group; none were considered by the investigator to be related to the intervention or to RSV.[236]

4.4.4 Results: effectiveness of extended half-life monoclonal antibodies against RSV-related disease in infants

As outlined in Section 4.2.1, the effectiveness of EHL-mAbs was informed by a systematic review of the effectiveness of nirsevimab published by Sumsuzzman et al. in January 2025. No effectiveness data were identified for clesrovimab, so the following summary is limited to nirsevimab data. The Sumsuzzman et al. review included 32 unique studies comprising 18 cohort and 14 case-control studies.[202] Not all of these studies were considered eligible per the criteria outlined in Table 4.2. Of note, a number of small data discrepancies were identified during cross-check that resulted in studies being recategorised based on their RSV testing method[237-241] or in terms of the availability of data for the age-group of interest.[170, 240] Studies were excluded if they compared outcomes across two different RSV seasons (n=5), were published as a preprint only (n=1), did not specify the testing method or did not report disaggregated data for those with PCR-confirmed RSV (n=11). This summary therefore reports on the 15 studies that were considered eligible for the HIQA review. An overview of the study selection process is presented in Figure 4.35. A summary of the characteristics of the included studies is provided in Table 4.9.

Figure 4.35 Study selection process



Key: HTA – health technology assessment; PCT – polymerase chain reaction; RADT –rapid antigen detection test; RSV – respiratory syncytial virus.

Of the 15 studies included in our reporting, seven studies were conducted in Spain,[170, 242-247] five in France[241, 248-251] and three in the USA[239, 240, 252]. All studies were published between April 2023 and June 2024. Eleven[170, 239, 242, 244-246, 248-252] were multicentre studies and four[240, 241 1773, 243, 247] were single-centre studies. Seven studies were conducted in inpatient care settings,[170, 239, 242, 243, 245, 247, 251] three in outpatient care settings,[240, 244, 249] four in emergency care[241 1773, 246, 248, 250] and one in multiple care settings.[252] Observational cohort (n=4) and test-negative (n=7) case-control, prospective case-control (n=3) and population-based case-control (n=1) studies provided effectiveness data for 96,392 unique individuals. Ten studies reported on RSV-related hospitalisations,[170, 239-242, 245, 247-249, 252] five on ICU admissions,[170, 242, 248, 249, 251] two on LRTI incidence,[243, 250] and three on the length of hospital stay among infants aged 12 months or younger.[242, 243, 249] Additionally, two studies considered RSV-related hospitalisations among children aged less than 24 months,[170, 240] with one study providing results,[240] which are reported below.

Table 4.9 Characteristics of included nirsevimab effectiveness studies

Author, year	Country Setting	Sample size, n Centres	Study design Funding	Sex, (% female) Age	Timeframe (month, year)	Outcomes Setting	Quality score~ RoB
Aguera et al.,[242] 2024	Spain Inpatient care	234 Multiple	Test-negative case-control NR	41 ≤12 months	November 2023 to February 2024	RSV-H, ICU-A, and LOHS	10 Low
Alejandre et al.,[243] 2024	Spain Inpatient care	52 Single	Prospective cohort NR	42 <12 months	September 2023 to February 2024	RSV-LRTI and LOHS	9 Low
Assad et al.,[248] 2024	France Emergency care	1035 Multiple	Prospective case-control The French National Agency for AIDS Research / Emerging Infectious Diseases (ANRS MIE)	48 <12 months	October 2023 to December 2023	RSV-H and ICU-A	10 Low
Carbajal et al.,[241] 2024	France Emergency care	2786 Single	Prospective case-control Not supported by any sponsor or funder	44 ≤12 months	October 2023 to February 2024	RSV-H	8 Low
Ezpeleta et al,[170] 2024	Spain Inpatient care	1177 Multiple	Prospective cohort Instituto de Salud Carlos III; EU	46 <6 months	October 2023 to February 2024	RSV-H and ICU-A	11 Low
Jabagi et al.,[249] 2025	France Outpatient care	82,474 Multiple	Population-based cohort Not supported by any sponsor or funder	47 ≤12 months	September 2023 to January 2024	RSV-H, ICU-A, and LOHS	11 Low
Lefferts et al.,[240] 2024	USA Outpatient care	472 Single	Test-negative case-control The US Centers for Disease Control and Prevention	47 <20 months*	October 2023 to June 2024	RSV-H	10 Low
Lenglart et al.,[250] 2025	France Emergency care	383 Multiple	Test-negative case-control Industry-funded: Sanofi, AstraZeneca	NR <12 months	October 2023 to February 2024	RSV-LRTI	9 Low
Lopez-Lacort et al.,[244] 2025	Spain Outpatient care	160 Multiple	Test-negative case-control Instituto de Salud Carlos III; EU	36 <12 months	November 2023 to February 2024	RSV-LRTI	9 Low

Author, year	Country Setting	Sample size, n Centres	Study design Funding	Sex, (% female) Age	Timeframe (month, year)	Outcomes Setting	Quality score~ RoB
Moline et al.,[239] 2024¥	USA Inpatient care	699 Multiple	Test-negative case-control The US Centers for Disease Control and Prevention	42 <8 months	October 2023 to February 2024	RSV-H	10 Low
Moline et al.,[252] 2025	USA Outpatient care and emergency care	1616 Multiple	Test-negative case-control The US Centers for Disease Control and Prevention	45 <60 months*	September 2023 to April 2024	RSV-H	10 Low
Nunez et al.,[245] 2025	Spain Inpatient care	4706 Multiple	Population-based case-control Instituto de Salud Carlos III	45 <12 months	April 2023 to March 2024	RSV-H	10 Low
Paireau et al.,[251] 2024	France Inpatient care	288 Multiple	Test-negative case-control Santé publique France; Laboratory of Excellence in Integrative Biology of Emerging Infectious Diseases (Labex IBEID)	45 <5 months	September 2023 to January 2024	ICU-A	9 Low
Reina et al.,[246] 2024	Spain Emergency care	278 Multiple	Prospective cohort Not supported by any sponsor or funder	NR <6 months	November 2023 to March 2024	RSV-EDV	5 Moderate
Rodriguez-Fernandez et al.,[247] 2024	Spain Inpatient care	32± Single	Prospective case-control Instituto de Salud Carlos III	43 <6 months	October 2023 to December 2023	RSV-H	8 Low

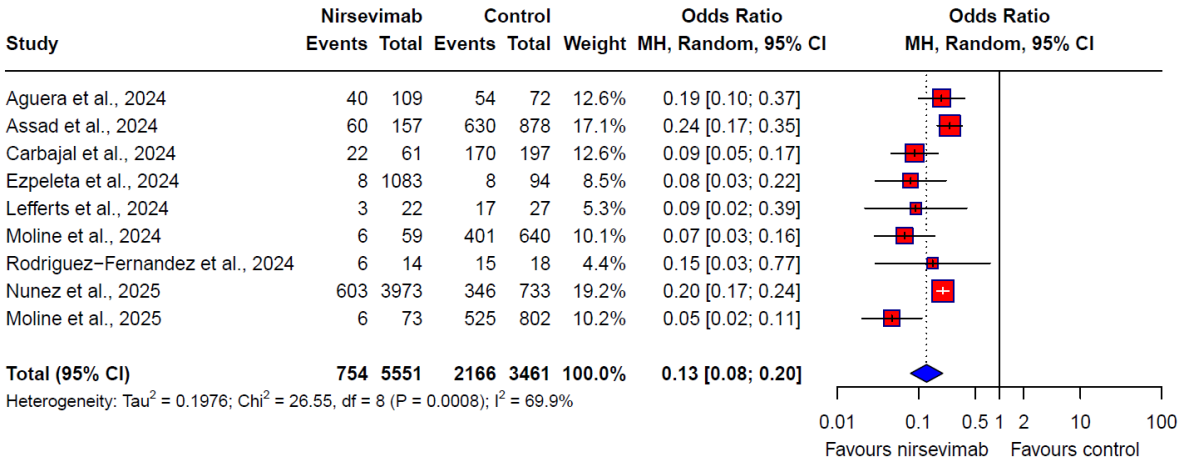
Key: EU – European Union; ICU-A - intensive care unit admission; LOHS - length of hospital stay; NR - not reported; RoB – risk of bias; RSV-EDV - respiratory syncytial virus-related-emergency department visit; RSV-H - respiratory syncytial virus-related hospitalisation; RSV-LRTI - respiratory syncytial virus-related lower respiratory tract infection incidence.
Note: ±Previously reported as 21 by Sumsuzzman et al. ¥The diagnosis method for this study was PCR which was previously not reported by Sumsuzzman et al. *Data for infants < 8 months were also reported. ~Quality assessment of included cohort and case-control studies used the JBI critical appraisal tool with a maximum score of 10 and 11 for case-control and cohort studies respectively with higher scores corresponding to higher quality and lower risk of bias.

Effectiveness outcomes of EHL-mAbs against RSV among infants aged 12 months or younger

RSV-related hospitalisation

Ten studies were identified as reporting on RSV-related hospitalisations among infants aged 12 months or younger.[170, 239-242, 245, 247-249, 252] All included studies related to nirsevimab. Nine studies were conducted among hospitalised populations, while the remaining study was based on an entire birth cohort and so was excluded from the pooled analysis, but is discussed narratively below.[249] All nine studies showed a statistically significant reduction in RSV-associated hospitalisations among infants who received nirsevimab, with the pooled effectiveness estimated at 87% (95% CI: 80% to 92%) (Figure 4.36). There is moderate statistical heterogeneity in this estimate (I^2=69.9%). The study reporting the results based on the birth cohort also reported a statistically significant reduction in RSV-associated hospitalisations among nirsevimab recipients, with an effectiveness of 65% (95% CI: 61% to 69%).[249]

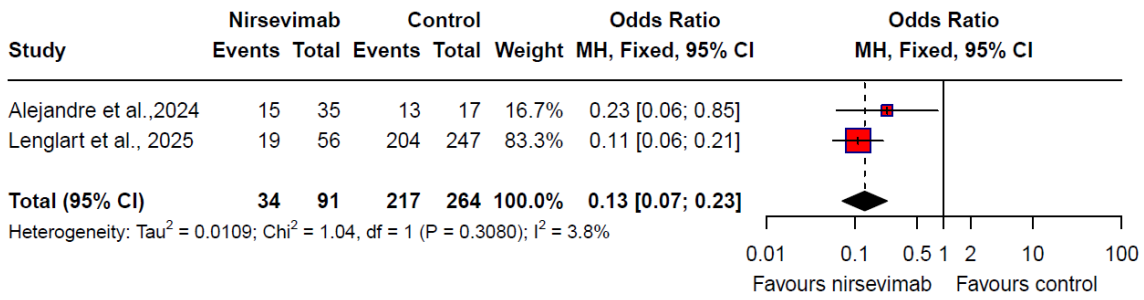
Figure 4.36 Effectiveness of nirsevimab against RSV-related hospitalisations in infants aged 12 months or younger



LRTI incidence

Two studies reported on the effectiveness of nirsevimab against RSV-related LRTI among infants aged 12 months or younger, with both reporting a statistically significant reduction in events among infants who received nirsevimab.[243, 250] The estimated pooled effectiveness of nirsevimab against RSV-related LRTI was 87% (95% CI: 77% to 93%), with low heterogeneity observed (I^2= 3.8%) (Figure 4.37).

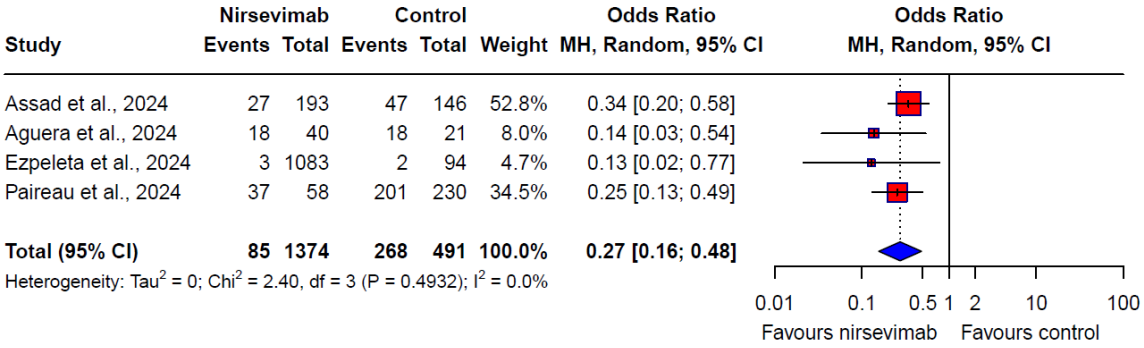
Figure 4.37 Effectiveness of nirsevimab against RSV-related LRTI in infants aged 12 months or younger



ICU admission

Five studies reported on the effectiveness of nirsevimab against ICU admissions in infants aged 12 months or younger,[170, 242, 248, 249, 251] of which one reported on an entire birth cohort;[249] this study was excluded from the pooled analysis, but is reported narratively below. All studies observed a statistically significant reduction in ICU admissions in nirsevimab recipients. The pooled analysis showed a 73% (95% CI: 52% to 84%) reduction in RSV-related ICU admissions in nirsevimab recipients, with no heterogeneity observed in this estimate (Figure 4.38). One study, which reported the effectiveness of nirsevimab against ICU admission based on an entire birth cohort, was excluded from the pooled analysis. This study reported the effectiveness of nirsevimab against ICU admission as 74% (95% CI 66% to 85%).[249]

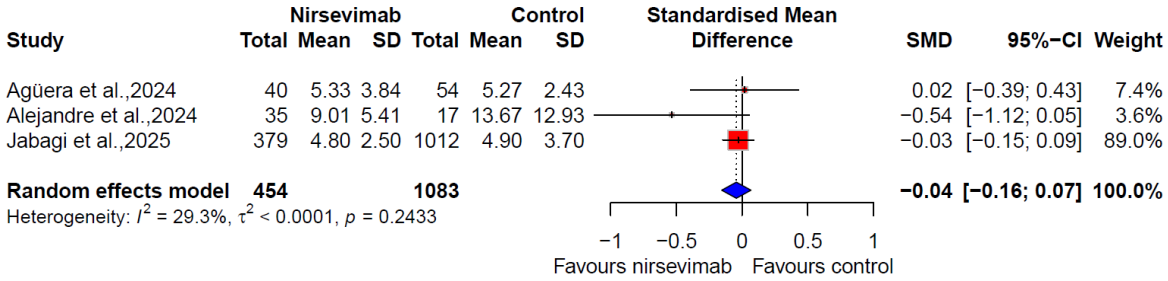
Figure 4.38 Effectiveness of nirsevimab against RSV-related ICU admission in infants aged 12 months or younger



Length of hospital stay

Three studies reported on the impact of nirsevimab on the length of hospital stay. [242, 243, 249] Mean length of stay differed between studies. None of the studies observed a statistically significant difference in the length of hospital stay between infants immunised with nirsevimab compared with the control group. The pooled estimate also indicated no significant difference in the mean length of hospital stay by immunisation status (Figure 4.39).

Figure 4.39 Effectiveness of nirsevimab on length of hospital stay in infants aged 12 months or younger



Effectiveness of EHL-mAbs against RSV-related hospitalisation among children aged 24 months or younger

One study from the United States reported on overall RSV-related hospitalisation among children aged up to 24 months from October 2023 through June 2024.[240] Comparing RSV-related hospitalisations in those who received nirsevimab (n=3/29) with those who did not (n=20/35) provided an estimated effectiveness of 91% (95% CI: 66% to 98%).

4.5 Quality appraisal

4.5.1 Quality appraisal of the ECDC systematic review

As noted in section 4.2, a systematic review undertaken on behalf of the ECDC was identified as the basis for the assessment of the effectiveness and safety of RSV vaccines for the passive immunisation of infants and active vaccination of older adults against RSV. Two reviewers independently appraised the quality of the updated review using the AMSTAR 2 tool.[253] The AMSTAR 2 tool is not designed to provide an overall quality score; however, the authors of the tool have proposed that the confidence in the quality of seven critical domains, which can substantially affect the validity of a review and its conclusions, can inform overall confidence in the results of the review.[203] No weakness were identified for the seven critical domains or the nine non-critical items. Overall, the review was therefore considered to be high quality.

4.5.2 Quality appraisal of the included vaccine efficacy and effectiveness studies

RCTs reporting on vaccine efficacy and safety

The ECDC review reported on four RCTs, three related to older adults (RSVPreF3, RSVpreF and RSV mRNA) and one to maternal vaccination (RSVpreF). For studies that were not otherwise updated, the risk of bias assessment as reported by the ECDC was used. Each of the bias domains were judged by the ECDC review authors as low risk of bias, meaning the overall judgement for these four RCTs was low risk of bias. Regarding the study by Simoes et al., reporting updated results of the MATISSE RCT, the reporting of interim results from this trial by Kampmann et al., was quality appraised in the ECDC review using the RoB 2 tool.[208] As this trial was initially quality appraised by the ECDC review authors, no new methodological concerns were identified in the updated publication, and no critical weaknesses or concerns were noted in the quality appraisal of the ECDC review and hence the HIQA evaluation team did not reassess the risk of bias for the updated publication.

Two reviewers independently assessed the risk of bias of the primary efficacy and safety outcomes over the trial periods reported in Ison et al. 2025 (an update of Papi et al. 2023) and Walsh et al. 2025 (an update of Walsh et al. 2023), which reported updated follow-up times of three seasons and two seasons, respectively. For outcomes reported over the total trial period, the risk of bias assessment found some potential concerns with respect to deviations from intended interventions for one study[219] and missing outcome data for both studies. For Ison et al., these concerns mainly relate to the loss to follow up of participants over the study period from the randomised total of 25,040 (100%) prior to season one to evaluable efficacy populations of 19,989 (79.8%) for season two and 18,726 (74.8%) for season three. While the characteristics of the excluded participants were not reported, the post-randomisation exclusions were balanced between the two groups and transparently reported by the study authors. For Walsh et al., approximately 22% of participants in both groups were lost to follow up, with no reporting of the time points and characteristics of these participants. For the outcome MA RSV-related LRTD, the risk of bias assessment found the potential for some concerns with respect to the selection of the reported result for both studies. For Walsh et al., this related to omission of data on events per season from the full report, with this data only provided in the appendix of a 2024 correspondence. For Ison et al., these concerns related to the reporting of this specific outcome as a post-hoc analysis. However, this was likely due to the inability to report on hospitalisations due to the very small number of events across the three seasons; the other outcomes reported were pre-specified in the study statistical analysis plan.

Observational studies reporting on vaccine effectiveness

Table 4.10 presents a summary of the risk of bias in the four non-randomised studies reviewed.[215-217, 220] Overall, three of the studies were deemed at moderate risk of bias with one study at serious risk of bias.[215] The domains deemed most at risk were bias due to confounding, bias in the selection of participants into the study and bias in the measurement of the outcome.

Each of the studies controlled for baseline confounding in multivariable logistic regression analyses. One study[215] was deemed at serious risk of bias as no information was identified in relation to controlling for time-varying confounding. Three studies adjusted for time varying confounding via inverse probability weighting[216, 217] and two considered time-varying adjustment alongside regression analysis.[216] In addition, one study included exact matching of cases and controls and a negative outcome control to assess residual confounding or ascertainment bias.[217] Two studies were considered at moderate risk of bias,[216, 220] and one at serious risk of bias.[215] This was because of the timing of when participants were vaccinated varied throughout the study period and an exclusion period for reporting outcomes after vaccination was used (14 days in two studies[216, 220] and 21 days in one study).[215] Although justified for allowing time for development of an adequate immune response, it introduces risk of immortal time bias (that is, a type of selection bias in which outcomes are excluded for a period after the intervention, potentially making the intervention group appear at lower risk because events occurring during this period are not counted). The study at serious risk of bias did not sufficiently account for potential selection bias such as through sensitivity analysis or use of inverse probability weighting, elevating the risk of bias judgement from moderate to serious. One study[217] was considered low risk for this domain due to exact matching between groups and the exploration of the effect of this exclusion period in sensitivity analysis. Each of the studies were deemed at moderate risk of bias in the measurement of the outcome domain as there was insufficient information available with respect to potential bias at the time of encounter or outcome assessment (such as knowledge of vaccination status).

Table 4.10 ROBINS-I version 2 quality appraisal

Domain	Tartof et al., 2024	Payne et al., 2024	Perez et al., 2025	Bajema et al., 2025
Bias due to confounding	Serious	Low	Low	Low
Bias in classification of interventions	Low	Low	Low	Low
Bias in selection of participants into the study	Serious	Moderate	Moderate	Low
Bias due to deviations from intended interventions	Low	Low	Low	Low
Bias due to missing data	Low	Low	Low	Low
Bias in measurement of the outcome	Moderate	Moderate	Moderate	Moderate
Bias in selection of the reported result	Low	Low	Low	Low
Overall risk of bias judgement	**Serious risk**	**Moderate risk**	**Moderate risk**	**Moderate risk**

Note: The interventions in Tartof et al., Payne et al., and Bajema et al. were RSVpreF and RSVPreF3. The intervention in Perez et al. was RSVpreF.

4.5.3 Quality appraisal of the Sevendal systematic review

As noted in section 4.1, a systematic review published by Sevendal et al.[201] in 2024 was updated as the basis for the assessment of the efficacy and safety of EHL-mAbs against RSV for infants. Two reviewers independently appraised the quality of the updated review using the AMSTAR 2 tool (described in section 4.2 above).[253] The main weaknesses identified were the lack of completion or reporting of the following elements: justification for selected study designs or publication restrictions; data extraction in duplicate or independent checks on some of the data extraction; use of a suitable tool to conduct risk of bias assessment of included studies; and reporting of funding sources in the included studies. Overall, the updated review was therefore considered to be of critically low quality. However, following scoping of the topic, given factors including the recency of publication of the Sevendal et al. review and the relevance of the population, intervention, comparator and outcomes to this HTA, the Sevendal review was selected for updating.

4.5.4 Quality appraisal of the included EHL-mAb efficacy and safety studies

Table 4.11 presents a summary of the risk of bias assessment for the four RCTs included in the efficacy and safety of EHL-mAbs review, of which three related to nirsevimab and one to clesrovimab. For the MELODY and HARMONIE trials, the risk of bias assessment was conducted on the overall trial rather than the individual publications.[229-231, 234, 235] The risk of bias assessment was completed for each efficacy and safety outcome individually, but as the individual judgements were in

agreement, only an overall summary judgement is presented for efficacy and safety. No study was identified to be at high risk of bias overall. Overall, some concerns of risk of bias were identified for one study (reported across two publications[230, 235]), while three studies (reported across five publications)[229, 231, 233, 234, 236] were deemed to be at low risk of bias. For the HARMONIE trial, some concerns were identified in relation to the measurement of the efficacy and safety outcomes as it was an unblinded study.[230, 235]

Table 4.11 Risk of bias 2 assessment of included studies – efficacy and safety of EHL-mAbs

Domain	MELODY	HARMONIE	Griffin et al., 2020	CLEVER
Efficacy outcomes:				
Randomisation process	Low	Low	Low	Low
Deviations from intended interventions	Low	Low	Low	Low
Missing outcome data	Low	Low	Low	Low
Measurement of the outcome	Low	Some concerns	Low	Low
Selection of the reported results	Low	Low	Low	Low
Overall risk of bias judgement	**Low**	**Some concerns**	**Low**	**Low**
Safety outcomes:				
Randomisation process	Low	Low	Low	Low
Deviations from intended interventions	Low	Low	Low	Low
Missing outcome data	Low	Low	Low	Low
Measurement of the outcome	Low	Some concerns	Low	Low
Selection of the reported results	Low	Low	Low	Low
Overall risk of bias judgement	**Low**	**Some concerns**	**Low**	**Low**

Note: The intervention in MELODY, HARMONIE and Griffin, 2020, was nirsevimab, and in CLEVER was clesrovimab.

4.5.5 Quality appraisal of the Sumsuzzman systematic review

Two reviewers independently appraised the quality of the systematic review of nirsevimab by Sumsuzzman et al. using the AMSTAR 2 tool.[253] No weakness was identified for the seven critical domains. One weakness was identified for one of the nine non-critical items (item 10), as the review authors stated that funding information for each study was extracted from the primary studies, but they did not include this information in the final publication. According to the AMSTAR-2 rating guidance, the systematic review was considered to be of high quality. It is worth

noting that there were some concerns relating to the assessment of the potential impact of risk of bias on the results of the meta-analysis and inclusion of one study at moderate risk of bias in the primary analysis. As this related to only one study, which had few events and a small sample size, it was not considered a strong enough concern to be considered a critical weakness for the systematic review overall.

A summary of the quality appraisal as reported in the systematic review using the JBI critical appraisal tool is provided in A4.19 in the appendix of this report. This summary is restricted to the 15 studies eligible for inclusion in the HIQA review and reported on in this chapter. Of these 15 studies, 14 were assessed to be at low risk of bias, while one study [246] was assessed to be at moderate risk of bias (Appendix A4 Table A4.19).

4.6 Pharmacovigilance

As outlined in Chapter 2, the three currently authorised RSV vaccines (RSVPreF3, RSVpreF and RSV mRNA) and the only authorised EHL-mAb (nirsevimab) are considered new active substances and new biologicals. As such, they are all subject to additional monitoring by regulatory authorities in the EU.[6-9] In Ireland, the Health Products Regulatory Authority (HPRA) operates the national system for recording and reporting details of suspected reactions/events. These are often based on observations of an unexpected or unwanted event and come from a variety of sources including healthcare professionals and patients. Reporting can be made directly using options from the HPRA website or indirectly from pharmaceutical companies through the European Medicines database, that is 'EudraVigilance'.[254] The following sections summarise the pharmacovigilance data for the agents as reported by the HPRA, other European regulatory authorities or through the product SmPCs, and as identified by the National Immunisation Advisory Committee (NIAC) in their updated recommendations for vaccination against RSV in older adults.[7-9, 135]

4.6.1 RSV vaccines

According to communication received by the HPRA for data up to 11 February 2025, there were fewer than five suspected adverse drug reaction (ADR) reports received associated with RSV vaccines, each relating to RSVPreF3. These adverse events related to pain, swelling, hypoaesthesia (that is, reduced sensation to touch, pain and temperature), insomnia, pain in extremity, and paraesthesia (that is, sensations like numbness, tingling, pins and needles). Note that uptake and hence pharmacovigilance data in Ireland for these products is likely to be limited as RSV vaccines are not currently nationally funded. Reports of a suspected drug reaction do not necessarily mean it has been caused by the medicine in question and such reports do not represent the opinion of the HPRA.

According to the respective EMA's SmPCs for each of the three vaccines authorised for use in older adults, while side effects are common (with the most common typically being injection site pain, tiredness, and headache) they are predominantly mild-to-moderate reactions.[255-257] Regarding the use of RSVpreF in pregnant women, the SmPC of the EMA states the vaccine is well tolerated. Moreover, it states that there is no indication of toxicity or safety signals in infants up to 24 months of age.[7]

There were some concerns noted by the Committee for Medicinal Products for Human Use (CHMP) in the summary of safety concerns in public assessment reports regarding missing information in relation to the use of RSVpreF and RSV mRNA vaccine in specific populations.[258, 259] For RSVpreF, these concerns related to missing safety data in population subgroups excluded from the pivotal clinical studies, including pregnant women who are immunocompromised and those who have high-risk pregnancies, as well as older adults who are immunocompromised, and older adults with renal or hepatic impairment. The CHMP required additional studies to be carried out in these populations as part of the risk management plan for RSVpreF.[260] Regarding the RSV mRNA vaccine, missing data were noted in relation to co-administration with other vaccines, use of the vaccine in persons who are immunocompromised and those with autoimmune or inflammatory disorders.[259] The pharmacovigilance plan for RSV mRNA vaccine includes post-authorisation safety studies to characterise the risk of predefined adverse events within subgroups defined by age, sex, immunocompromised status, co-administration of other vaccines, and status of autoimmune or inflammatory disorders.[259]

In terms of factors requiring additional or ongoing monitoring, the CHMP public assessment reports for RSVpreF and RSVpreF3 included specific comments relating to potential safety signals for Guillain-Barré syndrome (GBS) in older adults. [258, 261] For both of these vaccines, there is ongoing post-marketing surveillance for GBS risk in older adults. For RSVpreF, the EMA advised a causal relationship between RSVpreF and GBS is a reasonable possibility.[260] However, given the rarity of the event, it concluded that the overall benefit risk profile of RSVpreF remains favourable. For RVSPreF3, the EMA CHMP assessment stated that there was insufficient information available to draw a clear conclusion on the causal relationship between RSVPreF3 vaccination and pIMDs (such as GBS and acute disseminated encephalomyelitis (ADEM)), but noted that follow-up of pIMDs will occur in periodic safety update reports. In the US, the prescribing information for both RSVpreF and RSVPreF3 have been updated to advise that the results of a post-marketing observational study suggest an increased risk of GBS during the 42 days following vaccination.[262, 263] A report was published by the Medicines and Healthcare products Regulatory Agency (MHRA) in the UK on 7 July 2025.[264] According to the MHRA, in adults aged 75 to 79 years, preliminary unpublished post

marketing data from the UK Health Security Agency and Public Health Scotland studies suggest a combined excess of 15 to 25 cases of GBS per million RSVpreF vaccine doses in England and Scotland. The same report noted that the MHRA had received 21 reports of suspected GBS in older adults aged 75 to 79 years up until 2 June 2025, while 1.9 million doses of RSVpreF had been administered in this age group up to 26 May 2025. There were no reports received relating to RSVPreF3 as there was very limited use of RSVPreF3 in the UK during the same period. In the context of this report, the Commission on Human Medicines advised that the benefits of vaccination against RSV outweighs the small risk of developing GBS in older adults. NIAC recommendations in relation to GBS were additionally informed by analyses of pharmacovigilance data presented to the US and German NITAGs, which suggested a potential risk of 3 (95% CI: 0 to 10) to 10 (95% CI: 1.7 to 18.3) GBS cases per million doses of RSVPreF3, respectively, and 16 (9%% CI: 3 to 29) to 25.1 (95% CI: 6.7 to 43.3) GBS cases per million doses of RSVpreF, respectively, in those aged 60 years and older.[135]

The CHMP assessment reported that in an RSVPreF3 phase 3 efficacy and safety study, a statistically significant difference in atrial fibrillation events were reported (10 in the RSVPreF3 group and four in the placebo group); however, all events except one were observed in participants with pre-existing events of arrhythmias or with other risk factors or medical conditions.[261] In the US, the FDA has required a post-marketing study to evaluate atrial fibrillation in adults vaccinated with RSVPreF3.[265]

Regarding the RSV mRNA vaccine, the CHMP noted that in clinical trials of this vaccine there were two cases of pericarditis and two cases of myocarditis in the vaccinated group compared with one case of pericarditis and no cases of myocarditis in the placebo group. These were all evaluated to be unrelated to the intervention; however, the CHMP noted that myocarditis or pericarditis remains an important concern for the RSV mRNA vaccine as the risk of these adverse events with other mRNA vaccines was only discovered after widespread use.[259] The CHMP also discussed imbalances in duration of events of facial paralysis in the RSV mRNA vaccine arm compared with the placebo group.[259] Peripheral facial nerve paralysis was included as a rare adverse drug reaction in the SmPC based on an intervention-related SAE of facial paralysis in a vaccine.[9]

Regarding the use of RSVpreF in pregnant women, the CHMP noted a slightly higher number of preterm births in the vaccinated cohort compared with the placebo group. This difference was found to occur among mothers from upper-middle income countries, but overall was not found to be statistically significant.[258] The number of preterm deliveries and events of low birth weight are under continued monitoring. As highlighted in Chapter 2, the EMA authorised RSVpreF for administration to

pregnant women between 24 and 36 weeks' gestation. The US prescribing information for RSVpreF advises administration between 32 and 36 weeks' gestation, to avoid the potential risk of preterm birth.[262] The UK Medicines and Healthcare Product Regulatory Agency public assessment report lists premature birth as an important potential risk[266] and includes a warning that RSVpreF should not be used in pregnant individuals less than 28 weeks of gestation in order to minimise the potential risk of extremely premature birth.[267]

4.6.2 RSV extended half-life monoclonal antibodies

According to communication received from the HPRA, there were fewer than five ADR reports associated with nirsevimab up to 11 February 2025, all of which related to injection site redness. As highlighted in Chapter 2, nirsevimab was offered to all infants born in Ireland between September 2024 and February 2025 through the publicly-funded Pathfinder programme. Nirsevimab was also offered to all infants at high-risk of severe RSV disease and previously eligible for palivizumab, including those born prior to the start of the RSV season, as well as all children at high risk of RSV disease entering their second RSV season. A total of 22,444 infants were immunised, reflecting an overall uptake of 83%. Among infants at high risk of RSV disease (n=399), there was a higher uptake of 99%.

According to the SmPC for nirsevimab, the most frequently reported side effects (which may affect up to 1 in 100 people) are a rash occurring within 14 days after injection, and fever and injection site reactions occurring within seven days after injection.[6] The majority of cases of rash were mild to moderate in intensity, with injection site reactions classified as non-serious.

It is noted that anaphylaxis is a serious adverse event that has been reported following administration of nirsevimab; however, as it is a rare event the frequency is unknown.[6] As with other forms of immunisation, appropriate medical treatment and supervision should always be readily available in case of an anaphylactic event following administration. This product will continue to be closely monitored as part of routine pharmacovigilance activities.[268]

The EU risk management plan for nirsevimab acknowledges that the emergence of resistant variants of the RSV virus was a rare event in the pivotal trials.[268] The possibility of the RSV virus potentially developing resistance to nirsevimab will continue to be monitored closely and characterised through ongoing virologic assessment in post-marketing RSV molecular surveillance activities.

Data from the post-marketing surveillance of nirsevimab during the 2023/2024 RSV immunisation campaign in Spain were published in June 2025.[269] Based on these spontaneous notification data, no new safety concerns were identified beyond those

described in the product's SmPC. As these data come from spontaneous notifications, it is important to note that they may not represent all events and do not necessarily imply a causal relationship. In total, between September 2023 and May 2024, there were 67 cases reporting 141 suspected AEs (23.1 cases per 100,000 doses and 48.6 suspected AEs per 100,000 doses), with higher reporting rates in the initial months of the campaign. The most frequently reported suspected AEs were rash (n=12), drug ineffectiveness (n=10), and pyrexia (n=10). Of the 67 cases, 36 (54%) were reported as serious (54%) with 21 cases (31%) requiring hospitalisation. Of the 67 cases, the status of six (9%) was unknown at the time of publication, while 55 (82%) were listed as recovering or recovered; four (6%) had not recovered; and there were two reported deaths (3%) — one of which occurred after hospitalisation. None of the potential risks outlined in the EU Risk Management Plan were identified and no new safety signals or unexpected adverse events were identified in the referenced study. While causality cannot be implied from these data, the study authors emphasised the need for continued vigilance and monitoring, given the number of serious cases.

4.7 Discussion

This chapter considered the available evidence in relation to the efficacy, effectiveness and safety of approaches to immunisation against RSV for older adults and infants. This involved identifying and updating two systematic reviews: one commissioned by the ECDC that reported on RSV vaccination for the passive immunisation of infants through maternal vaccination and vaccination of older adults, and one from Sevendal et al.[201] that focused on immunisation with EHL-mAbs for infants and young children at increased risk of RSV-related disease. A third systematic review by Sumsuzzsman et al. focused on the effectiveness of nirsevimab in infants and children, with relevant studies from this review extracted and summarised in this chapter without update.

4.7.1 RSV vaccines

Overall, 12 studies relating to RSV vaccines were identified for inclusion in the updated review, comprising eight studies reporting on four RCTs, and four observational studies.[214, 215, 221-225] Seven of the 12 studies were newly identified by the HIQA update,[214, 215] while five studies were included from the ECDC living systematic review.[221-225] All studies reported on in this chapter are restricted to EMA-authorised vaccines against RSV (RSVPreF3, RSVpreF, RSV mRNA).

Relative efficacy and effectiveness of RSV vaccines in older adults

Six studies based on three RCTs reported on the efficacy and safety of RSV vaccines in adults aged 60 years and older,[218, 219, 221-224] while three observational studies reported on their effectiveness in this population.[215]

Based on pooled data from three RCTs, there was high certainty evidence that RSV vaccination (RSVPreF3, RSVpreF, RSV mRNA) is protective against RSV-related ARI and LRTD in older adults over one RSV season, with pooled vaccine efficacy (VE) estimates of 67% and 78%, respectively.[221-223] For the two RCTs that reported cumulative efficacy of a single RSV vaccine dose (RSVPreF3, RSVpreF) over two seasons,[224] pooled VE was estimated as 52% against RSV-related ARI and 67% against RSV-related LRTD. Heterogeneity was observed in the meta-analysis (I^2: 84.8% and 71.0%, respectively). This may be due to some differences in the outcome definitions, study settings and patient characteristics between the trials. Cumulative VE of a single dose of RSV vaccine (RSVPreF3) against RSV-related LRTD over three seasons was reported as 69% in one trial,[219] although per season VE estimates indicated that efficacy decreased over time, from 83% in season one to 56% and 48% in seasons two and three, respectively.

Based on data from two test-negative case-control studies, there was moderate certainty evidence that RSV vaccination (RSVpreF or RSVPreF3) reduces RSV-related hospitalisations in older adults over one season, with pooled vaccine effectiveness of 77%.[215, 216] Both studies selected participants for inclusion on the basis of having had hospital admissions or ED encounters. One RCT (RSVPreF3) reported on this outcome prospectively over two and three RSV seasons, but the results were not statistically significant, likely due to the very low number of events observed overall (that is, a total of eight RSV-related hospitalisations among approximately 25,000 participants across all three seasons).[224]

In the context of limited data regarding the efficacy of RSV vaccination against hospitalisation, two RCTs reported on MA RSV-related LRTD. As outlined in Table A4.6 in the appendix, both trials included cases that prompted general practitioner, specialist and ED visits, while one trial considered medically attended cases more broadly, and also included cases that resulted in telehealth consultations, urgent care visits and hospitalisation. This RCT reported vaccine efficacy (RSVpreF) against MA RSV-related LRTD with two or more symptoms as 60% over two seasons.[218] The other RCT reported a vaccine efficacy (RSVpreF3) against MA RSV-related LRTD visits of 74% over three seasons. The study authors suggested this as evidence that RSV vaccination is likely to reduce severe clinical conditions and the related burden on the healthcare system.[219] These conclusions of a reduction in burden on the

healthcare system are supported by the evidence from the observational studies reported above.

Neither the efficacy nor the effectiveness of vaccination against RSV-related ICU admissions and RSV-related mortality could be estimated, due to the limited data identified. No included studies reported on RSV-related ICU admissions and no evidence was identified relating to RSV-related mortality, with one study explicitly stating that no RSV-related deaths were reported during the study period.[221]

Safety of RSV vaccines in older adults

Unsolicited and solicited (any) adverse events were relatively common, with an increased risk following vaccination compared with receiving placebo. Based on three RCTs (RSVPreF3, RSVpreF, RSV mRNA), there was an increased risk of experiencing any unsolicited adverse event (pooled RR 1.30)[218, 221, 223] and based on two RCTs (RSVPreF3, RSV mRNA) there was an increased risk of experiencing solicited adverse events, including local and systemic reactions, among vaccinated participants compared with those who received a placebo (pooled RR: 1.81).[222, 223] Local and systemic reactions were relatively common among vaccine recipients; however, these were mostly mild-to-moderate in severity. Severe solicited adverse events were less commonly reported, but were more frequent in the vaccine than the placebo arms (RSVPreF3 RCT: 4.1% versus 0.9%; RSVpreF RCT: 6.2% versus 4.1%; RSV mRNA RCT: 6.2% versus 4.1%).

Overall, the RCT data indicate that SAEs related to RSV vaccination are rare. However, given the low certainty of the evidence (due to the small number of events and wider confidence intervals), it is unclear from these data whether authorised vaccines are associated with intervention-related SAEs. Pooled data from the three RCTs (RSVPreF3, RSVpreF, RSV mRNA) indicated that, in the first season after administration, there were 27 SAEs related to the intervention, with 17 (0.04%) occurring among RSV vaccine recipients and 10 (0.02%) among placebo recipients, and no significant difference between the trial arms.[221-223] The frequency of pIMDs that were considered related to the intervention were similar in both vaccine and placebo groups across the three studies.[221-223] Two of the three cases of related SAEs experienced by the vaccine group in one RCT (RSVpreF) were consistent with GBS and or a subset of GBS.[218, 222] No other cases of GBS were noted across the studies. Fatal SAEs related to the intervention were reported in one RCT (RSVPreF3) which provided follow up across three RSV seasons. A total of 496 (2%) participants died, with five of these deaths considered to be related to the vaccine (n=3) or placebo (n=2) during a blinded assessment.[219] No fatal adverse events related to vaccination or placebo were reported in the other two RCTs.

Aside from the included studies, an observational study published in May 2025 based on electronic health record data from approximately 4.7 million RSV vaccine recipients aged 60 years and older in the US reported an excess risk of GBS following vaccination. During the one-year study period, 102 GBS cases were reported across all participants. The authors estimated an excess of 18.2 (95% CI: 9.8 to 23.3) GBS cases per 1,000,000 doses of RSVpreF administered. For recipients of RSVPreF3, a clear excess risk of GBS was not evident, with an estimated 5.2 (95% CI: -0.9 to 9.2) excess cases per 1,000,000 doses administered.[270]

Several post-marketing surveillance studies are planned or underway to evaluate the risk of specific adverse events of special interest following RSV vaccination in older adults, including GBS. Regarding RSVPreF3, a post-marketing active surveillance study in the USA to evaluate the risk of GBS, acute disseminated encephalomyelitis, and atrial fibrillation in adults aged 50 years and older vaccinated with RSVPreF3 was planned to start in March 2025 with an estimated final study report due by the end of October 2031.[271] For RSVpreF, there are three post-authorisation safety studies concerning vaccination of older adults listed on the EMA website, one each assessing the risk of atrial fibrillation[272] and GBS[273] following vaccination, and one assessing vaccine safety among older adults who are immunocompromised, or who have renal or hepatic impairment.[274] As of 30 May 2025, there are no post-marketing safety surveillance studies listed by the EMA relating to the RSV mRNA vaccine. In July 2025, data from England and Scotland estimated a combined excess of 15 to 25 excess cases of GBS per million doses of RSVpreF vaccine among adults aged 75 to 79 years. In the context of this report, the Commission on Human Medicines advised that the benefits of vaccination against RSV outweighs the very rare risk of GBS among older adults.[264] Similarly, the risk of SAEs such as GBS was considered in the updated NIAC recommendations relating to the vaccination of older adults submitted to the Minister of Health in October 2025.[135] While noting some uncertainty over these potential adverse events, NIAC considered that these events remain rare and that the vaccines are generally well tolerated in this cohort, with the balance of benefits and harms favouring vaccination in those aged 75 years and older, and in those with risk factors for severe RSV disease.

Relative efficacy and effectiveness of maternal vaccination against RSV

Considering the passive immunisation of newborns and infants against RSV, one test-negative case control study and two studies reporting results of a single RCT of maternal vaccination were included.[214, 225] Regarding the RCT data, the results of this review were informed by the final updated analysis published in 2025.[214] The reported efficacy results relate to 180-days follow-up, which is equivalent to the estimated duration of protection offered by maternal vaccination.

Based on the results of this single RCT, there is moderate certainty evidence that maternal vaccination may reduce the risk of RSV-related LRTD and RSV-related hospitalisation in newborns and infants, compared with placebo.[214] Relative VE against RSV-related LRTD was estimated as 49%, but increased to 70% when restricted to severe RSV-related LRTD cases. Relative VE against RSV-related hospitalisation was estimated as 55%. The test-negative case control study provided further evidence of the effectiveness of RSV vaccination against hospitalisation up to 180 days after birth, reporting a vaccine effectiveness estimate of 71%. No RSV-related deaths were reported among the vaccine group; however, there was one death in a 120-day old full-term infant in the placebo group classified as caused by RSV-related ARI. The RCT did not report on efficacy against RSV-related ARI in infants.

Based on the RCT data, the estimated relative VE against RSV-related LRTD requiring oxygen-support (that is, either with oxygen saturation less than 90% or requiring supplemental oxygen) was 77% when these outcomes were combined. Subgroup analysis of these two outcomes was limited due to the small number of events (that is, 38 events in total among 7,307 infants). There were no differences observed between vaccine or placebo groups with respect to healthcare utilisation outcomes such as ICU admissions, asthma-related illness, bronchodilator use or antibiotic use.

In addition to the above studies, two additional studies that reported on maternal vaccination and RSV-related hospitalisation among infants, which were published as preprints, were identified in our search.[275, 276] One of these was subsequently published in July 2025.[275, 277] It reported on the results of a multicentre prospective cohort study that followed infants born after 12 August 2024 in Scotland and after 1 September 2024 in England that were hospitalised with acute LRTI up to 20 January 2025. When adjusted for site and month, age under three months, sex and prematurity, the adjusted vaccine effectiveness against RSV-related hospitalisation was 58% (95% CI: 28 to 75). When restricted to infants whose mothers were vaccinated more than 14 days before delivery, adjusted vaccine effectiveness was higher at 72% (95% CI: 48 to 85) The study also reported subgroup analyses considering clinical outcomes among RSV-positive infants born to mothers vaccinated more than 14 days before delivery compared with unvaccinated mothers.[275, 277] No statistically significant associations were observed for length of stay (p=0.9), risk of receiving high flow nasal cannulae respiratory support (p=0.4), risk of invasive mechanical ventilation (p=0.4), or risk of admission to PICU (p=0.4). The second preprint identified during our search assessed the impact of RSVpreF vaccination during pregnancy on RSV-related hospitalisations in infants in Argentina between March and August 2024.[276] This study reported adjusted vaccine effectiveness against RSV-related hospitalisations (adjusted for age, sex,

comorbidities and week of hospital admission) of 66% (95% CI: 30 to 84) in infants six months or younger. Vaccine effectiveness against hospitalisation (adjusted for age, sex and comorbidities) was higher at 81% (95% CI: 63 to 90) when restricted to those aged three months or younger. There was also evidence of vaccine effectiveness against RSV-related PICU admissions (87% (95% CI: 53 to 97)) and RSV-related hospital stays longer than 11 days (89% (95% CI: 62 to 97)).

Safety of maternal vaccination against RSV

SAEs related to the intervention were infrequent, with four cases reported for pregnant women (three among vaccine recipients and one in a placebo recipient) and no cases among newborns or infants.[214] Each of the intervention-related SAE were reported to have resolved.

In both pregnant women and infants, most adverse events reported in the period up to one month after vaccination were mild-to-moderate in severity. In pregnant participants, 14% of vaccine recipients and 13.2% of placebo recipients experienced an adverse event, while among newborns and infants, 38% and 35.4% experienced an adverse event in the vaccine and placebo groups, respectively. Severe events represented approximately 10% of all adverse events among both cohorts. No adverse events in the placebo group and less than 0.1% of events in the vaccine group were considered related to the intervention. Of 18 adverse events considered related to the study intervention among pregnant participants, four were categorised as pregnancy, puerperium and perinatal conditions; three occurred among the vaccine group and one in the placebo group.

No maternal deaths or stillbirths were judged as related to the study intervention. There was one maternal death reported, which occurred in the vaccine group. There were 19 stillbirths (vaccine group: n=10; placebo group: n=9) and three cases of spontaneous abortion (vaccine group: n=1; placebo group: n=2) reported in pregnant participants up to six months after delivery. Additionally, there were 22 deaths (vaccine group: n=8; placebo group: n=14) reported among newborns and or infants over a 24-month follow-up period, of which one case among the placebo group was determined to be caused by RSV-related ARI.

In terms of AESIs, preterm birth rates were reported as 5.7% in the RSVpreF group and 4.7% in the placebo group. A separate study described post-hoc analyses of preterm birth rates in this RCT, and reported that this equated to a non-significant relative risk of preterm birth (RR 1.20 (95% CI: 0.98 to 1.46)).[278] Most preterm births were late preterm (that is, 34 to less than 37 weeks' gestation), whereas 10.7% of preterm births in the vaccine group and 7% of preterm births in the placebo group took place at less than 34 weeks' gestation. In terms of the timing of vaccination, the risk of preterm birth was significantly higher with vaccination at 28

to less than 32 weeks' gestation (6.8% versus 4.8%; RR 1.43 (95% CI: 1.02 to 2.02)), but not significantly different at other administration times. A significant regional difference in preterm birth rates was also reported, specifically a higher risk of preterm birth among vaccine recipients (7%) compared with placebo recipients (4%) in non-high-income countries (RR 1.73 (95% CI: 1.22 to 2.47)).

In addition to the included studies, two preprints were identified that reported on RSV maternal vaccination and impact on infants.[275, 276] The preprint from the UK, subsequently published in July 2025,[277] reported that no infants recruited died during their time as an inpatient. The second preprint from Argentina noted that no deaths were recorded among the 323 infants included in their analysis and born to vaccinated mothers between 1 March and 9 November 2024.[276]

As noted in Section 4.6.1, regulatory agencies have adopted differing approaches to this safety signal (that is, preterm births), with agencies in the UK and US advising administration no earlier than 28 weeks and 32 weeks' gestation, respectively. RSVpreF also remains subject to additional monitoring. In addition to the published data included in this review, three post-marketing safety studies assessing the safety of RSVpreF maternal vaccination for pregnant women are planned or ongoing at the time of writing.[279-281]

Quality of the included studies

The updated HIQA review on RSV vaccines was based on the high-quality systematic review commissioned by the ECDC, which was quality assessed by the HIQA evaluation team using the AMSTAR 2 tool. For older adults, all three of the included RCTs (reporting on outcomes relating the first RSV season) were assessed to be at low risk of bias. Risk of bias assessments carried out by the HIQA evaluation team for the two RCTs that provided follow-up for subsequent seasons identified some concerns, primarily due to missing outcome data as participants were lost to follow-up. The three non-randomised studies relating to RSV vaccination in older adults that were included were deemed to be at moderate (two studies) to serious (one study) risk of bias, with the main sources of potential bias being confounding, the selection of participants into the study and the measurement of the outcome.

The single RCT relating to maternal vaccination was assessed as being at low risk of bias in the ECDC review. This assessment was not updated by the HIQA evaluation team, as no new methodological concerns were identified in relation to the additional study from this RCT included in the HIQA update. Moderate risk of bias due to measurement of the outcome was identified in the single non-randomised study included relating to maternal vaccination.

Strengths and limitations

The findings of this systematic review should be interpreted with consideration of its overall strengths and limitations. A robust approach to the review process was employed, with publication of a defined protocol. The review, which updated an existing draft systematic review commissioned by the ECDC, adhered to standard methods, ensuring methodological rigour at each stage. While the scope was restricted to currently authorised RSV vaccines for the passive immunisation of infants through maternal vaccination and the vaccination of adults aged 65 years and older, a comprehensive search strategy was used.

One of the aims of this systematic review was to inform national decision-making in Ireland with respect to the efficacy, effectiveness and safety of RSV vaccination among adults aged 65 years and older. While the identified evidence is directly relevant and largely applicable to this aim, there are limitations. The populations of interest in the included studies included adults aged 60 years and older, meaning a small proportion of participants included were aged up to five years younger than our cohort of interest. RCTs and observational studies differed in terms of the proportion of adults in older age groups included in the studies. Across the RCTs, the majority of adults were aged 60 to 69 years (56% to 64% of participants), while adults aged 80 years and older were poorly represented (6% to 8% of participants).[221-223] However, it is noted that a considerable proportion of those included in the observational studies had comorbid conditions, with these studies reflecting an older population. Two of the observational studies reported Charlson Comorbidity Index (that is, a tool predicting a patient's risk of mortality based on the presence of comorbid conditions) scores of three or higher for 41% and 75% of participants,[215, 217] respectively, while the third study reported that 84% of participants had two or more categories of comorbid conditions.[216]

The proportion of participants with immunocompromising conditions ranged from 11% to 23% across the three observational studies.[215-217] For two of the observational studies, the majority (56% and 60%, respectively)[215, 216] of participants were aged 75 years or older, and in the third observational study the majority (56%) of participants were aged 70 to 79 years .[217] Despite these differences in the demographics, the observational studies generally support the RCT findings that RSV vaccination likely reduces severe disease outcomes and the related burden on the healthcare system. Pooled subgroup analyses, such as for different age groups among older adults, were not conducted due to the small number of studies included and varied reporting practices across studies (for example, reporting of surveillance time for the total sample, but not by age group).

The identification of additional studies reflecting the latest available evidence up to 25 April 2025 is a strength of the current review; however, it also highlights the rapidly expanding nature of the evidence base regarding RSV vaccines. It is

reasonable to expect that further evidence will continue to emerge, particularly real-world evidence of the effectiveness and safety of RSV vaccines.

Current evidence in relation to the duration of protection for older adults is limited to a maximum follow-up of two (RSVpreF) or three (RSVPreF3) RSV seasons. Longer term follow-up data will be important to inform decision-making including the requirement for a booster, if any. Immunogenicity measures were outside the scope of this systematic review; however, inclusion of such measures could provide some additional insight in relation to the duration of protection.

Moreover, there is a lack of head-to-head trials for the available vaccines (or of the maternal vaccine compared with an EHL-mAb when considering the passive immunisation of infants), with differences in the end-point definitions between studies. These factors limit the ability to answer questions regarding the relative effectiveness of the different interventions. It is also noted that the included studies were not designed to estimate the protective effect of RSV vaccines against mild RSV illness as laboratory confirmation typically requires patients to seek medical care.

The RCT data for the RSV vaccines predominantly relate to the 2021/2022 RSV season (when there was extensive use of non-pharmacological interventions to limit the spread of SARS-CoV-2), while the observational data predominantly relate to the 2023-2024 RSV season. Given the potential for distinct seasonality with RSV and differences in disease severity, additional studies will be required to determine if the reported vaccine efficacy and effectiveness estimates are applicable across seasons.

In this update, the effects of the intervention were estimated using both per protocol and intention-to-treat approaches, where possible. The included trials, and the ECDC review, reported on the modified total vaccinated cohorts only (that is, the populations that were exposed to the intervention). Results of the respective analyses were broadly comparable, despite the different reporting approaches.

4.7.2 Monoclonal antibodies (efficacy and safety)

Relative efficacy and effectiveness of EHL-mAb in infants

Relative efficacy of EHL-mAb in infants

Three of the RCTs related to EHL-mAbs identified in this review involved nirsevimab; one RCT was identified relating to clesrovimab. There is high certainty of evidence based on three RCTs [233] [231] [236] that EHL-mAbs are effective at preventing MA LRTI in infants over one RSV season, with an estimated 69% (95% CI: 60% to 75%) reduction in events. However, based on data from the MELODY and CLEVER trials, this protection did not last over a second RSV season (days 362/365 to

511/515 post dose) (efficacy 1%, 95% CI: -46% to 33%, moderate certainty of evidence).[231, 236] Similarly, there is moderate certainty of evidence that EHL-mAbs protect against RSV-associated LRTI with hospitalisation, based on four trials, with an estimated 83% (95% CI: 75% to 88%) reduction in events over one season. Again, based on the MELODY trial, this protection does not appear to last into a second RSV season (efficacy 50%, 95% CI: -146 to 90).

Nirsevimab also protected against the requirement for ICU admission,[233] supplemental oxygen[233] and very severe RSV-associated LRTI compared to placebo or standard care over one season, but again with evidence that this protection does not extend to a second season.[231, 235] Similarly, clesrovimab protected against severe MA LRTI over one season, which included infants requiring supplemental oxygen or mechanical ventilation.[236] It should be noted that although there was a statistically significant difference between the groups for each of these outcomes, the incidence of these outcomes was typically very low.

There is high certainty of the evidence that EHL-mAbs protect against all-cause MA LRTI based on three studies.[231, 233, 236] As would be expected, the efficacy was lower for this outcome than for MA RSV LRTI (21% versus 69%). In the HARMONIE and CLEVER trials, EHL-mAbs protected against all-cause LRTI hospitalisations, with a lower pooled efficacy compared with RSV-associated LRTI hospitalisations (43% versus 83%).[231, 233] This outcome helps to provide an assessment of the impact of EHL-mAbs on the overall incidence of respiratory illnesses.

The trials differed in their definition of their primary efficacy outcome of MA RSV-associated LRTI as highlighted in Table A2.12, with fewer indicators of disease severity required in the clesrovimab study. However, a post-hoc analysis of the CLEVER trial, which used similar criteria for MA RSV-associated LRTI to that used in the MELODY study, suggests that clesrovimab effectiveness increases (88%, 95% CI: 76% to 94%) when more indicators of severe disease are included in the definition.

Relative effectiveness of EHL-mAb in infants

Effectiveness evidence for the EHL-mAbs were limited to nirsevimab, with no observational studies identified for clesrovimab. This likely reflects differences in the timing of authorisation by international regulatory authorities, with clesrovimab authorised on 9 June 2025 by the US FDA and a positive opinion adopted by the CHMP of the EMA on 18 September 2025 (awaiting a decision from the European Commission at the time of writing), thereby limiting the diffusion of this technology. In summary, 15 NRSIs reported on the effectiveness of passive immunisation with nirsevimab among infants aged 12 months and younger. Based on these data, there is moderate certainty evidence that nirsevimab is effective against RSV-related ICU

admission and LRTI. Observational data pooled from four studies estimated that nirsevimab is associated with a 73% reduction in RSV-related ICU admissions. Similarly, based on pooled data from two observational studies, it was associated with an 87% reduction in LRTI.

Based on pooled data from nine studies, nirsevimab was associated with an 87% reduction in RSV-related hospitalisations although the certainty of this evidence was judged to be low. For those patients that were admitted to hospital, no difference was found in the mean length of hospital stay between the immunised and control arms based on three studies.

The findings from the HIQA review broadly align with those reported in the original review by Sumsuzzman et al. in terms of the protective effect of nirsevimab against hospitalisation, ICU admission and LRTI incidence. However, variations were observed in the effectiveness estimates across these outcomes. These discrepancies were likely due to differences in the number of studies included in the pooled analyses, as well as differences in the effect sizes among the pooled studies. Preprints and studies using rapid antigen tests for RSV diagnosis were excluded from the focused analysis undertaken by HIQA. Additionally, a study based on birth cohort was excluded from the pooled analysis undertaken by HIQA as it was not seen to be appropriate to combine these data with the data from hospitalised patients; this may have further contributed to the observed differences.

While the findings of the observational studies were broadly consistent with the RCT data, that is, of a protective effect of nirsevimab, particularly against severe disease, comparisons were challenging due to differences in the endpoint definitions. For example, observational studies included in this review reported on total RSV-related LRTI cases and RSV-related hospitalisations, whereas the RCTs reported on MA LRTI and LRTI requiring hospitalisation. Data regarding RSV-related ICU admissions were only available from one RCT, which reported no events among nirsevimab recipients (n=969) and five events among the control group (n=484). This corresponded to an efficacy estimate of 96% (95% CI: 19% to 100%). Due to the low case numbers, the reliability of this estimate is uncertain, and is likely not suitable for direct comparison with the effectiveness estimate derived from the observational studies.

Safety of EHL-mAbs in infants

All four included RCTs reported on the incidence of any adverse events. No trial reported a significant difference in adverse events between the placebo/standard care and the nirsevimab groups, with point estimates around 1.00. In terms of AEs which were related to the intervention, they were of low incidence and were reported to be of low grade in terms of severity. For the placebo-controlled, blinded studies (Griffin et al., the MELODY RCT, and the CLEVER RCT), the incidence was

not found to be significantly different in the nirsevimab group compared with placebo. In the HARMONIE RCT, no AEs were considered related to the intervention in the standard care group; however, this may be due to the open-label design of this study.

No difference in the incidence of SAEs in the trials was reported. All four RCTs reported whether the SAEs were related to the intervention, with only two participants (out of 8,380) judged to have had an SAE which was related to EHL-mAbs, while one participant (out of 6,190) had an SAE related to placebo.

Recent post-marketing surveillance data support the overall safety of nirsevimab administration. In Ireland, the HPRA reported fewer than five ADR reports associated with nirsevimab up to 11 February 2025, all related to injection site redness. In Spain, there was an overall notification rate of 23 cases per 100,000 doses based on spontaneous notification data covering the 2024-25 RSV season;[269] however, it is noted that it is not possible to determine causality from these data. The study authors concluded the overall safety notification data were reassuring and support continued nirsevimab use, but highlighted the need for continued monitoring and vigilance due to the frequency of suspected severe events.

Quality of the included studies

The updated HIQA review on EHL-mAbs was based on the systematic review conducted by Sevendal et al. The quality of this review was assessed by the HIQA evaluation team using the AMSTAR 2 tool and was rated as critically low quality but was selected for updating due to the recency of the search and relevance of the population, intervention, comparator and outcomes to this HTA. Key weaknesses included insufficient justification for chosen study design or publication restrictions, absence of an appropriate risk of bias assessment tool and failure to report funding sources for the included studies. Risk of bias assessments were conducted by the HIQA evaluation team for the four RCTs included in this updated review, focusing on both efficacy and safety outcomes. No study was identified as having a high overall risk of bias. Three studies were considered low risk of bias across both efficacy and safety outcomes, while one study was assessed as having 'some concerns' for both efficacy and safety outcomes.

Observational studies reporting on the effectiveness of nirsevimab were identified from the systematic review by Sumsuzzman et al., the authors of which assessed the quality of the included studies using the JBI Critical Appraisal Checklist for Observational Studies. Of the 15 studies included in the HIQA reporting of this review, 14 were assessed to be at low risk of bias, while one study was assessed to be at moderate risk of bias.

Unpublished studies and ongoing studies

Two additional publications reporting on completed Phase III, double-blind RCTs (the MEDLEY[282, 283] and CLEVER trials[284]) were identified during the screening phase of HIQA's systematic review of efficacy and safety of EHL-mAbs. These trials were not included as the results of these studies were only available on a trial registry or as a letter to the editor at the time of undertaking this review. Both RCTs included infants at increased risk of severe RSV disease and followed them up for two RSV seasons. On 17 September 2025, the results of the phase IIb-III CLEVER trial were published and subsequently incorporated into this HTA as a post-hoc update.[236]

The MEDLEY trial, which enrolled 925 infants prior to the 2019 and 2020 RSV seasons across 126 sites in 25 countries in both the northern and southern hemispheres, compared nirsevimab with palivizumab.[282] According to the results listed on clinicaltrials.gov, the incidence of MA LRTI and hospitalisation due to RSV through 150 days were similar across the two arms of the study (0.6% versus 1% for MA LRTI; 0.3% versus 0.6% for hospitalisation, in the nirsevimab and palivizumab groups, respectively). Per the results published in a letter to the editor, similar rates of AEs, treatment-related AEs, SAEs, treatment-related SAEs and AESIs through 360 days were reported across the arms of the study. No treatment-related deaths were reported in either arm of the study.

A further two trials were identified during the screening phase of HIQA's systematic review of efficacy and safety of EHL-mAbs.[228, 232] Both were Phase Ib/IIa double-blind RCTs, one investigated the effects of nirsevimab versus placebo (Domachowske et al. 2018)[232], while the other compared clesrovimab with placebo (Madhi et al. 2025)[228]. These trials were not included as both studies included EHL-mAb doses which were lower than the authorised dose (nirsevimab) or the dose included as part of the authorisation application (clesrovimab), limiting their generalisability. Both RCTs included healthy infants aged 12 months of age or younger; Domachowske et al. included preterm infants only,[232] while Madhi et al. included both preterm and term infants.[228]

The search of the trial registries as part of this review also identified two ongoing double-blind RCTs (the CHIMES[285] and SMART trials[286]). CHIMES is a Phase III trial involving healthy preterm and term infants, comparing nirsevimab with placebo and is due to complete in the winter of 2025. SMART is a Phase III trial involving infants and children at increased risk for severe RSV disease, comparing clesrovimab with palivizumab, and is due to complete in the summer of 2025.

Strengths and limitations

The systematic review by Sevendal et al. provided a comprehensive review of the literature that identified studies evaluating RSV-specific mAbs and antiviral therapies in human clinical trials between 2000 and 2023. This update expanded on the review by Sevendal et al. by including three additional publications related to nirsevimab, reflecting the latest available evidence up to 23 April 2025. While this update had a narrowed scope with a focus on RSV-specific EHL-mAbs in infants, a key strength is its rigorous and methodologically robust approach, employing a rigorous search strategy, dual and independent screening, double data extraction, using the ROB-2 standardised quality appraisal tool, and GRADE assessments to ensure reliability and minimise bias. However, the review is limited by the small number of eligible studies available; only three completed RCTs met the inclusion criteria for the update, which reduces statistical power for robust conclusions.

As noted, while the findings of the observational studies were broadly consistent with the RCT data, that is, of a protective effect of nirsevimab, particularly against severe disease, comparisons were challenging due to differences in the endpoint definitions. As with the data relating to the RSV vaccines, the included studies were not designed to estimate the protective effect of the EHL-mAbs against mild RSV illness as laboratory confirmation typically requires patients to seek medical care.

The RCT data for nirsevimab and clesrovimab predominantly relate to a number of RSV seasons (some of which may have been impacted by the COVID-19 pandemic when there was extensive use of non-pharmacological interventions to limit the spread of SARS-CoV-2), while the available observational data relate to the 2023/2024 RSV season. Following the COVID-19 pandemic, an increased intensity was observed in seasonal RSV outbreaks internationally, possibly influenced by immune depletion due to previously reduced RSV circulation. Given the potential for distinct seasonality with RSV and differences in disease severity, along with potential for nirsevimab resistance, additional studies will be required to determine if the reported efficacy and effectiveness estimates are applicable across seasons. There was no evidence of multi-season protection or increased RSV-associated disease severity in a second season after administration in the RCTs for these EHL-mAbs. Recent observational data suggest that nirsevimab may result in a lower incidence of severe RSV-related outcomes in hospital settings in a second season after administration, with no indication of increased severity in the second season.[287]

4.8 Conclusion

Based on clinical trial data from three RCTs and real world evidence from three observational studies, there is evidence to indicate that the currently authorised RSV prefusion vaccines reduce the risk of RSV-related LRTD and ARI in older adults. For two vaccines (RSVPreF3 and RSVpreF), there is evidence from a single RCT for each

to support the duration of protection over a second RSV season and in the case of one vaccine (RSVPreF3), a third season. However, in season data provide evidence of waning immunity over time. In terms of reactogenicity and safety outcomes in older adults, RCT data indicate that adverse events were mostly mild-to-moderate, while severe or related SAEs are rare. Post-marketing surveillance studies evaluating the safety of vaccination with RSVPreF3 or RSVpreF suggest a small potential increase in GBS cases with vaccination, although these events remain rare.

Based on clinical trial data from a single RCT and one observational study, there is evidence that the currently authorised maternal vaccine may reduce the risk of RSV-related hospitalisation in newborns and infants up to six months of age. Additionally, based on data from the single RCT, there is evidence that the currently authorised maternal vaccine may reduce the risk of RSV-related LRTD, severe RSV-related LRTD, and RSV-related LRTD requiring oxygen support in newborns and infants up to six months of age. The evidence indicates that this vaccine is safe for pregnant women and their infants, as severe reactions or related SAEs were rare.

Clinical trial data from four RCTs, indicate that the authorised EHL-mAbs, nirsevimab and clesrovimab, reduce the risk of MA RSV-associated LRTI, hospitalisation with RSV-associated LRTI and the severity of RSV-associated LRTI over one RSV season. While local and systemic events were common, these were mostly mild-to-moderate in severity with no indication from these RCTs of safety concerns up to one year after randomisation or dosing. Based on data from observational studies on nirsevimab, there is evidence that nirsevimab possibly reduces RSV-related LRTI and ICU admission. At the time of writing, there were no published observational studies which met the inclusion criteria for this review, on the effectiveness or safety of clesrovimab for the prevention of RSV and associated complications.

In summary, there is consistent evidence that all currently authorised RSV immunisation products are safe and effective for the prevention of RSV and associated complications, over one season. While local and systemic events are common, these are mostly mild-to-moderate in severity; SAEs are rare. For older adults, there is evidence of waning immunity over time, with current data limited to a maximum of three years' follow-up. The potential harms that are associated with immunisation must be considered in the context of the potential for clinical benefit within that population.

5 Review of methodology for economic modelling studies of RSV immunisation strategies

Key points

- The most recent systematic review of economic modelling studies of RSV immunisation strategies with a focus on modelling inputs was published in 2021, based on a literature search conducted up to 2020. However, it did not include studies relating to the newly authorised forms of RSV vaccination or extended half-life monoclonal antibodies (EHL-mAbs).
- To establish and assess the most up-to-date international evidence on the approaches taken to the economic modelling of immunisation strategies, a rapid review of studies published since 2020 was undertaken with 16 studies identified.
- Ten studies reported funding from various non-industry funding sources such as government agencies, research bodies and or charitable foundations. Three studies received EU funding, two of which also received funding from industry. The remaining three studies were solely industry-funded.
- Thirteen of the 16 included studies employed a static modelling approach, while two used dynamic transmission models. One study presented a model comparison of three static models and two dynamic transmission models. The time horizon varied across the studies ranging from one RSV season to 10 years with some studies including longer time horizons for long-term outcomes or in secondary analyses. Models that included death as one of the health states used a lifetime analytical horizon to account for costs and consequences of premature deaths within the followed timeframe.
- Seven studies conducted their analysis from a healthcare perspective, a further two studies adopted a societal perspective, while the remaining seven studies adopted a dual perspective (considering both the healthcare and societal perspective) in the base-case analysis.
- While the overall appraisal did not raise major concerns about the quality of included studies, there were some concerns with regard to inconsistency in the inclusion of the health states; transparency of structural assumptions and data identification; and the description of model validation in a minority of studies.
- This rapid review identified several notable modelling features for consideration when developing an economic model of immunisation of young children and

adults, all of which will be considered in the development of a de novo economic model for Ireland.

- While included studies found immunisation of infants and adults to be cost effective, this was typically sensitive to the assumed unit price (or price per dose delivered) of the interventions and was frequently at significant reductions relative to their list price. Moreover, for infants, the optimal strategy (maternal vaccination or EHL-mAB) was sensitive to their relative prices.

5.1 Introduction

This chapter describes a review of published international economic evaluations of RSV immunisation strategies. The review specifically examines the approaches taken to modelling the expected costs and benefits of RSV immunisation in young children less than two years and adults aged 65 years and older. The purpose of this review is to inform the development of a de novo economic model to assess the cost effectiveness of RSV immunisation strategies in young children and adults in Ireland (Chapter 6).

5.2 Background

A total of 13 different considerations for modelling economic evaluations of immunisation strategies were used as guidance for this review.[288] These considerations include:

- model selection
- time horizon of models
- natural disease history
- measures of vaccine-induced protection
- duration of vaccine-induced protection
- indirect effects
- target population
- model calibration and validation
- handling uncertainty
- discounting
- health-related quality of life
- cost components
- perspective adopted.

A scoping exercise was undertaken by the evaluation team to identify published systematic reviews of economic evaluations of RSV immunisation that provide detail on the economic models employed and the model input parameters. A relevant

systematic review was identified that assessed the cost effectiveness of RSV immunisation in young children and adults aged 65 years and older and which provided data on the type of model employed, model input parameters, vaccine characteristics and economic results.[289] The review was published in 2021 and contained searches up until October 2020, prior to the authorisation of any RSV vaccinations or extended half-life monoclonal antibody interventions. Therefore, a rapid review was conducted by the evaluation team to identify economic evaluations of RSV immunisation that have been published since 2020 (to cover the last search date for the most recent systematic review) up to 10 September 2024.

5.3 Rapid review methods

5.3.1 Research question

Research question: What approaches have been used to model the expected costs and benefits of RSV immunisation in young children and those aged 65 years and older?

The Population, Interest, Context (PICo) framework that was developed to address the above research question is outlined in Table 5.1.

Table 5.1 PICo for a rapid review of methodology for respiratory syncytial virus (RSV) immunisation economic modelling studies

Population	Young children and or adults in the general population being immunised against RSV.
Interest	Approaches to modelling the expected costs and benefits of RSV immunisation in children and or adults, including, but not limited to: ▪ Model structure – type of model – perspective adopted – time horizon – discount rate for costs and outcomes – age at immunisation – dosing schedule – immunisation type (that is, vaccine and or monoclonal antibody) – comparator – waning immunity. ▪ Model input parameters – immunisation efficacy and or effectiveness – immunisation coverage – direct and indirect costs – direct and indirect benefits – utility values for cost-utility analysis. ▪ Model outputs

	– economic model results that include a ratio of (incremental) costs to (incremental) benefits or net monetary benefit (NMB) – epidemiological model outputs used in a related economic model.
Context	RSV immunisation in high-income countries (as defined by the OECD)[+]

Key: OECD - Organisation for Economic Cooperation and Development; RSV – respiratory syncytial virus.
Note: [+]OECD: WDI - The World by Income and Region (worldbank.org)

5.3.2 Eligibility criteria

The following studies were eligible for inclusion: economic modelling studies of RSV immunisation in children and those aged 65 years and older in high-income countries that describe the approach to modelling, provide detail on the model structure and model input parameters, include both costs and outcomes in the analysis and report a ratio of (incremental) costs to (incremental) benefits.

5.3.3 Search strategy

A comprehensive electronic search was conducted in MEDLINE Complete via EBSCOhost, Embase via Ovid, CINAHL via EBSCOhost, The Cochrane Library and INAHTA database from 22 October 2020 to 10 September 2024. The electronic search strategy was developed by a librarian and peer reviewed by a second independent librarian using the Peer Review of Electronic Search Strategies (PRESS) checklist.[290] A forward citation search was undertaken in Google Scholar of the most recent systematic review.[289] No language restrictions were applied. The database search strings, dates of searches and search results are provided in Appendix A5.1 and are also available on Zenodo.[291]

5.3.4 Study selection and data management

Results were exported to Covidence software and screened by three reviewers for relevance.[292] The full texts of potentially eligible articles were retrieved and independently assessed for eligibility by two reviewers according to the pre-specified inclusion and exclusion criteria outlined in Table 5.2 and Section 5.3.2. Any uncertainty with screening or inclusions was resolved through discussion or, if necessary, involvement of a third reviewer.

5.3.5 Data extraction and quality appraisal

Table 5.2 details the data that were extracted for each included study. Data extraction for each study was conducted by one reviewer using a standardised, pre-piloted electronic data extraction form and checked by a second reviewer. A critical appraisal of all included studies was undertaken using the framework proposed by Philips et al. for the quality assessment of decision-analytic models.[293] The

framework assesses the quality of models under three key themes, *Structure, Data and Consistency*. Quality appraisal was conducted by two reviewers and checked by a third. Disagreements in data extraction and quality appraisal were resolved through discussion. All incremental cost-effectiveness ratio (ICER) values were extracted as reported by the study authors at time of publication, with no adjustments made for inflation, and no currency conversions carried out.

Table 5.2 Data extracted from each included study, where available

General study characteristics	Author name Year of publication DOI
	Region or country
	Type of economic evaluation
	Population
	Funding
Model characteristics	Model type
	Perspective
	Time horizon
	Comparator
	Discount rates
	Sensitivity analysis
Intervention	Type of immunisation
	Dosing schedule
	Strategies
	Age at immunisation
	Coverage rate
Model input parameters	Efficacy/effectiveness
	Waning
	Costs included - direct and indirect
	Effects included - direct and indirect
Economic results	Type of summary ratio
	Overall payer perspective result
	Overall societal perspective result
Epidemiological results	Overall epidemiological result
Authors conclusions	Overall study conclusion

Key: DOI – digital object identifier.

5.3.6 Data synthesis

Summary characteristics of included studies in addition to the immunisation interventions and strategies considered in the models are presented in table format. The reporting of this review adheres to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 criteria.[210]

5.4 Results

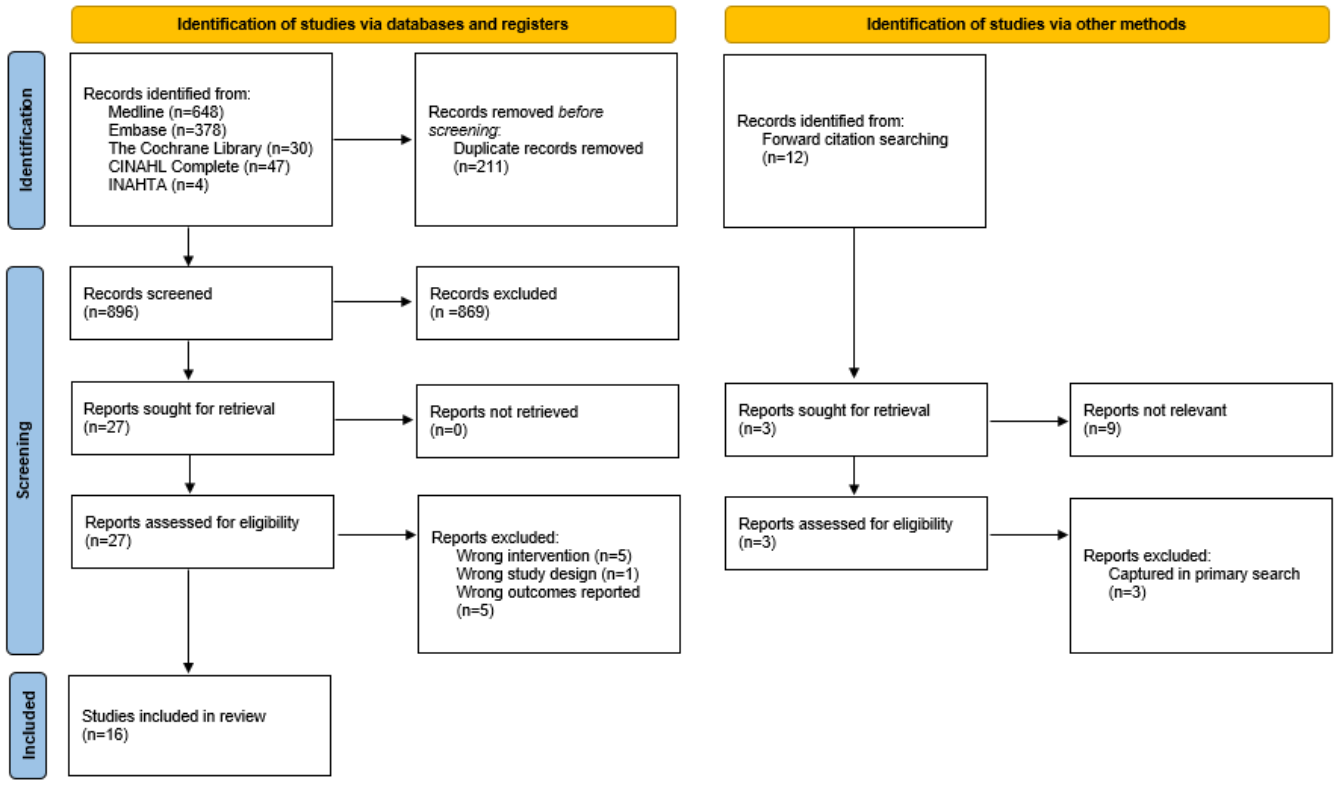
A total of 1,107 articles were identified in the database searches. Following the removal of duplicates, 211 articles remained. Three eligible articles identified through forward citation searching were captured in the primary database searches. All articles were screened by title and abstract; after exclusions, a total of 27 articles remained for full-text review. Following full-text review and subsequent exclusion, 16 studies were included (Figure 5.1). Full data extraction tables for included studies are provided in Appendix A5.2 and A5.3.

5.4.1 Characteristics of included studies

A total of 16 model-based studies published since 2020 met the inclusion criteria for this rapid review. Of these, one was published in 2021,[294] two were published in 2022,[295, 296] five were published in 2023,[297-301] and eight were published in 2024.[302-309] Seven studies were conducted for European countries, four of which included multiple countries or regions in their analysis. Of these four multi-region studies, two included England and Wales,[296, 304] one included Denmark, England, Scotland, Finland, Italy and the Netherlands,[298] and one was conducted using model input parameters from Norway, the United Kingdom and the Netherlands.[297] The remaining three European studies were conducted from a single country perspective, with one each in the United Kingdom,[307] Norway,[295] and Spain.[302] Of the nine studies conducted outside of Europe, five were conducted for Canada,[294, 299, 303, 308, 309] two for the United States,[300, 305] and one each for Japan[306] and Hong Kong.[301] An overview of general study characteristics and information on the model structure for included studies is provided in Table 5.3 and Table 5.4.

All studies conducted a cost-utility analysis (CUA) using quality-adjusted life year (QALY) health effects. Six of the 16 studies explicitly reported funding from various non-industry funding sources such as government agencies, research bodies and or charitable foundations. Two of these six studies were from Canada,[294, 309] two from England and Wales,[296, 305] one from the USA,[305] and one from Hong Kong.[301] One multi-centre study received EU funding alone.[297] Two studies received joint funding from the EU and industry, one of which was a multi-centre study[298] and one was based in Norway.[295] Three of the 16 included studies were industry-funded: one each from Spain,[302] the United Kingdom[307] and Japan.[306] Four studies (three from Canada[299, 303, 308] and one from the USA)[300] did not explicitly state funding sources, but financial supports for individual authors were acknowledged.

Figure 5.1 PRISMA flow diagram of included studies



Source: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71. For more information, visit: http://www.prisma-statement.org/

Table 5.3 General study characteristics of included studies in infants

Study Year	Country / Region	Model type	Time horizon	Type of economic evaluation	Perspective	% Discount rate (costs/health effects)	Funding source
Alvarez Aldean J[302] 2024	Spain	Static cohort model with a Markov-type process	1 RSV season Lifetime (premature RSV-deaths)	CUA	Healthcare system	3.0/ 3.0	Industry
Gebretekle[303] 2024	Canada	Static cohort model	1 year Lifetime (costs and consequences for long-term outcomes)	CUA	1. Healthcare system 2. Societal	1.5/ 1.5	Not reported>
Getaneh[298] 2023	Europe	Static cohort model	5 years	CUA	1. Healthcare system 2. Societal (Partial)	3.5/ 3.5¥ 3/ 3 4%/1.5	European Union~ and industry
Hodgson[296] 2022	England and Wales	Dynamic transmission model	10 years	CUA	Healthcare system	3.5/ 3.5	Government, research body and charitable foundation
Hodgson D[304] 2024	England and Wales	Dynamic transmission model	10 years	CUA	Healthcare system	3.5/ 3.5	Government, research body and charitable foundation
Ishiwada[306] 2024	Japan	Static Markov model with decision tree	11 months and lifetime horizon (premature RSV-related deaths only)	CUA	1. Healthcare system 2. Societal	2.0/ 2.0	Industry
Kieffer A[307] 2024	United Kingdom	Static decision-analytic model	1 RSV season 3 years (recurrent wheezing) Lifetime (premature RSV-deaths)	CUA	Healthcare system	3.5/ 3.5*	Industry
Li X[295] 2022	Norway	Static cohort model with decision tree	5 years (base case) and 13 years (scenario analysis of recurrent wheezing and asthma)	CUA	Healthcare system	4.0/ 4.0	European Union+ and industry

Study Year	Country / Region	Model type	Time horizon	Type of economic evaluation	Perspective	% Discount rate (costs/health effects)	Funding source
Li X[297] 2023	Europe	Static (n=3): Multi-cohort stochastic decision tree, deterministic decision tree and multi-cohort deterministic Markov model Dynamic (n=2): Deterministic compartmental transmission models	1 year (static models) and 10 years (dynamic models)	CUA	1. Healthcare system 2. Societal	3.0/ 3.0	European Union⁺ and industry
Nourbaksh[294] 2021	Canada	Static discrete event simulation model	1 year	CUA	Healthcare system	N/A^	Government and research body
Shoukat A[299] 2023	Canada	Static discrete event simulation model	1 year	CUA	1. Healthcare system 2. Societal	1.5/ 1.5	Not reported>

Key: CUA - cost-utility analysis; N/A – not applicable; QALY – quality-adjusted life year; RSV - respiratory syncytial virus.
Note: *Risk of recurrent wheezing, and associated management cost, discounted at 3.5% per annum for 2 years. Not stated otherwise. ⁺EU Horizon 2020 and European Foundation of Pharmaceutical Industries and Associations. ^No discount rate was applied. ~RSV Consortium in Europe funded through European Union's Horizon 2020 and the European Federation of Pharmaceutical Industries and Associations. ¥3.5%/3.5% for Denmark, England and Scotland, 3%/3% for Finland and Italy and 4%/1.5% for The Netherlands. >Funding source not stated but financial support for individual authors acknowledged.

Table 5.4 General study characteristics of included studies in older adults

Study Year	Country / Region	Model type	Time horizon	Type of economic evaluation	Perspective	% Discount rate (costs/health effects)	Funding source
Hutton[305] 2024	USA	Static decision-analytic simulation model	2 years and lifetime for RSV-related death	CUA	Societal	3.0/ 3.0	Government
Moghadas[300] 2023	USA	Static discrete event simulation model with decision tree	Primary analysis: 1 RSV season Secondary analysis: 2 RSV seasons	CUA	Societal	3.0/ 3.0	Not reported[>]
Shoukat[308] 2024	Canada	Static discrete event simulation model with decision tree	2 RSV seasons	CUA	1. Healthcare system 2. Societal	1.5/ 1.5	Not reported[>]
Tuite[309] 2024	Canada	Static individual-based model	3 years and lifetime for RSV-related death	CUA	1. Healthcare system 2. Societal	1.5/ 1.5	Government
Wang[301] 2023	Hong Kong	Static decision-analytic model with decision tree	2 years	CUA	Healthcare system	3.0/ 3.0	Academia

Key: CUA - cost-utility analysis; RSV - respiratory syncytial virus.
Note: [>]Funding source not stated but financial support for individual authors acknowledged.

5.4.2 Model characteristics of included studies

Model

Thirteen of the 16 included studies employed a static modelling approach,[294, 295, 298-303, 305-309] while two used dynamic transmission models.[296, 304] One study presented a model comparison of three static models and two dynamic transmission models.[297] Of note, two of the static models included in the model comparison study[297] were the same as those used by the Li et al. 2022[295], Kieffer et al. 2024[307] and Getaneh et al. 2023 studies,[298] while one of the dynamic transmission models employed in the model comparison study was the same as that used in the Hodgson et al. 2022[296] and Hodgson et al. 2024 studies.[304]

Across the studies that employed a static modelling approach, 12 unique models were identified of which two were a discrete event simulation model,[294, 299] four were a Markov model,[297, 299, 302, 303] three were a decision tree model,[295, 297, 301] two were a discrete event simulation model with a decision tree[300, 308] and one was a Markov model with a decision tree.[306] Where studies did not clearly indicate the model type,[298, 303, 305, 307, 309] the included diagrammatic representations were used for categorisation which suggested that three were decision tree models[298, 305] and two were Markov models.[303, 309] Among the five Markov models, three applied a monthly cycle length,[297, 302, 309] while the cycle length was not clearly stated for the remaining two models.[303, 306]

An overview of the model characteristics of the included studies is provided in Table 5.5 and Table 5.6.

Irrespective of model type, the economic evaluations included some or all of the following health states:

- symptomatic RSV infection
- primary care visit
- outpatient care
- emergency department (ED) visit
- hospitalisation
- admission to intensive care unit (ICU)
- death.

For the 11 studies in the infant population, two considered longer-term complications of RSV infection such a wheezing or asthma.[295, 307] Adverse events from the intervention were not considered in the infant studies. Of the five included older adult population studies, two specifically considered the requirement for mechanical ventilation in their models,[300, 308] and one considered adverse events after vaccination.[301]

Time horizon

The time horizon varied across studies, with some studies including longer time horizons for long-term outcomes or in secondary analyses. The most frequently adopted time horizon was up to one year (or one RSV season), which was used by eight studies.[294, 297, 299, 300, 302, 303, 306, 307] Four studies adopted a two-year (or two RSV seasons) time horizon[300, 301, 305, 308] (one of which including it as a secondary analysis)[300]; one a three-year (or three RSV seasons) time horizon;[309] two a five-year time horizon;[295, 298] and three studies reporting on the two dynamic transmission models adopted a 10-year time horizon.[296, 297, 304] Six of the 16 studies adopted a lifetime analytical horizon for RSV-related mortality outcomes.[302, 303, 305-307, 309] In addition, two studies included separate time horizons for the outcome recurrent wheezing, reported as three years in one study,[307] and as a scenario analysis with a 13 year time horizon in the other study.[295]

Perspective

Seven of the 16 studies conducted the analysis from the perspective of the payer only, where the payer could represent the tax payer, healthcare payer, or the healthcare system.[294-296, 301, 302, 304, 307] Two studies conducted the analysis from the societal perspective only.[300, 305] Seven studies conducted the analysis from both the payer and societal perspectives.[297-299, 303, 306, 308, 309]

Discount rates

The same discount rates were applied for both costs and outcomes in 14 of the 15 studies in which discounting was noted. Differential discounting was applied in one study (the Netherlands), with discount rates of 4% and 1.5% for costs and outcomes, respectively.[298] One study from Canada, with a one-year time horizon, did not apply discounting to costs or outcomes.[294] Discount rates ranged from 1.5% for Canada; [299, 303, 308, 309] 2% for Japan;[306] 3% for Spain,[302] Finland and Italy,[298] USA,[300, 305] Hong Kong,[301] and the European cohort in the model comparison study;[297] 3.5% for Denmark,[298] England,[296, 298, 304] Scotland[298] and Wales;[296, 304] and separately for the United Kingdom;[307] and 4% for Norway.[295] Hyperbolic discounting was not applied in any of the included studies.

5.4.3 Intervention and immunisation strategies

A number of different immunisation strategies were assessed across the 16 included studies, as summarised in Table 5.5 and Table 5.6.

Strategies for the immunisation of infants

Intervention and comparator

For this review, the eligibility criteria for interventions were restricted to those that are currently authorised by the EMA or HPRA. Specifically, these included the passive immunisation of infants in the general population through the extended half-life monoclonal antibody, nirsevimab, or via maternal vaccination with RSVpreF. This review did not identify any study evaluating clesrovimab as an intervention. Included also was the short-acting monoclonal antibody, palivizumab, which is indicated for the passive immunisation of infants up to two years of age at high risk of severe disease. Studies that only considered non-authorised interventions were excluded from the review, while data extraction was limited to the authorised interventions in studies that included more than one alternative.[294, 295, 297, 298] For clarity, studies that included both the monoclonal antibody (either palivizumab or nirsevimab), and a maternal vaccine as intervention were categorised as studies with a combination strategy.

There were 11 studies that assessed strategies for the passive immunisation of infants against RSV. Seven studies considered multiple strategies that included maternal vaccination, nirsevimab administration, or a combination strategy;[294, 295, 297-299, 303, 304] however, only three of these seven included the authorised maternal vaccine, RSVpreF, in their base case.[299, 303, 304] Two studies reported only on strategies that included nirsevimab.[296, 307] Two studies included maternal vaccination, either alone,[302] or alongside palivizumab.[306] The choice of comparator in these studies was no intervention,[294, 295, 297-299, 302] palivizumab,[296, 303, 304, 306, 307] and or a comparison against alternative strategies.[294, 295, 298, 303]

Timing of administration

Overall, the studies considered a variety of approaches to the immunisation of infants against RSV, including year-round,[295-299, 302-304, 306] seasonal[295-298, 303, 304] and or seasonal with catch-up strategies.[294-299, 303, 304, 307] Multiple approaches were also considered within individual studies. Nine of 11 infant population studies considered a year-round immunisation strategy[295-299, 302-304, 306] of which six studies assessed nirsevimab,[295-298, 303, 304] five assessed maternal vaccination,[295, 299, 302-304, 306] one considered strategies combining maternal vaccination and palivizumab, and two assessed a programme based on a combination strategy (maternal vaccination plus nirsevimab).[299, 303] Six of 11 studies considered seasonal immunisation strategies of which five considered nirsevimab only,[295-298, 303, 304] and one study included maternal vaccination with palivizumab.[304] Nine studies examined seasonal with catch-up strategies for nirsevimab.[294-299, 303, 304, 307]

Of the nine studies assessing the cost effectiveness of nirsevimab,[294-299, 303, 304, 307] eight considered administration as a single dose at birth for the seasonal and year-round strategies; one study considered a single dose administered up to two months

after birth.[294] For the general population of infants who received nirsevimab as part of a catch-up programme, it was typically offered to infants aged one to six months at the start of RSV season,[295, 297-299, 303, 304] although one study included infants up to seven months old[296] and two studies included catch-up for infants at either eight, 12 or 16 weeks old (to coincide with the existing National Immunisation Programme immunisation appointments in England).[296, 307] Additionally, four studies specified catch-up administration of nirsevimab for infants at increased risk of RSV-related disease.[294, 299, 303, 310] Among these studies, the age of the cohort eligible for catch-up with nirsevimab varied. One study noted that infants considered at moderate and high risk that were born from June to October would be eligible for catch-up administration in November.[303] In one study, infants born preterm aged up to five months old and infants with chronic illness aged up to 12 months old were eligible.[294] One study had a catch-up for infants at increased risk of RSV-related disease up to six months old at the start of the RSV season.[303] One study stated catch-up for high-risk infants followed national guidelines for palivizumab-eligible infants, with varying eligibility depending on the underlying condition.[307]

Within the five studies assessing the cost effectiveness of the maternal vaccines, the specific window of administration differed across the studies. One study administered a single dose of the vaccine during the third trimester of pregnancy[299] while four studies administered a single dose of the vaccine during a window that spanned the late second trimester (from 24 wGA) and third trimester of pregnancy.[302-304, 306]

Irrespective of whether included as an intervention or as a comparator, palivizumab was administered during the RSV season once per month, up to five doses in all except one study from Japan,[306] in which it was administered up to six times during the RSV season as part of a combination strategy alongside maternal vaccination.

Immunisation coverage

Assumed immunisation coverage varied considerably across the included studies. The immunisation coverage of nirsevimab was assumed to range from 71% to 100% across eight studies,[295-299, 303, 304, 307] while one study did not report coverage rates.[294] Four studies provided the basis for the nirsevimab coverage estimate,[295, 297, 304, 307] while the remaining studies either did not comment or the estimate was based on uncited assumptions or unpublished data.[296, 298, 299, 303] Nirsevimab coverage estimates were based on infant rotavirus vaccine coverage in two studies,[295, 297] vitamin K supplementation coverage at birth in one study,[304] and assumed to be similar to the primary series of vaccinations in infants under five years old in one study.[307]

Maternal vaccine coverage was assumed to range from 60% to 100% across five studies.[299, 302-304, 306] Three of these studies noted that maternal vaccine coverage estimates were based on influenza and or pertussis vaccination uptake among pregnant women.[299, 303, 304] A fourth study employed similar assumptions in their scenario analysis, but assumed 100% coverage in the base case without elaborating further.[299] For one study, the maternal vaccine coverage estimate was informed by COVID-19 vaccine uptake in pregnant women.[306] Four studies provided coverage estimates for palivizumab, which ranged from 46.2% to 95%.[296, 303, 306, 307]

Strategies for the immunisation of older adults

Intervention and comparator

Five studies assessed strategies for the vaccination of older adults against RSV and all included both RSVpreF vaccine (Abrysvo®) and the RSVPreF3 vaccine (Arexvy®).[300, 301, 305, 308, 309] No studies were identified that used the recently licensed mRNA RSV vaccine (mRESVIA®). The choice of comparator in these studies was no vaccination[300, 301, 305, 308, 309] and or a comparison against alternative strategies.[301, 309]

Timing of administration

Three of the five studies specified that vaccination would begin in September.[300, 308, 309] One study followed the timing observed for influenza vaccination, with the model run in August with 0% anticipated vaccine uptake in that month, increasingly monthly thereafter with uptake largely plateauing in January.[305] Information regarding the time of administration was not identified for the remaining study.[301] The vaccine was administered as a single dose in each of the five studies.

Population

Four studies included adults aged ≥60 years[300, 301, 305, 308] and one study included adults aged ≥65 years.[305] One study included setting-specific strategies, which comprised vaccinating residents of long-term care homes and community-dwelling adults.[308] Age-stratified vaccine eligibility was considered in one study for adults aged ≥60, ≥65, ≥70, ≥75, and ≥80 years. This study also stratified groups by the presence of at least one chronic medical condition.[309].

Immunisation coverage

Vaccination coverage varied across the included studies, ranging from 20% to 100% across the five studies.**[300, 301, 305, 308, 309]** In four of the studies, coverage estimates were based on influenza seasonal vaccine uptake, while one study assumed a limited uptake of newly recommended vaccines. The assumed time taken to achieve

vaccination coverage was stated in four studies. In two studies coverage was achieved within two months of model entry[300, 309] while another study assumed five months to match the timing of influenza vaccination.[305] In one study the time taken to achieve coverage differed by setting, assumed as four weeks for residents of long-term care homes and eight weeks for community-dwelling adults.[308]

5.4.4 Intervention characteristics

The 16 included studies used parameter values obtained from published randomised controlled trials (RCTs) for their intervention efficacy estimates. For nirsevimab, these included the phase 2b and MELODY trials;[233, 234] a pooled analysis of these two trials and the MEDLEY study;[282, 311] the HARMONIE study.[230] For the maternal vaccine, the MATISSE trial was cited.[225] In addition, one study from Japan noted that modelled efficacy values by term status were informed by a conference abstract of an observational sero-epidemiology study of RSV antibody transplacental transfer in naturally infected individuals.[312]

In terms of adult immunisation, for RSVpreF (Abrysvo®) the RENOIR trial was cited.[222] For RSVPreF3 (Arexvy®) the phase 3 trial[221] was cited, with one study[309] also including the 2024 trial data across two RSV seasons.[224]

Immunisation efficacy for infants

The majority of studies reported separate intervention efficacy parameter values for multiple RSV-associated health outcomes, while two studies reported modelled efficacy parameter values for only medically attended (MA) RSV-related lower respiratory tract infection (LRTI).[296, 304]

The efficacy rates against the outcomes included in the studies are presented in Table 5.5. Each of the nine studies that included nirsevimab assumed it was effective from the day of administration. Studies differed in how efficacy parameter values were modelled, reporting either initial, constant or mean efficacy parameter values over time. Nine studies modelled efficacy parameter values relating to RSV-related LRTI with four describing efficacy values against the outcome RSV-related LRTI in their models,[296, 299, 303, 304] while four referred to efficacy values against primary care visits due to RSV,[295, 297, 298, 307] and one study described RSV outpatient visits.[294] Six of these nine studies modelled constant efficacy over five months,[294, 295, 297, 298, 303, 307] ranging from 47% to 80%. Three studies modelled different mean efficacy over 150 days,[296, 299, 304] ranging from 74.5% to 79.5%. Seven studies modelled nirsevimab efficacy parameters against RSV-related hospitalisation: six studies modelled constant efficacy over 5 months,[294, 295, 297, 298, 303, 307] ranging from 23.5% to 83.2%. One study modelled mean efficacy of nirsevimab against RSV-related hospitalisation over five months of 77.3%.[299]

The lowest efficacy parameter values were reported by Nourbaksh et al., informed by results from a phase 2b RCT in preterm infants.[233]The other studies were additionally informed by results from phase 3 RCTs that included preterm and term infants (MELODY, HARMONIE).[234]

Of the nine studies that modelled nirsevimab efficacy, three used mean efficacy over 150 days after administration.[296, 299, 304] Efficacy was assumed to wane thereafter following a time-varying protection curve of continuous waning in one analysis;[304] via a sigmoidal decay function to 0% by 10 months after administration;[299] and through an exponential loss of protection with a mean duration of protection of 150 days.[296] Five studies modelled constant efficacy estimates for nirsevimab to 150 days after administration, after which efficacy was assumed to be 0%.[294, 295, 298, 303, 307] One study was a model comparison study, in which three static models and one dynamic transmission model assumed constant efficacy over 150 days followed by no protection, and one dynamic transmission model used mean efficacy over 150 days with exponential decline over time.[297] In two studies, efficacy estimates for nirsevimab differed by subpopulation.[294, 307] The first study grouped cohorts as late preterm and term infants (35 weeks' gestational age (wGA) or greater), preterm infants (between 29 wGA and less than 35 wGA) and palivizumab-eligible infants (born less than 29 wGA or having chronic lung disease or congenital heart disease).[307] The second study grouped infants as healthy term infants aged up to two months, chronically ill infants aged less than one year, and preterm infants (no cut-off specified) aged up to five months.[294]

Each of the five studies that modelled maternal vaccination strategies considered year-round maternal vaccination, while one additionally considered seasonal maternal vaccination as a potential strategy. The studies differed in their approaches to modelling efficacy parameters (Table 5.5). Two studies specifically considered vaccine efficacy by infant term status and assumed low vaccine efficacy among preterm and or late preterm infants compared with full term (≥37 wGA at birth) infants.[302, 306] The same two studies assumed that vaccine efficacy would be 0% among infants born less than two weeks after administration of the maternal vaccine, irrespective of term status at birth.[302, 306] Four studies modelled efficacy parameters against multiple health outcomes,[299, 302-304, 306] while one study considered only MA RSV-related LRTI.[304] Each of the studies modelled efficacy parameter values against MA RSV-LRTI: three described this specifically as MA RSV-LRTI; one study described this as RSV related primary care outcomes; and one study described this as RSV related outpatient visits. Two reported initial efficacy ranging from 47.6% to 62%;[302, 306] two studies described mean efficacy over 90 days after birth ranging from 57.1% to 58.3%,[299, 304] and one study reported constant efficacy over 180 days after birth of 52.5%.[303] Four studies modelled maternal vaccine efficacy parameter values against RSV-related hospitalisation: two studies described

initial efficacy values of 88.1%;[302, 306] one study used constant efficacy over 180 days after birth of 56.4%;[303] one study reported mean efficacy over 90 days after birth of 67.9%.[299]

One study referred to initial efficacy with a duration of protection of 180 days after birth, after which immunity waned linearly to 0% by nine months after birth.[306] One study assumed constant efficacy for 150 days after birth, after which efficacy was assumed to be 0%.[303] Two studies described mean efficacy estimates that waned over time, with duration of protection differing between the studies: one study described mean efficacy over 180 days, after which protection waned over time until the proportion protected in the model by 365 days was 0.093;[304] the second study described mean efficacy over 90 days after birth, which declined via a sigmoidal decay function to 0% by 10 months after birth.[299] The fifth study described monthly vaccine efficacy estimates from 0 to 1 month after birth with linear waning to 0% by between 9 to 10 months after birth.[302] Two of the five studies stratified efficacy estimates by infant preterm birth status, grouped as full term or late preterm infants in one study,[302] and in the second study as full term (37wGA or more), preterm (two groups: 26 to 32 wGA; 28 to 31 wGA) and high-risk infants.[306]

Interventions for the immunisation of older adults

The five studies that examined vaccination of older adults against RSV-related disease were largely consistent in their reporting of vaccine efficacy parameters for health outcomes. Each study modelled separate efficacy values for RSVpreF and RSVPreF3, respectively. No information was identified from these studies regarding the time after vaccine administration from which immunity was assumed to be conferred. Three studies used similar approaches and based parameter values on efficacy against RSV-related LRTI for outpatient care (RSVpreF, 65.1%; RSVPreF3, 82.6%) and efficacy against severe RSV LRTD for hospitalisations (RSVpreF, 88.9%; RSVPreF3, 94.1%).[300, 308, 309] Two of these studies reported initial vaccine efficacy,[300, 308] while one described mean efficacy over seven months.[309] The other two studies used the same parameter values based on efficacy against medically attended RSV-related acute respiratory infection ARI (RSVpreF, 65.2%; RSVPreF3, 79.0%) and medically attended RSV-related LRTI (RSVpreF, 84.6; RSVPreF3, 87.5%).[301, 305] One of these two applied different parameter values for outpatient care (medically attended RSV-related ARI) and for hospitalisation and ED encounters (medically attended RSV-related LRTI).[305]

Each of the studies reported vaccine efficacy estimates for both RSVPreF3 and RSVpreF vaccines over a maximum of two years.[300, 301, 305, 308, 309] One study assumed fixed efficacy estimates for season one and season two.[301] Two of the five studies described modelling mean vaccine efficacy estimates, and two modelled

combination approaches to vaccine efficacy (initial, fixed and mean), over an assumed duration of protection, after which efficacy declined to 0%. Assumptions relating to the duration of protection, waning, and modelled efficacy estimates differed between vaccines and across the four studies, as outlined in Table 5.6. Hutton et al. described mean vaccine efficacy estimates for both RSV vaccines for the first seven months after administration, followed by mean efficacy estimates for RSVPreF3 and RSVpreF between 8 to 18 months and 8 to 14 months after administration, respectively.[305] Protection waned linearly between seasons and to 0% by 24 months. Tuite et al. described a similar assumption for vaccine efficacy over two seasons, with linear waning between seasons and 0% efficacy assumed by 24 months in the base case. However, the same duration of protection was assumed for both RSVPreF3 and RSVpreF in this study (0 to 7 months in season one and 12 to 18 months in season 2).[309] The remaining two studies both modelled two different approaches to waning immunity in their model, considering sigmoidal decline in immunity to 0% over 24 months and a linear decline in protection after 18 months to 0% by 24 months after administration.[300, 308] In both studies, one approach used an initial vaccine efficacy for the beginning of season 1, which followed a sigmoidal decline in immunity reflecting a mean vaccine efficacy over 18 months, decline to 0% by 24 months after vaccination. In the second approach, fixed vaccine efficacy was modelled for season 1 (0 to 8 months follow-up) and for season two (12 to 18 months follow up), with a linear decline in immunity between seasons and a linear decline to 0% between 18 to 24 months after vaccination.

Table 5.5 Immunisation strategies and intervention characteristics considered in the models of studies in infants

Study Year	Intervention type Dosing schedule	Comparator	Population	Administration time	Intervention efficacy/ effectiveness	Estimated effectiveness over time/ Duration of protection	Intervention coverage
Álvarez Aldean J[302] 2024	MV (RSVpreF) 1 dose	No vaccination	Pregnant women: 2nd/ 3rd trimester¥	MV: ▪ Year-round	Initial monthly efficacy from 0-<1 month to 9-<10 months. RSV-Primary care/ ED visit ▪ Full term infants: 62.0% Late preterm infants: 51.7% RSV-Hospitalisation ▪ Full term infants: 88.1% ▪ Late preterm infants: 73.4%	Primary care/ ED visit by 5-<6 months: Full term infant: 40.3% Preterm infant: 33.6% Hospitalisation by 5-<6 months: Full term infant: 47.9% Late preterm infant: 39.9% Linear waning to 0% by 9-<10 months after birth	70%
Gebretekle GB[303] 2024	MV (RSVpreF) EHL-mAb (nirsevimab) 1 dose (MV, nirsevimab)	Palivizumab for infants at high-risk Each alternative strategy	Pregnant women: 2nd/ 3rd trimester¥ Infants: Birth / 1-6 months old (catch-up)	MV: ▪ Year-round mAb: ▪ Year-round ▪ Seasonal Seasonal plus catch-up	RSV-LRTI ▪ MV: 52.5% (95% CI: 28.7 to 68.9%) ▪ Nirsevimab: 80% (95% CI: 70 to 87%) RSV-hospitalisation ▪ MV: 56.4% (95% CI: 5.2 to 81.5%) ▪ Nirsevimab: 81% (95% CI: 64 to 90%)	Effectiveness of nirsevimab constant over 5 months after administration, after which assumed 0%. Effectiveness of MV constant over 5 months after birth, after which assumed 0%	MV: 64.8% Nirsevimab: ▪ infants at low/moderate risk: 71% ▪ infants at high risk: 80%

Study Year	Intervention type Dosing schedule	Comparator	Population	Administration time	Intervention efficacy/ effectiveness	Estimated effectiveness over time/ Duration of protection	Intervention coverage
					RSV-ICU admission ▪ MV: 56.4% (95% CI: 5.2 to 81.5%) Nirsevimab: 90% (95% CI: 54 to 98%)		
Getaneh AM[298] 2023	MV^ EHL-mAb (nirsevimab) 1 dose	No vaccination Each alternative strategy	Infants: Birth / 1-6 months (catch-up)±	EHL-mAb: ▪ Year-round ▪ Seasonal Seasonal plus catch-up	Constant efficacy over 5 months after administration RSV-primary care visit ▪ EHL-mAb: 74.5% (95% CI: 53.2 to 90.3%) RSV-hospitalisation ▪ EHL-mAb: 62.3% (95% CI: 12.1 to 98.0%)	Duration of protection: EHL-mAb: 5 months after administration Assumed no protection after 5 months.	Base case: 90%
Hodgson D[296] 2022	EHL-mAb (nirsevimab) 1 dose	Palivizumab	Infants: Birth / 8, 12 or 16 weeks* / 1-6 months§ (catch-up)	EHL-mAb ▪ Year-round ▪ Seasonal Seasonal plus catch-up	Mean efficacy over 150 days after administration RSV-LRTI: 74.5% (95% CI: 49.6 to 87.1%)	Duration of protection 150 days after administration, after which assumed exponential loss of protection at rate of λ=1/150	Base case: 90% Scenario analysis: 70%
Hodgson D[304] 2024	MV (RSVpreF) EHL-mAb (nirsevimab)	Palivizumab and alternate intervention strategies	Pregnant women: 2nd/ 3rd trimester¥ Infants: Birth/ 1-6 months	MV: ▪ Year-round ▪ Seasonal	RSV-LRTI Mean efficacy over 90 days after birth ▪ MV: 58.3 % (95% CrI: 41.5 -72.8%)	RSV-LRTI Mean MV efficacy over 120, 150, and 180 days after birth: Over 120 days after birth:	MV: 60% EHL-mAb: 90%

Study Year	Intervention type Dosing schedule	Comparator	Population	Administration time	Intervention efficacy/ effectiveness	Estimated effectiveness over time/ Duration of protection	Intervention coverage
	1 dose			mAb: ▪ Year-round ▪ Seasonal ▪ Seasonal plus catch-up	Mean efficacy over 150 days after administration ▪ EHL-mAb: 77.3% (95% CI: 65.4 to 86.5%)	MV: 55.7% (95% CI: 39.5 -68.7%) Over 150 days after birth: MV: 52.8% (95% CI: 37.2 – 65.2%) Over 180 days after birth: MV: 49.8% (95% CI: 34.2 to 62.1%) Proportion protected by 365 days after birth (MV) or after administration (EHL-mAb): MV: 9.3% (95% CI: 0.1 to 23.7%) EHL-mAb: 14.8% (95% CI: 1.5 to 33.8%)	
Ishiwada N[306] 2024	MV (RSVpreF) mAb (palivizumab) 1 dose (MV) Up to 6 monthly	Palivizumab (infants with risk factors born ≤31 wGA, 32-26 wGA and ≥37 wGA; infants without risk factors born ≤31 wGA and 32-35 wGA)	Pregnant women: 2nd/ 3rd trimester¥ Infants: ≤ 5 months S1: Infants with risk factors born ≤31 wGA, 32 to 26 wGA and ≥37 wGA. Infants without risk factors born <31	MV: ▪ Year-round mAb: Year-round	Initial effectiveness of RSVpreF RSV-outpatient visit ▪ ≥37 wGA: 47.6% ▪ 32 to 36 wGA: 39.6% ▪ ≤31 wGA/High-risk: 0% Hospitalisation ▪ ≥37 wGA: 88.1%	Trial based waning of RSVpreF over 180 days after birth, after which assumed linear loss of protection in the next 3 months until 0% by 9 months after birth.	MV: 80% Palivizumab: ▪ ≤36 wGA: 46.2% High risk: 95%

Study Year	Intervention type Dosing schedule	Comparator	Population	Administration time	Intervention efficacy/ effectiveness	Estimated effectiveness over time/ Duration of protection	Intervention coverage
	doses (palivizumab)		wGA. Infants without risk factors born 32 to 36 wGA to unvaccinated mothers or within 2 weeks of maternal vaccination. S2: Infants with risk factors born ≤31 wGA. Infants with risk factors born 32 to 26 wGA and ≥37 wGA to unvaccinated mothers or within 2 weeks after maternal vaccination. Infants without risk factors born ≤31 wGA. Infants without risk factors born 32 to 36 wGA to unvaccinated mothers or within 2 weeks after maternal vaccination.		▪ 32 to 36 wGA: 73.4% ▪ ≤31 wGA/High-risk: 0% ED visit ▪ ≥37 wGA: 47.6% ▪ 32 to 36 wGA: 39.6% ▪ ≤31 wGA/High-risk: 0% Initial effectiveness of palivizumab against RSV-LRTI: 56%		
Kieffer A[307] 2024	EHL-mAb (nirsevimab) 1 dose	Palivizumab	Infants: Birth / 8, 12 or 16 weeks* ≤ 5 months / ≤1 year*	EHL-mAb: ▪ Seasonal plus catch-up	Constant efficacy RSV-primary care/ED visits ▪ Nirsevimab: ○ palivizumab-eligible group: 51.0% (95% CI: 40.8 to 61.2%)	Duration of protection: 150 days after administration. No residual efficacy assumed after this period.	Nirsevimab: 91% (95% CI: 72.8 to 100%)

Study Year	Intervention type Dosing schedule	Comparator	Population	Administration time	Intervention efficacy/ effectiveness	Estimated effectiveness over time/ Duration of protection	Intervention coverage
					○ preterm group: 86.2% (95% CI: 68 to 94%) ○ term group: 74.5% (95% CI: 49.6 to 87.1%) RSV-hospitalisation ▪ Nirsevimab: ○ palivizumab-eligible group: as above ○ preterm/term groups: 83.2% (95% CI: 67.8 to 92%) All-cause LRTD-hospitalisation ▪ Nirsevimab: ○ Preterm group: 58.04%		
Li X[295] 2022	MV^ EHL-mAb (nirsevimab) 1 dose	No intervention and alternate interventions	Pregnant women Infants: Birth / 1-6 months	MV: Year-round EHL-mAb: ▪ Year-round ▪ Seasonal	Constant efficacy RSV-Primary care visit: ▪ 74.5% (95% CI: 53.2 to 90.3%) RSV-hospitalisation/ outpatient visit: ▪ 62.3% (95% CI: 12.1 to 98.0%)	Base case: duration of protection fixed at 5 months after administration Scenario analysis: Duration of protection varied to 6 months	92%

Study Year	Intervention type Dosing schedule	Comparator	Population	Administration time	Intervention efficacy/ effectiveness	Estimated effectiveness over time/ Duration of protection	Intervention coverage
				▪ Seasonal with catch-up			
Li X[297] 2023	MV^ EHL-mAb (nirsevimab) 1 dose	No intervention	Pregnant women Infants: Birth / 1-6 months	EHL-mAb: ▪ Year-round ▪ Seasonal ▪ Seasonal plus catch-up	RSV-Primary care visit: 70% (95% CI: 52.3 to 81.2%) RSV-hospitalisation/ outpatient visit: 78% (95% CI: 52 to 90)	Base case: duration of protection of 150 days after administration Scenario analyses: varied ▪ Static models assumed all or nothing protection with a stepwise function for 150 days, then no protection. Dynamic models ▪ The SPD model assumed an all or nothing protection with a stepwise function for 150 days. ▪ The LSHTM model assumed all or nothing protection with an exponential decline function for individuals moving out of the protected comparted over 150 days.	94%

Study Year	Intervention type Dosing schedule	Comparator	Population	Administration time	Intervention efficacy/ effectiveness	Estimated effectiveness over time/ Duration of protection	Intervention coverage
Nourbakhsh S[294] 2021	MV^ mAb (palivizumab) EHL-mAb (nirsevimab) 1 dose (MV, nirsevimab) Up to 5 monthly doses (palivizumab)	1: No intervention 2: mAb for preterm infants ≤ 5 months + chronically ill infants <1 yr during Jan - June 3: EHL-mAb for preterm infants ≤ 5 months + chronically ill infants aged <1 yr during Jan -June	Pregnant women Infants: ≤ 2 months/ ≤ 5 months / ≤1 year‡	EHL-mAb/mAb: ▪ Seasonal plus catch- up	Constant efficacy RSV-outpatient visit: ▪ Palivizumab ○ All groups: 48% (95% CI: 4 to 80%) ▪ Nirsevimab ○ All groups: 47% (95% CI: 20 to 80%) RSV-hospitalisation ▪ Palivizumab/ Nirsevimab ○ Preterm/chronically ill 0-2/3-5 months: 20% to 90% ○ Preterm/chronically ill 6-11 months: 20% to 67% ○ Healthy 0-2 months: 23.5% RSV-ICU admission ▪ Palivizumab/ Nirsevimab ○ Preterm/chronically ill all ages: 63.9% ○ Healthy 0-2 months: 43.9%	Duration of protection: Palivizumab: 30 days Nirsevimab: 150 days	NR

Study Year	Intervention type Dosing schedule	Comparator	Population	Administration time	Intervention efficacy/ effectiveness	Estimated effectiveness over time/ Duration of protection	Intervention coverage
Shoukat A[299] 2023	MV (RSVpreF) EHL-mAb (nirsevimab) 1 dose	No intervention	Pregnant women: 3rd trimester~ Infants: Birth /1-6 months	MV: ▪ Year-round mAb: ▪ Seasonal plus catch-up	Mean efficacy over 90 days after birth (MV) and over 150 days after administration (nirsevimab) RSV-LRTI ▪ MV: 57.1% (95% CI: 14.7 to 79.8%) ▪ mAb: 79.5% (95% CI: 65.9 to 87.7%) RSV-hospitalisation ▪ MV: 67.9% (95% CI: 34.6 to 84.2%) ▪ mAb: 77.3% (95% CI: 50.3 to 89.7%) RSV-ICU admission ▪ MV: 81.8% (95% CI: 40.6 to 96.3%) ▪ mAb: 86% (95% CI: 62.5 to 94.8%)	Duration of protection: MV: 90 days after birth mAb: 150 days after administration Base case: after initial period of protection, sigmoidal decay in efficacy to 0% by 10 months. Sensitivity analyses: after initial period of protection, linear decline in efficacy to 0% by 10 months	Base case: 100% Scenario analyses: MV: 60% mAb: 80%

Key: CI – confidence interval; ED – emergency department; EHL-mAb – extended half-life monoclonal antibody; ICU – intensive care unit; LRTD – lower respiratory tract disease; mAb – monoclonal antibody; MV – maternal vaccine: RSV – respiratory syncytial virus; RSVpreF – respiratory syncytial virus prefusion F vaccine; wGA – weeks' gestational age.
Note: ¥24 to 36 wGA. ~28 to before 33 wGA. *Catch-up administration of nirsevimab for infants born before the RSV season during regular National Immunisation Programme (NIP) appointment (8, 12 or 16 weeks after birth) closest to but not later than the start of RSV season. ‡Palivizumab-eligible population: up to five monthly doses throughout the RSV season for infants born during the season or as a catch-up for infants born before the season. ‡For both Palivizumab and Nirsevimab the age at immunisation was preterm infants aged 0 to 5 months, chronically ill infants aged under 1 year and healthy full-term infants aged 0 to 2 months. ±Catch-up programme in October for children up to 4 months, born in May to September (inclusive). §Seasonal and catch-up strategy that is not NIP-integrated includes children aged <7 months in October. ^Hypothetical vaccine – not extracted

Table 5.6 Immunisation strategies and intervention characteristics considered in the models of studies in older adults

Study Year	Intervention type Dosing schedule	Comparator	Cohort vaccinated	Intervention efficacy/ effectiveness	Estimated effectiveness over time/ Duration of protection	Intervention coverage
Hutton DW[305] 2024	RSV vaccines (RSVpreF and RSVPreF3) 1 dose	No vaccination	Adults: ▪ ≥65 years ▪ 60 to <65 years ▪ 65 to <70 years ▪ 70 to <75 years ▪ ≥75 years	Mean efficacy over 7 months after administration (season 1) Outpatient visit ▪ RSVpreF: 65.2% (95% CI: 36.0 to 82.0%) ▪ RSVPreF3: 79.0% (95% CI: 54.3 to 91.5%) Hospitalisation/ ED visit ▪ RSVpreF: 84.6% (95% CI: 32.0 to 98.3%) ▪ RSVPreF3: 87.5% (95% CI: 58.9 to 97.6%)	Mean efficacy from 8 to 14 months (RSVpreF) and from 8 to 18 months (RSVPreF3) after administration (season 2) RSV-outpatient visit: ▪ RSVpreF: 55.0% (95% CI: 0.0 to 82.0%) ▪ RSVPreF3: 27.8% (95% CI: 0.0 to 60.4%) RSV-hospitalisation: ▪ RSVpreF: 75.0% (95% CI: 0.0 to 97.4%) ▪ RSVPreF3: 52.9% (95% CI: 0.0 to 81.2%) After these periods efficacy assumed to wane linearly to 0% by 24 months	20%
Moghadas SM[300] 2023	RSV vaccines (RSVpreF and RSVPreF3) 1 dose	No vaccination	Adults: ▪ ≥60 years	Initial vaccine efficacy at start of season 1: RSV-outpatient visit	Season 2 efficacy estimates: RSV-outpatient visit	Base case: 66% Scenario analysis: 100%

Study Year	Intervention type Dosing schedule	Comparator	Cohort vaccinated	Intervention efficacy/ effectiveness	Estimated effectiveness over time/ Duration of protection	Intervention coverage
				▪ RSVpreF: 65.1% (95% CI: 35.9 to 82.0 ▪ RSVPreF3: 82.6% (95% CI: 57.9 to 94.1) RSV hospitalisation ▪ RSVpreF: 88.9% (95% CI: 53.6 to 98.7) ▪ RSVPreF3: 94.1% (95% CI: 62.4 to 99.9)	▪ RSVpreF: 48.9% (95% CI: 13.7 to 70.5) ▪ RSVPreF3: 67.2% (95% CI: 48.2 to 80.0) RSV-hospitalisation ▪ RSVpreF: 78.6% (95% CI: 23.2 to 96.1) ▪ RSVPreF3: 78.8% (95% CI: 52.6 to 92.0) Two approaches to waning immunity: 1) Sigmoidal waning profile: mean efficacy estimates over 24 months (with an 18 month follow-up period for each RSV vaccine), with 0% efficacy by 24 months. 2) Linear waning profile: fixed efficacy estimates for each season (season 1 0-8 months, season 2 12-18 months). Modelled over an 18 month follow-up, with a linear decline between seasons and to 0% from 18 months to 24 months.	

Study Year	Intervention type Dosing schedule	Comparator	Cohort vaccinated	Intervention efficacy/ effectiveness	Estimated effectiveness over time/ Duration of protection	Intervention coverage
Shoukat A[308] 2024	RSV vaccines (RSVpreF and RSVPreF3) 1 dose	No vaccination	Adults: ▪ ≥60 years	Initial vaccine efficacy estimates at start of season 1: RSV-outpatient visit ▪ RSVpreF: 65.1% ▪ RSVPreF3: 82.6% RSV-hospitalisation ▪ RSVpreF: 88.9% ▪ RSVPreF3: 94.1%	Season 2 efficacy estimates: RSV-outpatient visit ▪ RSVpreF: 48.9% ▪ RSVPreF3: 56.1% RSV-hospitalisation ▪ RSVpreF: 78.6% ▪ RSVPreF3: 64.2% Two approaches to waning immunity: 1) Sigmoidal waning profile: mean efficacy estimates over 24 months (with an 18 month follow-up period for each RSV vaccine), with 0% efficacy by 24 months. 2) Linear waning profile: fixed efficacy estimates for each season (season 1 0-8 months, season 2 12-18 months). Modelled over an 18 month follow-up, with a linear decline between seasons and to 0% from 18 months to 24 months	Long-term care home residents: 90% Community dwelling adults: 74%

Study Year	Intervention type Dosing schedule	Comparator	Cohort vaccinated	Intervention efficacy/ effectiveness	Estimated effectiveness over time/ Duration of protection	Intervention coverage
Tuite AR[309] 2024	RSV vaccines (RSVpreF and RSVPreF3) 1 dose	No vaccination Each alternative strategy	Age-only eligibility: ▪ ≥60 years ▪ ≥65 years ▪ ≥70 years ▪ ≥75 years ▪ ≥80 years Age with medical risk eligibility (with ≥1 chronic condition): ▪ ≥60 years ▪ ≥65 years ▪ ≥70 years ▪ ≥75 years ▪ ≥80 years Age plus medical risk-only eligibility: As above for age-only eligibility and people from 50 or 60 years of age with ≥1 chronic medical condition	Mean vaccine efficacy over 7 months after administration (season 1) RSV-outpatient visit ▪ RSVpreF: 65.1% ▪ RSVPreF3: 82.6% RSV-hospitalisation ▪ RSVpreF: 88.9% ▪ RSVPreF3: 94.1%	Mean vaccine efficacy from 12 to 18 months after administration (season 2). Protection was assumed to decline linearly between seasons. Season 2 (12-18 months follow-up) RSV-outpatient visit ▪ RSVpreF: 48.9% ▪ RSVPreF3: 56.1% RSV-hospitalisation ▪ RSVpreF: 78.6% ▪ RSVPreF3: 64.2% Season 3 in the base case was 0%. Scenario analysis assumed efficacy for season 3 was one third of Season 2: RSV outpatient visit ▪ RSVpreF: 16.3% ▪ RSVPreF3: 18.7% RSV hospitalisation ▪ RSVpreF: 26.2% RSVPreF3: 21.4%	With chronic medical condition: ▪ 50 to 59 years: 58.6% ▪ 60 to 64 years: 59.9% ▪ 65 to 69 years: 65.2% ▪ 70 to 79 years: 82.7% ▪ ≥80 years: 83.4% Without chronic medical condition: ▪ 50 to 59 years: 36.7% ▪ 60 to 64 years: 49.4% ▪ 65 to 69 years: 61.1%

Study Year	Intervention type Dosing schedule	Comparator	Cohort vaccinated	Intervention efficacy/ effectiveness	Estimated effectiveness over time/ Duration of protection	Intervention coverage
						▪ 70 to 79 years 74.9% ≥80 years: 74.8%
Wang Y[301] 2023	RSV vaccines (RSVpreF and RSVPreF3) 1 dose	No vaccination Each alternative strategy	Adults: ▪ ≥60 years	Constant vaccine efficacy estimates for season 1: RSV-ARI ▪ RSVpreF: 65.2% (95% CI: 36.0 to 82.0%) ▪ RSVPreF3: 79% (95% CI: 54.3 to 91.5%) RSV-LRTD ▪ RSVpreF: 84.6% (95% CI: 32.0 to 98.3%) ▪ RSVPreF3: 87.5% (95% CI: 58.9 to 97.6%)	Constant vaccine efficacy estimates for season 2: RSV-ARI ▪ RSVpreF: 55.0% (95% CI: 3.4 to 82.0%) ▪ RSVPreF3: 27.8% (95% CI: 0 to 60.4%) RSV-LRTD ▪ RSVpreF: 75.0% (95% CI: 25.3 to 97.4%) ▪ RSVPreF3: 52.9% (95% CI: 0 to 81.2%)	48.2%

Key: ARI – acute respiratory infection; CI: confidence interval; ED – emergency department; LRTD – lower respiratory tract disease; RSV – respiratory syncytial virus; RSVpreF – respiratory syncytial virus prefusion F vaccine; RSVpreF3 – respiratory syncytial virus prefusion F3 vaccine.
Note: Efficacy against RSV-associated acute respiratory infection (ARI) or lower respiratory tract disease (LRTD) was typically applied as an estimate of outpatient visits. Efficacy against severe RSV-associated lower-respiratory tract disease (LRTD) was typically applied against hospitalisation.

5.4.5 Costs (direct and indirect)

Direct costs

Across the 16 studies, direct costs detailed in the economic models conducted from either a healthcare perspective or a societal perspective, or both, generally included some or all of the following:

- Direct medical costs:
  - GP visits
  - outpatient visits
  - hospitalisation
  - emergency department visits
  - ICU costs.
- Intervention costs:
  - intervention procurement
  - intervention administration
  - programme implementation
  - immunisation-related severe adverse events
  - immunisation-related serious adverse events.
- Patient-borne costs:
  - over-the-counter medication
  - prescription medication
  - transportation.

Four studies considered costs of wheezing as a long-term complication of RSV-related disease,[295, 298, 299, 307] and one study considered the cost of all-cause LRTD hospitalisations.[307] Three studies considered intervention wastage.[294, 303, 309] Three studies included the cost of vaccine-related serious adverse events, all related to the vaccination of older adults.[301, 305, 309]

Indirect Costs

For studies that conducted their economic analysis from the societal perspective,[297-300, 303, 305, 306, 308, 309] indirect costs detailed in the economic models varied but generally included some or all of the following:

- productivity losses associated with
  - illness due to RSV
  - hospitalisation due to RSV
  - RSV-related mortality
  - work absenteeism for caregivers of those with RSV

  - time costs for patients due to immunisation.

5.4.6 Effects (direct and indirect)

Direct effects

Across all studies, the direct effects of immunisation against RSV included in the economic modelling generally incorporated some or all of the following:

- RSV infection
  - medically attended RSV cases
  - non-medically attended RSV cases
- primary care visit
- outpatient visit
- hospitalisation
- emergency department visit
- ICU admission
- long-term complications of RSV infection
  - recurrent wheezing and or asthma
- RSV-related mortality.

Three of the five studies that examined vaccination of older adults against RSV reported that adverse events related to vaccination were incorporated into the model, and included:[301, 305, 309]

- systemic reactions
- injection site reactions
- severe adverse events
- serious adverse events.

Model parameters for adverse events were obtained from published RCT data for each of the three studies. One study provided a list of severe adverse events, which comprised injection site pain, redness and swelling for grade three solicited local reactions; and fatigue, fever, headache, gastrointestinal symptoms and muscle pain for systemic reactions.[301]

Indirect effects

Two of the studies incorporated indirect effects in their analyses with a proportion of each healthcare outcome averted attributable to the indirect protection from the immunisation programme.[296, 304]

Utility values for quality-adjusted life years (QALYs)

Infants

Of the 11 infant studies included, three studies clearly reported baseline utility values used in the analyses.[299, 302, 306] Two of these studies specified using country-specific baseline utility values derived from the EuroQol five-dimension (EQ-5D) instrument for children older than one year to account for the long term effect of RSV.[302, 306]

A summary of the disutility values and QALY losses associated with specific health states reported by studies is presented in Table 5.7. Utility weights or utility decrements due to RSV and accompanying health states, used to calculate QALYs, were clearly reported in three studies,[294, 299, 302] with one of these studies also reporting associated calculated QALY losses.[302] All of these studies sourced the disutility values from the same study[313] and hence the reported values were consistent across the studies. Eight further studies reported QALY losses associated with the health states.[295, 297, 298, 302-304, 306, 307] These values were sourced from different studies[314-316] and varied for the same health states.

Table 5.7 Disutility values and QALY losses for health states associated with RSV used in studies in infants

Health state	Lowest reported value	Highest reported value	Number of studies	Referenced in
QALY loss				
Non-medically attended RSV	0.001448 (≥5 years)	0.0036	3	(297, 304, 307)
GP/PC visit	0.001448 (≥5 years)	0.0063	5	(295, 297, 298, 304, 307)
Outpatient settings*	0.0038	0.00845	5	(295, 297, 302, 303, 306)
ED visit	0.0038	0.0135	4	(297, 303, 306, 307)
Hospitalisation	0.00299 (≥5 years)	0.0169	8	(295, 297, 298, 302-304, 306, 307)
ICU admission	0.00299 (≥5 years)	0.0245	4	(297, 303, 304, 307)
Recurrent wheezing	0.0366¥ (≤1year)	0.0392± (≤1 year)	3	(295, 298, 307)
Disutility				
Non-medically attended RSV	0.05~	0.12≠	1	(294)
Outpatient settings*	0.16	0.16>	3	(294, 299, 302)

Hospitalisation	0.41	0.41>	3	(294, 299, 302)
ICU admission	0.60	0.60	2	(294, 299)
Wheezing episode	0.04	0.04	1	(299)

Key: ED – emergency department; GP – general practitioner; ICU – intensive care unit; LRTD – lower respiratory tract disease; PC – Primary Care; QALY – quality-adjusted life year; RSV – respiratory syncytial virus.
Note: All QALY loss values reported are for infants <1 year of age unless otherwise stated. All disutility values reported are for infants <1 year of age. QALY loss due to adverse events related to RSV immunisation were not reported in this cohort.
*Outpatient settings described in the reviewed studies may include both hospital outpatient care and primary care settings.
¥This value is the QALY loss for palivizumab-eligible cohort in year 3 of recurrent wheezing. ±QALY loss per year of recurrent wheezing. ^This relates to a palivizumab-eligible cohort. ~Without previous RSV infection or RSV related outpatient visit.
≠With previous RSV infection. >Disutility values were calculated by subtracting illness utility from the reported baseline utility without RSV.

Adults

All five studies conducted among older adults reported the baseline utility values; four studies reported them by age band[300, 305, 308, 309] and one study reported for the overall study cohort (adults aged 60 years and older).[301] One study specified that the baseline utility values were adjusted for sex and age.[305] Two studies clearly reported that the baseline utility values were derived using EQ-5D instruments.[301, 309]

A summary of the utility values and QALY losses associated with specific health states and adverse events due to immunisation reported by studies is presented in Table 5.8. In terms of utility decrements due to RSV, three studies reported utility weights associated with different health states.[300, 301, 308]. Two of these studies applied utility weights associated with different health states to age-specific utility values.[300, 308] The method used to derive the utility scores was only reported by one study.[301] QALY losses associated with different health states were reported by three studies,[300, 305, 309] with two of these studies[305, 309] also reporting QALY losses resulting from adverse events due to immunisation.

Table 5.8 Utility values and QALY losses for health states associated with RSV used in studies in older adults

Health state	Lowest reported value	Highest reported value	Number of studies	Referenced in
QALY loss				
ED visit	0.0056 (≥ 50 years)	0.0056 (≥ 50 years)	1	(309)
Hospitalisation	0.0193 (≥ 60 years)	0.02 (≥ 50 years)	2	(305, 309)
Outpatient settings~	0.0056 (≥ 50 years)	0.0185 (≥ 60 years)	2	(305, 309)
Death	1.49 (≥85 years)	20.26 (50-59 years)	2	(300, 309)
Utility*				
Non-medically attended RSV	0.82	0.88	3	(300, 301, 308)

Outpatient settings~	0.75	0.76	3	(300, 301, 308)
GP/ PC visit	0.76	0.76	2	(300, 308)
ED visit	0.76	0.76	2	(300, 308)
Hospitalisation	0.35	0.576	3	(300, 301, 308)
ICU admission	0.1	0.1	2	(300, 308)
Adverse events related to RSV immunisation				
QALY loss				
Systemic reaction (non-severe)	0.0011 (50-64 years)	0.0031 (≥65 Years)	1	(305)
Severe local adverse event	0.0003 (≥50 years)	0.0003 (≥50 years)	1	(301, 305, 309)
Severe systemic adverse event	0.0004 (≥50 years)	0.0006 (≥60 years)	2	(301, 309)
Serious adverse events	0.141 (≥60 years)	0.141 (≥60 years)	1	(305)

Key: ED – emergency department; GP – general practitioner; ICU – intensive care unit; LRTD – lower respiratory tract disease; PC – Primary Care; QALY – quality-adjusted life year; RSV – respiratory syncytial virus.
Notes: All utility values reported are for ≥ 60 years old.
~Outpatient settings described in the reviewed studies may include both hospital outpatient care and primary care settings.
* Reported values appear to reflect utility weights (rather than disutility values or health state utility values) which were applied to age-specific baseline utility estimates to calculate the age-specific QALY loss.

5.4.7 Economic results

Among the 16 included studies, 15 reported an ICER and one study calculated the incremental net monetary benefit.[295, 304] One study reported both incremental cost per QALY gained and incremental cost per life year gained.[305]

Table 5.9 provides an overview of the economic evaluations examining the cost effectiveness of immunisation strategies in infants and young children. Note that all of the included figures are as reported by the study authors at time of publication, with no adjustments made for inflation, and no currency conversions carried out.

Maternal vaccination strategies

Four studies assessed the cost effectiveness of an authorised maternal vaccine, with different approaches to the timing of administration including year-round or both year-round and seasonal administration. In these studies, the comparator was either no intervention, standard of care, and or alternative strategies. Results relating to studies for non-authorised maternal vaccines are not presented.[294, 295, 297, 298] This section provides a summary of the main cost effectiveness results reported across these five studies. Of note, two of these studies also assessed the cost effectiveness of extended half-life monoclonal antibodies, the results of which are described in the next section.[299, 303]

- An industry-funded study found a year-round maternal vaccination strategy to dominate (that is, more effective and less costly) no vaccination from a Spanish healthcare perspective at a willingness to pay (WTP) threshold of €25,000/QALY. The assumed vaccine price was €166.50 and an additional administration cost of €6 per vaccination was included in the model. This study applied higher vaccine efficacy (VE) against GP visits (62% vs 51.7%), hospitalisations (88.1% vs 73.4%) and ED visits (62% vs 51.7%) for full term infants compared with late preterm infants.[302]

- When compared with no vaccination, a year-round strategy of maternal vaccination in Canada was found to be cost effective from both a healthcare (ICER: CAD $41,321/QALY) and societal perspective (ICER: CAD $25,825/QALY) at a WTP threshold of CAD $50,000/QALY on the basis of a maximum price per dose (PPD) of CAD $160 and CAD $200, respectively using sigmoidal VE profiles. The strategy was found to be cost effective from both a healthcare and societal perspective at higher PPDs of CAD $185 and CAD $235, respectively, under constant VE assumptions. The authors reported the probabilities of a year-round strategy being cost effective at its maximum PPD were 68% using sigmoidal VE profiles and 87% using constant VE profiles.[299]

- Another Canadian study reported that, for any of the infant programmes to be cost effective, a substantial reduction in product prices would be required. The cost per dose in the model based on list price was CAD $230 for RSVpreF and CAD $952 for nirsevimab, with administration cost assumed to be CAD $14.7 per dose. From both a healthcare and societal perspective a standalone year-round maternal vaccination was dominated (that is, was less effective and more costly) by a combination strategy of year-round maternal vaccination with nirsevimab for infants at high-risk of severe disease.[303] However, sensitivity analysis indicated that the combination strategy would dominate if nirsevimab was priced at greater than CAD $110 to CAD $290 per dose and the price of RSVpreF was less than CAD $60 to CAD $155 per dose at a WTP threshold of CAD $50,000 per QALY.

- A study based in England and Wales was conducted from the healthcare perspective, assuming a WTP threshold of GBP £20,000 per QALY, and reported the optimal strategy based on the product's combined cost of purchasing and administration (CCPA) in £5 intervals from £0 to £200. The authors reported that a year-round maternal vaccination programme was optimal up to a CCPA of £35 and a seasonal maternal vaccination programme was optimal at a CCPA between £36 to £80 if nirsevimab is priced above a CCPA of £84.[304]

Extended half-life monoclonal antibody strategies

Nine studies evaluated the cost effectiveness of year-round, seasonal and or seasonal with catch-up interventions based on extended half-life monoclonal antibodies. The comparator in these studies was either no intervention, standard care or alternate strategies. This section provides a summary of the main cost-effectiveness results across these nine studies.

- Gebretekle et al. reported that, for all infant programmes to be cost effective, a substantial reduction in product prices would be required. The cost per dose in the base case was CAD $952 for nirsevimab and $1,227 for palivizumab, while administration costs were assumed as CAD $14.7 per dose. At these prices, seasonal nirsevimab for infants at moderate- and at high-risk with catch-up was cost effective with ICER CAD $27,891/QALY compared with palivizumab programme from both the Canadian healthcare payer and societal perspectives. The authors presented an incremental analysis in which other infant strategies, including all infant programmes, were either dominated or had ICERs higher than commonly accepted WTP thresholds. In a scenario analysis undertaken from the healthcare perspective payer which assumed higher hospitalisation rates and healthcare costs, seasonal nirsevimab for all infants with catch-up dominated all other strategies except year-round maternal vaccination plus nirsevimab for infants at high-risk of RSV-related disease. Sensitivity analysis indicated that, at a WTP threshold of CAD$ 50,000, all of the modelled infant nirsevimab programmes could be cost effective if nirsevimab is priced below CAD $110–190 per dose.[303]

- Another Canadian study reported a year-round approach providing nirsevimab to all infants as a cost-effective strategy at a PPD of up to CAD $290 from a societal perspective and at a PPD of up to CAD $215 from a healthcare payer perspective based on a WTP threshold of CAD $50,000 per QALY gained.[299]

- A study published in 2021 reported that replacing palivizumab with nirsevimab for immunisation of infants at high risk was cost saving in all scenarios of mild, moderate and severe seasons from a healthcare perspective in Canada. Further, the authors reported that expanding eligibility of nirsevimab to all infants in addition to high-risk infants was deemed to be moderately cost effective (ICER: $39,414 per QALY) in a mild season, highly cost effective (ICER: $5,255 per QALY) in a moderate season, and cost saving in a severe season. Mild, moderate and severe seasons were defined as 30-50%, 50-70%, 70-90% of households having at least one infant under one year of age infected with RSV, respectively. The study assumed the immunisation cost of palivizumab and nirsevimab to be equal. The age-specific cost of

immunisation per dose was CAD$1,065 for infants aged 0 to 2 months, CAD$1,567 for those aged 3 to 5 months, and CAD$2,048 for infants aged 6 to 11 months. These costs include a 5% wastage rate and a CAD$50 administrative fee.[294]

- A study conducted in Norway reported that, from a healthcare payer perspective, at a price of €51 per dose for both nirsevimab and maternal vaccine, the most cost-effective strategy at a WTP threshold of NOK 390,000 (~€40,000) per QALY gained was a four-month seasonal nirsevimab programme administered between November to February, while the six-month season programme was cost effective at a higher WTP threshold of NOK 500,000 (~€50,000) per QALY gained. All other programmes evaluated in the incremental analysis including the year-round maternal vaccination, year-round nirsevimab and seasonal with catch-up programmes were (extendedly) dominated.[295]

- A government-funded study published in 2024 informed the UK Joint Committee on Vaccination and Immunisation's (JCVI) recommendations for an RSV immunisation programme to protect newborns and infants in England and Wales.[304] At a WTP threshold of £20,000 per QALY gained, this study reported a seasonal nirsevimab strategy to be optimal between £55 to £83 CCPA, and a seasonal nirsevimab with a catch-up programme to be optimal up to £55 CCPA when the CCPA for the maternal vaccine is above £80. The year-round nirsevimab programme was dominated by the seasonal nirsevimab with an annual catch-up programme across all CCPAs (in £5 intervals from £0 to £200).[304]

- Another study based in England and Wales reported that replacing the palivizumab programme with a nirsevimab programme was cost effective at a WTP threshold of GBP £20,000 per QALY gained from a healthcare perspective. The study reported a seasonal nirsevimab programme with a pre-season catch-up as the optimal strategy at a PPD of £32 dose or less, a seasonal programme without a catch-up as the optimal strategy at a PPD between £33-£63 and a seasonal nirsevimab programme restricted to infants at high-risk as the optimal strategy at a PPD of £64 and over.[296]

- An industry-funded study based in the UK estimated that providing nirsevimab to all infants, including infants considered eligible to receive palivizumab, in a seasonal plus catch up programme was cost effective if the price of nirsevimab (including administration cost) was equal to or less than £243 and £274 at WTP thresholds of £20,000 and £30,000 per QALY, respectively.[307]

- A 2023 model comparison study compared three static and two dynamic models using a common input parameter set for a hypothetical birth cohort of 100,000 infants. The authors reported that all models estimated ICERs in favour of seasonal programmes versus the year-round programmes when compared with no intervention when considered from either a healthcare payer or societal perspective.[297] The assumed price per dose was €37.5 forRSVpreF vaccine, with an additional €5 for year-round administration and €11.36 for seasonal administration. The EHL-mAb was priced at €50 per dose, with an additional administration cost of €8.32.
- A multi-country analysis of six European countries (Denmark, England, Finland, Italy, the Netherlands and Scotland) compared different strategies from both societal and healthcare perspectives. For all countries except the Netherlands, seasonal nirsevimab plus catch-up dominated alternate strategies (such as year-round maternal vaccination, year-round and seasonal mAb administration) in an incremental analysis at a price of €50 per dose for each intervention from a societal perspective. The societal perspective considered all direct costs plus the economic cost of total time loss including leisure time by caregivers due to RSV. For the Netherlands, seasonal nirsevimab without catch-up dominated all other programmes from a societal perspective. From the healthcare payer perspective, seasonal nirsevimab plus catch-up was cost saving in Scotland, while it was cost effective at WTP values of €20,000 (England, Finland), €30,000 (Denmark) or €50,000 (Veneto region Italy) per QALY gained. From a healthcare perspective for the Netherlands, a seasonal nirsevimab with catch-up programme was preferred only at a WTP threshold above €120,000.[298] In a scenario analysis, International Classification of Diseases (ICD)-coded RSV hospitalisations were included instead of the base case estimates based on time series analysis. Using the ICD-coded RSV-hospitalisations led to substantially lower hospitalisation rates, resulting in none of the intervention programmes being cost effective for England, the Veneto region (Italy), and the Netherlands at all WTP thresholds considered. For the remaining countries, the seasonal nirsevimab was cost effective at substantially higher WTP values.[298]

Combined strategies of mAb and maternal vaccination

Three studies assessed the cost effectiveness of a combined strategy of year-round maternal vaccination and administration of a mAb compared with no intervention.[299, 303, 306] or standard of care. Results from an additional study that used a hypothetical maternal vaccine are not presented.[294]

- A 2024 Canadian study found that a combined strategy of year-round maternal vaccination for all pregnant women plus year-round nirsevimab offered to infants at high-risk of RSV-related disease was not cost effective in an incremental analysis at WTP thresholds of CAD $50,000 or $100,000, from both a healthcare payer (ICER: CAD $204,621 per QALY gained) and societal (ICER: CAD $ 343,421 per QALY gained) perspective.[303] The cost per dose in the base case were based on list prices of CAD $230 for RSVpreF and CAD $952 for nirsevimab, with an assumed administration cost of CAD $14.70 per dose.

- Another study based in a Canadian setting, published in 2023, reported that a combined strategy was cost effective.[299] The authors found that a combined programme of a year-round maternal vaccination followed by seasonal administration of nirsevimab to infants at high-risk of RSV-related disease was cost effective at various combinations of PPD values, compared with no intervention. From the healthcare perspective at a WTP threshold of CAD $50,000 per QALY, the combined strategy was reported to be cost effective for a combined PPD of $615 for nirsevimab and $140 for RSVpreF (ICER: CAD $3,853 per QALY gained) with 100% probability. From the societal perspective, the combined strategy was reported to be cost effective with a PPD of $705 for nirsevimab and $180 for RSVpreF with 98% probability. These results assumed sigmoidal efficacy waning profiles for both interventions. Under the linear efficacy waning assumptions, the combined strategy was cost effective at various combinations of PPD values with higher ICER values from both perspectives.

- An industry-funded study in a Japanese setting published in 2024 assessed the cost effectiveness of a combined programme of year-round maternal vaccination for all pregnant women plus palivizumab targeted to infants based on their gestational age and risk of RSV-related disease. A combined programme of providing maternal vaccination and palivizumab to all premature infants (≤ 31 wGA), high risk infants and infants born unprotected at 32–36 wGA was found to be cost effective at the threshold value of ¥5 million per QALY gained (equivalent to $38,052) when the price of the maternal vaccine was equal to or less than JPY 23,948 (equivalent to $182) compared with a palivizumab-only programme, from both a healthcare perspective (ICER: US $38,043 per QALY gained) and a societal perspective (ICER: US $35,301 per QALY gained). When palivizumab was offered to all premature infants, infants born unprotected at 32–36 wGA, and high risk infants born unprotected at greater than 32 wGA, the combined programme was dominant from both a healthcare and a societal perspective.[306]

Table 5.9 Results of the economic evaluations examining the cost effectiveness of different RSV immunisation strategies in infants and young children

Study Year Published	Country/ region	Intervention	Comparator	Strategy/strategies	ICER - Healthcare Perspective	ICER - Societal Perspective	WTP threshold	Author's Conclusions
Álvarez Aldean J[302] 2024	Spain	MV (RSVpreF)	No vaccination	Year round MV	Year round MV dominant over no vaccination	N/A	€25,000 /QALY	MV dominant over no vaccination at a RSVpreF vaccine price of €166.5 and administration cost of €6.
Gebretekle[303] 2024	Canada	MV (RSVpreF) EHL-mAb (Nirsevimab) mAb (Palivizumab)	Palivizumab for infants at high-risk Each alternative strategy	Strategy 1 (S1): Year-round EHL-mAb to all infants Strategy 2 (S2): Seasonal EHL-mAb to all infants without catch-up Strategy (S3): Seasonal EHL-mAb with catch-up to all infants Strategy (S4): Year-round EHL-mAb to infants at moderate- and high-risk	Most cost-effective strategy S6 : ICER CAD $27,891 / QALY compared to S9 Non-dominated strategies: S8: ICER CAD $204,621 /QALY compared with S6 S3 ICER CAD $512,265 /QALY compared with S8	Strategies on the efficient frontier: S6: ICER CAD $14,948 /QALY S8: ICER CAD $343,421 /QALY Strategy 3: ICER CAD $476,746 /QALY	CAD $50,000 /QALY CAD $100,000 /QALY	At the cost per dose prices of CAD $952 for nirsevimab, CAD $1,227 for palivizumab, CAD $230 for RSVpreF with administration costs of CAD $14.7 all-infants nirsevimab and year-round RSVpreF programs were not cost-effective. All infants nirsevimab programme could be cost effective if nirsevimab is priced below CAD $110–190 per dose at WTP of CAD$ 50,000 per QALY. Year round MV plus nirsevimab for infants could be cost effective if nirsevimab was priced at greater than CAD $110

Study Year Published	Country/ region	Intervention	Comparator	Strategy/strategies	ICER - Healthcare Perspective	ICER - Societal Perspective	WTP threshold	Author's Conclusions
				Strategy (S5): Seasonal EHL-mAb without catch-up to infants at moderate- and high-risk Strategy (S6): Seasonal EHL-mAb with catch-up for infants at moderate- and high-risk Strategy (S7): Year-round MV for all pregnant women Strategy (S8): A combined program of a year-round MV for all pregnant women plus year-round EHL-mAb to infants at high-risk Strategy (S9): Palivizumab for				to CAD $290 per dose and the price of RSVpreF was less than CAD $60 to CAD $155 per dose at a WTP threshold of CAD $50,000 per QALY.

Study Year Published	Country/ region	Intervention	Comparator	Strategy/strategies	ICER - Healthcare Perspective	ICER - Societal Perspective	WTP threshold	Author's Conclusions
				infants at high-risk				
Getaneh[298] 2023	Denmark England Scotland Finland Italy The Netherlands	MV* EHL-mAb (Nirsevimab)	No vaccination Each alternative strategy	Strategy 1(S1): Year-round MV Strategy 2(S2):Year-round EHL-mAb Strategy 3 (S3):Seasonal EHL-mAb Strategy 4 (S4):Seasonal EHL-mAb plus catch-up	**Incremental analysis** **Denmark** S4 (ICER: €24,664/QALY) and S3 (ICER: €9,129/QALY) dominate all other strategies **England** S4 (ICER: €8,864/QALY) and S3 (ICER: €4,444/QALY) dominate all other strategies **Scotland** S4 dominates all other strategies **Finland**	**Incremental analysis** **Denmark, England, Scotland, Finland, Italy Veneto Region:** S4 dominates all other strategies **The Netherlands** S4 dominates all other strategies	A range of WTP threshold values were considered across the six countries.	Seasonal EHL-mAb with or without catch-up is preferred over year-round MV and EHL-mAb programmes when both products are priced equally (€50 per dose for each intervention).

Study Year Published	Country/ region	Intervention	Comparator	Strategy/strategies	ICER - Healthcare Perspective	ICER - Societal Perspective	WTP threshold	Author's Conclusions
					Seasonal EHL-mAb plus catch-up (ICER:€ 13,373/QALY) dominate all other strategies **Italy Veneto Region** Seasonal EHL-mAb plus catch-up (ICER: € 42,245/QALY) and seasonal mAb (ICER: €23,814/QALY) dominate all other strategies **The Netherlands** Seasonal EHL-mAb plus catch-up (ICER: € 130,308) and seasonal EHL-mAb(€21,187/QA			

Study Year Published	Country/ region	Intervention	Comparator	Strategy/strategies	ICER - Healthcare Perspective	ICER - Societal Perspective	WTP threshold	Author's Conclusions
					LY) dominate all other strategies			
Hodgson[296] 2022	England Wales	EHL-mAb (Nirsevimab)	Palivizumab	Strategy 1 (S1):Year-round EHL-mAb to all infants S2: Seasonal EHL-mAb to infants at very high-risk S3: Seasonal EHL-mAb to all infants S4: Seasonal EHL-mAb with catch-up S5: Seasonal EHL-mAb with NIP integrated catch-up	S1 and S5-Dominated at all price range (£0–100) S4 optimal when PPPD is less than or equal to £32 S3 optimal when PPPD is between £33-63 S2 optimal when PPPD is £64 and over	N/A	£20,000 /QALY	Nirsevimab is preferable to the existing palivizumab programme at various PPDs.
Hodgson D[304] 2024	England Wales	MV (RSVpreF) EHL-mAb (Nirsevimab)	mAb (Palivizumab) and alternate interventions	Strategy (S1):Year-round MV	S1 is optimal up to £35 CCPA and S2 is optimal between £36 to £80 CCPA if EHL-	N/A	£20,000 /QALY	MV and EHL-mAb are optimally cost-effective at various CCPAs.

Study Year Published	Country/ region	Intervention	Comparator	Strategy/strategies	ICER - Healthcare Perspective	ICER - Societal Perspective	WTP threshold	Author's Conclusions
				Strategy (S2): Seasonal MV Strategy (S3): Year-round EHL-mAb Strategy (S4): Seasonal EHL-mAb Strategy (S5): Seasonal EHL-mAb plus catch-up	mAb is priced above £84. S4 is optimal up to £55–83 CCPA, and S5 is optimal up to £55 CCPA if MV is priced above £80. S3 dominated by S5 at all CCPAs.			
Ishiwada[306] 2024	Japan	MV (RSVpreF) mAb (Palivizumab)	Palivizumab (all infants born ≤35 wGA and all infants with risk factors)	S1: Year-round MV plus palivizumab to all premature infants (≤31 wGA), all high risk infants and no-risk infants (32-36wGA) unprotected by maternal vaccine⁑ S2: Year-round MV plus palivizumab to all premature	S1: JPY 4,998,847 (USD $38,043) /QALY Strategy 2: Dominant	S1: JPY 4,638,509 (USD $35,301) /QALY Strategy 2: Dominant	JPY 5 million ($38,052) /QALY	A combined programme of year-round MV and palivizumab was cost effective compared with palivizumab only programme at RSVpreF vaccine price of US $182 per dose.

Study Year Published	Country/ region	Intervention	Comparator	Strategy/strategies	ICER - Healthcare Perspective	ICER - Societal Perspective	WTP threshold	Author's Conclusions
				infants, no-risk infants (32–36 wGA) and high-risk (≥ 32 wGA) infants unprotected by maternal vaccine				
Kieffer A[307] 2024	United Kingdom	mAb (Palivizumab) EHL-mAb (Nirsevimab)	mAb Palivizumab	Seasonal EHL-mAb plus catch-up	Cost saving	N/A	£20,000 /QALY £30,000 /QALY	Seasonal with a catch up strategy based on nirsevimab to all infants could be cost-effective compared with palivizumab to palivizumab-eligible population at price between £243 at £20,000 WTP threshold and £274 at £30,000 WTP threshold.
Li X[295] 2022	Norway	EHL-mAb (Nirsevimab) MV*	No intervention and alternate interventions	Stratey (S1): Year-round MV Strategy (S2): Year-round EHL-mAb Strategy(S3): Seasonal EHL-mAb (28 seasonal EHL-	S3 cost-saving Other programmes extendedly dominated	N/A	CEA assessed for a range of WTP values	Seasonal EHL-mAb programmes are cost effective over year-round MV at WTP threshold up to €40,000 per QALY when both interventions are equally priced at €51 per dose.

Study Year Published	Country/ region	Intervention	Comparator	Strategy/strategies	ICER - Healthcare Perspective	ICER - Societal Perspective	WTP threshold	Author's Conclusions
				mAb programmes)^ Strategy (S4): Seasonal EHL-mAb with catch-up				
Li X[297] 2023	Norway UK The Netherlands	MV* EHL-mAb (nirsevimab)	No intervention	Strategy(S1): Year-round MV Strategy (S2): Seasonal MV Strategy (S3): Year-round EHL-mAb Strategy (S4): Seasonal EHL-mAb Strategy (S5): Seasonal EHL-mAb plus catch-up	**S1:** UA (static): €402,349/QALY NV(static): €463,979 /QALY SPS (static): €366,437/QALY SPD (dynamic): €1,973,816 /QALY LSHTM (dynamic): €178,322 /QALY**S2:** UA (static): €129,280/QALY NV (static): €182,852 /QALY	**S1:** UA (static): €332,952/QALY NV (static): €375,702/QALY SPS (static): €297,665/QALY SPD (dynamic): €1,901,299 /QALY LSHTM (dynamic): €162,266/QALY **S2:** UA (static): €129,280/QALY NV (static): €	N/A	All models estimated ICERs more in favour of seasonal programs versus the year-round programs from both perspectives. The assumed price per dose were €37.5 for RSVpreF vaccine (additional €5 for year-round administration and €11.36 for seasonal administration) and €50 for mAb (additional administration cost of €8.32).

Study Year Published	Country/ region	Intervention	Comparator	Strategy/strategies	ICER - Healthcare Perspective	ICER - Societal Perspective	WTP threshold	Author's Conclusions
					SPS (static): € 142,378/QALY SPD (dynamic): €1,733,256/QALY LSHTM (dynamic): €131,423/QALY **S3:** UA (static): €71,522 /QALY NV (static): €69,419 /QALY SPS (static): €61,626 /QALY SPD (dynamic): €101,282 /QALY LSHTM (dynamic): €54,272 /QALY **S4:** UA(static): Dominant NV(static):	94,579/QALY SPS (static): €73,568/QALY SPD (dynamic): €1651046/QALY LSHTM (dynamic): €115,186/QALY **S3:** UA (static): €11,658 /QALY NV (static): Dominant SPS(static): €1635 /QALY SPD (dynamic): €34,327 /QALY LSHTM (dynamic): €35,205 /QALY **S4:** UA (static):		

Study Year Published	Country/ region	Intervention	Comparator	Strategy/strategies	ICER - Healthcare Perspective	ICER - Societal Perspective	WTP threshold	Author's Conclusions
					Dominant SPS(static): Dominant SPD (dynamic): €16,807/QALY LSHTM (dynamic): €36,376 /QALY **S5:** UA (static): €14,640/QALY SPS (static): €14,240 /QALY SPD (dynamic): €38,168 /QALY LSHTM (dynamic): €33,548/QALY	Dominant NV (static): Dominant SPS (static): Dominant SPD (dynamic): Dominant LSHTM (dynamic): €15,352 /QALY **S5:** UA (static): Dominant SPS (static): Dominant SPD (dynamic): Dominant LSHTM (dynamic): €16,705/QALY		
Nourbaksh(294)	Canada	MV* mAb	1: No intervention	Strategy 1 (S1): No intervention	**Mild RSV Season:**	N/A	CAD20,000 /QALY	Switching from palivizumab to nirsevimab to infants at

Study Year Published	Country/ region	Intervention	Comparator	Strategy/strategies	ICER - Healthcare Perspective	ICER - Societal Perspective	WTP threshold	Author's Conclusions
2021		(Palivizumab) EHL-mAb (Nirsevimab)	2: Palivizumab for preterm infants ≤ 5 months + chronically ill infants <1 yr 3: Nirsevimab for preterm infants ≤ 5 months + chronically ill infants aged <1 yr	Strategy 2(S2): Palivizumab for preterm infants ≤ 5 months + chronically ill infants <1 yr Strategy 3(S3): Nirsevimab for preterm infants ≤ 5 months + chronically ill infants aged <1 yr Strategy 4(S4): Maternal vaccine Strategy 5(S5): Maternal vaccine + Nirsevimab for preterm and chronically ill infants Strategy 6(S6): S2 + Palivizumab for healthy infants Strategy 7(S7): S3+ Nirsevimab	S2 vs S1: CAD $1,011,139 /QALY S3 vs S1: Cost-saving S4 vs S1: CAD $227,286/QALY S5 vs S1: Cost-saving S6 vs S2: CAD $ 441,023 /QALY S7 vs S3: CAD $ 39,414 /QALY **Moderate RSV season:** S2 vs S1: CAD $13,926 /QALY S3 vs S1: Cost-saving S4 vs S1: Cost-saving S5 vs S1: Cost-saving		(strongly recommended) •CAD100,000 /QALY (moderately recommended)	high risk was deemed cost saving when the cost of immunisation per dose was assumed to be equal for both interventions (CAD$1,065 - CAD$2,048 based on infants' weight)

Study Year Published	Country/ region	Intervention	Comparator	Strategy/strategies	ICER - Healthcare Perspective	ICER - Societal Perspective	WTP threshold	Author's Conclusions
				for healthy infants	S6 vs S2: CAD $208,015 /QALY S7 vs S3: CAD $5,255 /QALY **Severe RSV season** S2 vs S1: Cost-saving S3 vs S1: Cost-saving S4 vs S1: Cost-saving S5 vs S1: Cost-saving S6 vs S2: CAD $129,726 /QALY S7 vs S3 : Cost-saving			
Shoukat A[299] 2023	Canada	MV (RSVpreF) EHL-mAb (Nirsevimab)	No intervention	Strategy 1 (S1):EHL-mAb to preterm infants ≤32 wGA and infants with CLD or CHD	**Sigmoidal vaccine efficacy profiles** S1: CAD $49,577 /QALY at maximum PPD	**Sigmoidal vaccine efficacy profiles** S1: CAD $49,467 /QALY at	CAD $50,000 /QALY	Standalone nirsevimab and MV programmes were deemed cost effective at different PPDs.

Study Year Published	Country/ region	Intervention	Comparator	Strategy/strategies	ICER - Healthcare Perspective	ICER - Societal Perspective	WTP threshold	Author's Conclusions
				Strategy (S2):EHL-mAb to preterm infants ≤36 wGA and infants with CLD or CHD Strategy (S3):EHL-mAb to preterm infants ≤36 wGA, infants with CLD or CHD and term infants born during RSV season Strategy 4(S4):EHL-mAb to all infants S5: Year-round MV Strategy (S6):combined programme with year-round MV followed by seasonal EHL-mAb to preterm	CAD $615 S2: CAD $45,924 /QALY at maximum PPD CAD $375 S3: CAD $34,331 /QALY at maximum PPD CAD $300 S4: CAD $4,200 /QALY at maximum PPD CAD $215 S5: CAD 41,321 /QALY at maximum PPD CAD $160 S6: Nirsevimab PPD 615, RSVpreF PPD 140: CAD 3,853 /QALY Nirsevimab PPD 215, RSVpreF PPD 155: CAD 18,913	maximum PPD 705 S2: CAD $49,618 /QALY at maximum PPD 455 S3: CAD $28,634 /QALY at maximum PPD 385 S4: CAD $46,749 /QALY at maximum PPD 290 S5: CAD $25,815 /QALY at maximum PPD 200 S6: Nirsevimab PPD CAD $705, RSVpreF CAD $PPD 180: CAD $5,797 /QALY Nirsevimab PPD		Combined programme of MV and nirsevimab to infants at high risk of severe disease cost-effective at different PPD combinations.

Study Year Published	Country/ region	Intervention	Comparator	Strategy/strategies	ICER - Healthcare Perspective	ICER - Societal Perspective	WTP threshold	Author's Conclusions
				infants ≤32 wGA and infants with CLD or CHD	/QALY **Constant vaccine efficacy profiles** S1: CAD 46,135 /QALY at maximum PPD 610 S2: CAD 36,306 /QALY at maximum PPD 370 S3: CAD 24,716 /QALY at maximum PPD 295 S4: CAD 27,348 /QALY at maximum PPD 215 S5: CAD 34,041 /QALY at maximum PPD 185 S6:	CAD $290, RSVpreF PPD 195: CAD $15,511 /QALY **Constant vaccine efficacy profiles** S1: CAD $45,987 /QALY at maximum PPD CAD $700 S2: CAD $44,162 /QALY at maximum PPD CAD $450 S3: CAD $29,422 /QALY at maximum PPD CAD $380 S4: CAD $31,187 /QALY at maximum PPD CAD $285 S5: CAD $ 30,317 /QALY at		

Study Year Published	Country/ region	Intervention	Comparator	Strategy/strategies	ICER - Healthcare Perspective	ICER - Societal Perspective	WTP threshold	Author's Conclusions
					•Nirsevimab PPD 610, RSVpreF PPD 165: CAD 17,243 /QALY •Nirsevimab PPD 215, RSVpreF PPD 180: CAD 32,932 /QALY	maximum PPD CAD $235 S6: •Nirsevimab PPD CAD $700, RSVpreF PPD CAD $215 CAD $33,598 /QALY •Nirsevimab PPD CAD $285, RSVpreF PPD CAD $230 CAD $42,805 /QALY		

Key: CAD – Canadian dollar; CCPA - combined cost of purchasing and administration; CEA – cost effectiveness analysis; EHL-mAb - extended half-life monoclonal antibody; HCP – healthcare payer; ICER – incremental cost-effectiveness ratio; JPY – Japanese Yen; LRTD - lower respiratory tract disease; LSHTM -London School of Hygiene and Tropical Medicine; MA – medically Attended; mAb – monoclonal antibody; MV – maternal vaccine; N/A – not applicable; NOK – Norwegian Krone; NR – not reported; NV - Novavax model; PPD – price per dose; PPPD - purchasing price per dose; QALY – quality-adjusted life year; RSV- respiratory syncytial virus; RSVpreF – respiratory syncytial virus prefusion F vaccine; S – Strategy; SPD- Sanofi Pasteur dynamic model; SPS - Sanofi Pasteur static model; UA -University of Antwerp model; wGA – weeks' gestational age; WTP – willingness to pay.
Note: * Hypothetical vaccine candidate- not extracted in datasheet. ^ A single-month program or any combination of consecutive months during the RSV season to prevent RSV disease from October to April. ‡If their mothers were unvaccinated or infants born within 2 weeks after maternal vaccination.

Strategies for the immunisation of older adults

Table 5.10 provides an overview of the economic evaluations examining the cost effectiveness of immunisation strategies in older adults. The cost-effectiveness results of five economic evaluations evaluating the impact of providing RSVpreF (Abrysvo®) or RSVPreF3 (Arexvy®) are summarised below.

- A study conducted for Hong Kong assessed the cost effectiveness of vaccination with RSVpreF and or RSVPreF3 in a population of adults aged 60 years and older, compared with no vaccination.[301] The analysis was conducted from the healthcare perspective considering US vaccine prices of $200 for RSVpreF and $270 for RSVPreF3 and a WTP threshold value of $49,594 per QALY gained. The ICERs were $26,209 and $47,485 per QALY gained for RSVpreF and RSVPreF3, respectively, assuming a vaccine cost of 25% of the US vaccine price level. When the assumed cost of the vaccines were set to 50%, 75%, and 100% of the US vaccine price levels, the ICERs for both vaccines exceeded the WTP threshold. The study also reported that RSVPreF dominated RSVpreF3 at all four US vaccine price levels.[301]
- A study published in 2023 and based in the US investigated the cost effectiveness of three strategies of vaccinating adults aged 60 years and older: a single dose vaccination with RSVPreF3 only, RSVpreF only and a combined strategy of either vaccine (assuming a 50% probability of either vaccine being administered), compared with no vaccination. The authors reported that at a WTP of $95,000 per QALY gained, compared with no vaccination, these strategies may be cost effective for a PPD up to $127, $118 and $122, respectively from a societal perspective over a single RSV season with 68% vaccine coverage and a sigmoidal vaccine efficacy assumptions. The corresponding maximum PPDs for linear vaccine efficacy profiles were $132, $117 and $126, respectively.[300]
- Another study based in the US found that compared with no vaccination, vaccination of adults aged 75 years and older resulted in ICERs of $101,567 and $92,664 per QALY gained for RSVPreF3 and RSVpreF, respectively. For adults aged 80 years and older, they reported ICERs of $110,830 and $100,726 per QALY gained for RSVPreF3 and RSVpreF, respectively. The authors stated that both sets of results may be considered cost effective from a societal perspective at a WTP threshold of $100,000 or $150,000 per QALY gained. In a sub-group analysis that stratified by five-year age bands, the estimated ICERs for the groups aged 60 to 64 years and 65 to 69 years were higher than the commonly accepted WTP thresholds to be considered cost-effective. In scenario analyses, the ICERs were more favourable (closer to the

commonly accepted WTP thresholds) when vaccine prices were lower compared with those estimated in the base case ($280 for RSVPreF3 and $295 for RSvpreF), when vaccine efficacy was assumed to last beyond two seasons, and when a higher hospitalisation rate was applied.[305]

- A Canadian study, published in 2024, conducted an incremental analysis to compare ICERs of various vaccination strategies based on age only, medical risk only, and age plus medical risk-based eligibility criteria for RSVpreF and RSVPreF3. The analysis considered base case vaccine prices of CAD $230 per dose of either RSVpreF or RSVPreF3. The study reported that a programme focused on vaccinating people with at least one chronic medical condition aged 70 years and older was the optimal strategy for both vaccines from both a healthcare and a societal perspective at a WTP of CAD $50,000 per QALY gained.[309]
- Another Canadian study, also published in 2024, reported on single dose RSV vaccination of residents of long-term care homes aged 60 years and older. The authors reported that this approach, compared with no vaccination, was cost effective for a PPD up to $139 for RSVPreF3 and $137 for RSVpreF from a healthcare perspective at the WTP threshold of CAD$ 50,000 per QALY gained. When the programme was extended to include community-dwelling older adults aged 60 years and older in the analysis, the strategies were cost effective at lower PPDs of $69 for RSVPreF3 and $68 for RSVpreF. The maximum PPD at which the strategies were cost effective were higher for linear vaccine efficacy profiles than sigmoidal vaccine efficacy profiles.[308]

Table 5.10 Results of the economic evaluations examining the cost effectiveness of different RSV immunisation strategies in adults aged 65 years and older

Study Year	Country/ Region	Intervention	Comparator	Strategy	ICER - Healthcare Perspective	ICER - Societal Perspective	WTP threshold	Study Conclusions
Hutton[305] 2024	USA	RSV vaccines (RSVpreF and RSVPreF3)	No vaccination	RSV vaccination: Strategy 1(S1): ≥60 yrs Strategy 2(S2): ≥65 yrs Strategy 3(S3): ≥70 yrs Strategy 4(S4): ≥75yrs Strategy 5(S5): ≥80 yrs Strategy 6(S6): 60 to < 65 yrs Strategy 7(S7): 65 to < 70 yrs Strategy 8(S8): 70 to <75 yrs Strategy 9(S9): 75 to <80 yrs Strategy 10 (S10): ≥80 yrs	N/A	**S1:** RSVPreF3 $196,842 /QALY RSVpreF $176,557 /QALY **S2:** RSVPreF3 $162,138 /QALY RSVpreF $146,543 /QALY **S3:** RSVPreF3 $134,742 /QALY RSVpreF $122,296 /QALY **S4:** RSVPreF3 $101,567 /QALY RSVpreF $92,664 /QALY **S5:** RSVPreF3 $110,830 /QALY RSVpreF $100,726 /QALY **S6:** RSVPreF3 $385,829 /QALY	No universally accepted threshold for the US $100,000 /QALY or $150,000 /QALY are commonly used	A single dose vaccination may be cost effective for adults aged ≥65 years ICERs for age groups 60 to <65 years, 65 to <70 years, 70 to <75 years not cost effective under commonly accepted WTP thresholds

Study Year	Country/ Region	Intervention	Comparator	Strategy	ICER - Healthcare Perspective	ICER - Societal Perspective	WTP threshold	Study Conclusions
						RSVpreF $331,486 /QALY **S7:** RSVPreF3 $253,967 /QALY RSVpreF $225,521 /QALY **S8:** RSVPreF3 $233,472 /QALY RSVpreF $207,453 /QALY **S9:** RSVPreF3 $92,438 /QALY RSVpreF $84,652 /QALY **S10:** RSVPreF3 $110,830 /QALY RSVpreF $100,726 /QALY		
Moghadas[300] 2023	USA	RSV vaccines (RSVpreF and RSVPreF3)	No vaccination	Strategy 1 (S1): ≥60yrs with 66% vaccine coverage Strategy 2 (S2): ≥60yrs with 100% vaccine coverage	N/A	**S1**With sigmoidal vaccine efficacy profiles RSVPreF3 $93,981 /QALY RSVpreF $94,651 /QALY	$95,000 /QALY	A single dose vaccination to adults aged 60 years and older may be cost effective at

Study Year	Country/ Region	Intervention	Comparator	Strategy	ICER - Healthcare Perspective	ICER - Societal Perspective	WTP threshold	Study Conclusions
						RSVPreF3 and RSVpreF $94,234 /QALY **S1** With linear vaccine efficacy profiles RSVPreF3 $94,035 /QALY RSVpreF $94,664 /QALY RSVPreF3 and RSVpreF $94,848 /QALY **S2** with sigmoidal vaccine efficacy profiles RSVPreF3 $93,968 /QALY RSVpreF $94,471 /QALY		various PPDs.

Study Year	Country/ Region	Intervention	Comparator	Strategy	ICER - Healthcare Perspective	ICER - Societal Perspective	WTP threshold	Study Conclusions
						RSVPreF3 and RSVpreF $95,004 /QALY **S2** With linear vaccine efficacy profiles RSVPreF3 $93,978 /QALY RSVpreF $93,906 /QALY RSVPreF3 and RSVpreF $94,081 /QALY		
Shoukat[308] 2024	Canada	RSV vaccines (RSVpreF and RSVPreF3)	No vaccination	Strategy 1 (S1): Residents of LTCHs ≥60yrs (90% coverage) Strategy 2 (S2): Residents of LTCHs ≥60yrs (90% coverage) +community-dwelling adults ≥60yrs (74% coverage)	**S1** With sigmoidal vaccine efficacy profiles RSVPreF3 CAD $49,653/QALY RSVpreF CAD $49,806 /QALY With linear vaccine efficacy profiles	**S1** With sigmoidal vaccine efficacy profiles RSVPreF3 CAD $49,653 /QALY RSVpreF CAD $49,806 /QALY	CAD $50,000 /QALY	A single dose vaccination to community-dwelling older adults in addition to LTCH residents at high risk of severe outcomes could be

Study Year	Country/ Region	Intervention	Comparator	Strategy	ICER - Healthcare Perspective	ICER - Societal Perspective	WTP threshold	Study Conclusions
					RSVPreF3 CAD $49,984 /QALY RSVpreF CAD $49,977 /QALY **S2** With sigmoidal vaccine efficacy profiles RSVPreF3 CAD $49,669 /QALY RSVpreF CAD $49,788 /QALY With linear vaccine efficacy profiles RSVPreF3 CAD $49,457 /QALY RSVpreF CAD $49,931 /QALY	With linear vaccine efficacy profiles RSVPreF3 CAD $49,984 /QALY RSVpreF CAD $49,977 /QALY **S2** With sigmoidal vaccine efficacy profiles RSVPreF3 CAD $49,478 /QALY RSVpreF CAD $49,711 /QALY With linear vaccine efficacy profiles RSVPreF3 CAD $49,698 /QALY		cost-effective depending on PPD.

Study Year	Country/ Region	Intervention	Comparator	Strategy	ICER - Healthcare Perspective	ICER - Societal Perspective	WTP threshold	Study Conclusions
						RSVpreF CAD $49,175 /QALY		
Tuite[309] 2024	Canada	RSV vaccines (RSVpreF and RSVPreF3)	No vaccination Each alternate strategy	RSV vaccination: **Age-only eligibility** ≥60yrs, ≥65yrs, ≥70yrs, ≥75yrs and ≥80yrs **Age with medical risk eligibility*** ≥60yrs, ≥65yrs, ≥70yrs, ≥75yrs and ≥80yrs **Age-only eligibility plus medical risk eligibility^** (≥60yrs plus 50-59 with ≥1 CMC; ≥65yrs plus 50-64/60-64 with ≥1 CMC; ≥75yrs plus 50-74/60-74 with ≥1 CMC; ≥80yrs plus 50-79/60-79 with ≥1 CMC)	Vaccinating ≥70yrs with at least one chronic condition optimal strategy in an incremental analysis with ICER CAD 49,439 /QALY (RSVPreF3) and CAD 46,542 /QALY (RSVpreF) compared with vaccinating people with at least one chronic medical condition aged 75 years and older.	Vaccinating ≥70yrs with at least one chronic condition optimal strategy in an incremental analysis with ICER CAD 43,255 /QALY (RSVPreF3) and CAD 41,632 /QALY(RSVpreF) compared with vaccinating people with at least one chronic medical condition aged 75 years and older.	CAD 50,000 /QALY	Age-based vaccination was deemed to be never cost effective compared with risk-based or risk and age-based strategies. A single dose vaccination to those aged ≥70yrs with at least one chronic condition was deemed to be the optimal strategy.

Study Year	Country/ Region	Intervention	Comparator	Strategy	ICER - Healthcare Perspective	ICER - Societal Perspective	WTP threshold	Study Conclusions
Wang[301] 2023	Hong Kong	RSV vaccines (RSVpreF and RSVPreF3)	No vaccination Each alternative strategy	1. ≥60yrs vaccinated with RSVpreF 2. ≥60yrs vaccinated with RSVPreF3	**Compared with no vaccination:** 25% of US vaccine price: ▪ RSVpreF $26,209 /QALY ▪ RSVPreF3 $47,485 /QALY 50% of US vaccine price: ▪ RSVpreF $63,441 /QALY ▪ RSVPreF3 $104,756 /QALY 75% of US vaccine price: ▪ RSVpreF $100,674 /QALY ▪ RSVPreF3 $162,027 /QALY 100% of US vaccine price: ▪ RSVpreF $137,907 /QALY	N/A	$49,594 /QALY	The cost effectiveness of RSVPreF3 or RSVpreF is highly subject to vaccine price and RSV attack rate.

Study Year	Country/ Region	Intervention	Comparator	Strategy	ICER - Healthcare Perspective	ICER - Societal Perspective	WTP threshold	Study Conclusions
					▪ RSVPreF3 $219,299 /QALY **Incremental analysis:** RSVpreF dominated RSVPreF3 at all four US vaccine prices			

Key: CAD – Canadian dollar; CCPA - combined cost of purchasing and administration; CMC – chronic medical condition; ICER – incremental cost-effectiveness ratio; JPY – Japanese Yen; LRTD - lower respiratory tract disease; LTCH –long term care homes; MA – medically attended; mAb – monoclonal Antibody; MV – maternal vaccine; N/A – not applicable; NOK – Norwegian Krone; NR – not reported; PPPD - purchasing price per dose; QALY – quality-adjusted life year; RSV- respiratory syncytial virus; RSVpreF – respiratory syncytial virus prefusion F vaccine; RSVpreF3 – respiratory syncytial virus prefusion F3 vaccine; wGA – weeks' gestational age; WTP – willingness to pay; yrs - years.

Note: *People in these age categories with at least one chronic medical condition are eligible. ^In this strategy people were eligible to receive the vaccine if they met an age requirement, or if they were ≥50 or ≥60 years and had at least 1 chronic medical condition.

5.4.8 Critical appraisal

Given that the objective of this rapid review was to assess the published international evidence on the approaches taken to modelling the economic evaluations of RSV immunisation strategies, a critical appraisal of all included studies was undertaken using the framework proposed by Philips et al. for quality assessment of decision-analytic models.[293] Overall, no major concerns were identified with the quality of the included studies. However, within each of the three domains (structure, data, consistency) assessed there were some concerns.

In terms of the 'structure' domain, there were some minor concerns regarding quality. The 16 studies considered the burden of medically attended RSV health-related outcomes, although the specific health events and what was included within the model pathway differed across studies. Seven studies included non-medically attended RSV burden in their model, in addition to medically attended events such as primary care visits and hospitalisation.[296, 297, 300, 301, 304, 307, 308] Another study did not include outpatient or emergency department events due to a lack of data,[298] while other approaches taken by studies incorporated events such as emergency visits within the primary care visit model input.[295]

Other minor quality issues relating to model structure included consideration of all feasible and practical options for strategies and comparators. Of the five studies of RSV vaccination in older adults,[300, 301, 305, 308, 309] one study stratified the study population by age and risk group,[309] while scenario analyses were performed in another two studies comparing different age sub-groups.[305, 308] Regarding studies that considered maternal vaccination, two studies did not explicitly justify excluding a seasonal maternal vaccination strategy in their models.[299, 302]

In terms of the 'data' domain, no major concerns were identified with the quality of the included studies, as the data incorporated into all the models were described and data sources referenced in sufficient detail. However, there was a lack of transparency around the initial data identification steps, with respect to specifying if systematic methods were used to identify the data inputs. Only three studies explicitly referred to performing a literature search to identify model parameter values.[301-303] Although each study indicated a preference to use country- or region-specific data if available, only one study was identified as explicitly explaining how choices were made in scenarios where multiple such data sources may have been identified.[301]

Further while all studies did assess uncertainty, it was not considered a fully comprehensive assessment in four studies, either because they noted that the lack of a probabilistic sensitivity analysis was a limitation [303, 306, 307]; because the deterministic sensitivity analysis merely assumed a deviation of 20% for many

parameters[307]; or because the model was not run separately for relevant sub-groups.[301]

Lastly, for the 'consistency' domain, no major concerns were identified with the quality of the included studies. However, only three studies were considered to have provided a sufficient description of model validation.[294, 307, 309]

5.4.9 Conclusions from studies

The four studies assessing standalone maternal vaccination as an intervention to prevent RSV among infants differed in their conclusions. One study concluded that a year-round maternal vaccination strategy was cost saving compared with no intervention from the chosen perspective.[302] Another study reported a year-round maternal vaccination programme was cost effective compared with no intervention from both a healthcare and societal perspective if the PPD was lower than that for the monoclonal antibodies.[299] A study analysing a year-round maternal vaccination strategy found it to be dominated by year-round maternal vaccination combined with nirsevimab for infants at high-risk, from both a healthcare and societal perspective.[303] One study reported that, if nirsevimab is priced above £84, the CCPA for the maternal vaccine needs to be up to £35 for the year-round programme to be optimal and needs to be between £36 and £80 for the seasonal programme to be optimal.[304]

In terms of monoclonal antibodies, three studies concluded that replacing palivizumab with nirsevimab was cost saving or cost effective when considered from a healthcare or a societal perspective.[294, 296, 307] Another three studies concluded that a seasonal nirsevimab programme is preferred to a year-round programme from the chosen perspective.[295, 297, 298] Three studies provided the maximum price of nirsevimab for a seasonal with catch-up programme to be cost effective compared with either palivizumab or no vaccination from a healthcare perspective, ranging from a PPD of GBP £32 to a CCPA of GBP £243 (at a WTP threshold of GBP £20,000 per QALY gained) or a PPD of CAD $215 (at a WTP threshold of CAD $50,000 per QALY gained).[296, 299, 304, 307] One study provided a maximum CCPA of nirsevimab for a seasonal with catch-up programme to be optimal at £55 from a healthcare perspective in the context of the maternal vaccine CCPA being above £80.[304] Two studies provided a maximum CCPA of nirsevimab for a seasonal programme without a catch-up to be optimal from a healthcare perspective, ranging from GBP £63 to GBP £83 when compared with either palivizumab or the maternal vaccine respectively and at a WTP threshold of GBP £20,000 per QALY gained.[296, 304] Three studies evaluated a combined programme with year-round maternal vaccination plus a monoclonal antibody (either nirsevimab or palivizumab) for premature infants and those at high risk who are unprotected through maternal vaccination.[299, 303, 306] Two studies provided the maximum PPDs at which the strategy could be cost-effective

compared with no vaccination from the chosen perspective,[299, 306] the third study did not find the strategy to be cost effective in an incremental analysis comparing standalone seasonal and year-round programmes based on nirsevimab and maternal vaccine.[303]

Studies assessing a single vaccination with RSVpreF or RSVPreF3 for older adults concluded that the cost effectiveness was dependent on the age group, product and the vaccine PPDs. A study from the US undertaken from a societal perspective concluded that a single-dose vaccination strategy could be cost effective compared with no vaccination, particularly for the oldest age groups, that is, those aged above 75 years, at vaccine prices of US$200 for RSVpreF and US$270 for RSVPreF3. The authors also reported that evidence of efficacy beyond two RSV seasons would make the vaccination more cost effective.[305] A second study from the US concluded that the vaccination programmes could be cost effective compared with no vaccination from the societal perspective at a PPD up to $127 with RSVPreF3 and $118 with RSVpreF over the first RSV season.[300] A study from Hong Kong which considered US vaccine prices of $200 for RSVpreF and $270 for RSVPreF3 found that vaccination with RSVpreF or RSVPreF3 was cost effective only at 25% of these prices from a healthcare perspective.[301] A Canadian study reported universal age-based vaccination strategies not to be cost effective compared with risk-based strategies. The authors found vaccinating adults aged 70 years and older with one or more chronic medical condition to be optimal from both a healthcare and societal perspective.[309] A second study from Canada concluded that vaccinating all older adults aged 60 years and older including those residing in the LTCHs was cost effective compared with no vaccination from both a healthcare and societal perspective based on a PPD of $69 for RSVPreF3 and $68 for RSVpreF.[308] The maximum PPD at which the strategies were cost effective were higher for linear vaccine efficacy profiles than sigmoidal vaccine efficacy profiles.

5.5 Discussion

5.5.1 General and model characteristics

Most of the studies in this review were conducted for countries spread across Europe, North America, and the Asia-Pacific region. Of the 16 included studies, three were industry-funded and two studies were jointly funded by the European Union and industry. Static decision-tree models (n=6 studies),[295, 297, 298, 301, 305, 307] were most commonly used followed by static Markov models (n=5),[297, 302, 303, 306, 307, 309] dynamic transmission models (n= 4 studies)[296, 297, 304] and static discrete event simulation models (n=4 studies).[294, 299, 300, 308] One study compared the cost effectiveness results between two dynamic and three static models.[297] The five Markov models adopted monthly time cycles.

Most of the studies used a time horizon of one to three years, while dynamic models included in the review employed a 10-year time horizon. When death was included as a health state in the model, studies adopted a lifetime analytical horizon to account for costs and consequences of premature deaths within the timeframe. A total of seven studies conducted the analysis from both the payer and societal perspectives, seven conducted the analysis from the healthcare perspective only and two adopted the societal perspective.[300, 305] The same discount rates were applied to both costs and outcomes in 15 studies, ranging from 1.5% for Canada to 4% for Norway.[295, 309] In the multicentre study, differential discounting was applied for the Netherlands with a discount rate of 4% for costs and a rate of 1.5% for health effects.[298]

Dynamic transmission modelling can be used to model the direct and indirect effects that may arise from a communicable disease control programme.[317] They are particularly important when considering an intervention's impact on strain selection and disease transmission;[318] however, they are more complex and have increased data requirements compared with static models. Static models are considered acceptable when the target group for an intervention is not epidemiologically influential.[318] Thirteen studies used static modelling approaches, while three studies reported on two dynamic transmission models, including a model comparison study that compared the findings of three static models and two dynamic transmission models. Two of the three studies that reported on dynamic transmission models noted model assumptions that infants play a limited role in RSV transmission given that they have few contacts with others outside the household, and therefore that immunisation of this cohort is unlikely to have a noticeable effect on herd protection.[296, 297] In addition, the model comparison study reported similar outcomes for medically attended RSV cases between the static and dynamic models.[297]

In terms of health states, the majority of studies (n=10) did not account for non-medically attended RSV cases.[294-298, 302-305, 309] Four studies conducted in infants population considered the long-term complications of RSV such as asthma and recurrent wheezing either in base case or scenario analysis with different follow-up periods.[295, 298, 299, 307]

5.5.2 Intervention and immunisation strategies

The majority of studies that focused on infant populations modelled alternative infant immunisation strategies with variations in administration time and immunisation forms, except for one study that only analysed a single strategy.[302] Regarding the studies focused on older adults, the majority of these evaluated universal vaccination for adults aged 60 years and older in the general population.[300, 301, 305, 308] Only one study considered offering vaccination to different

age groups in the base-case analysis,[309] while two other studies considered age stratification in the scenario analysis.[305, 308] Similarly, despite higher reported incidence of severe RSV-related disease outcomes among older adults with a chronic medical condition, only one study analysed a risk-based vaccination strategy.[309] This may be due to the limited data availability on the incidence of RSV among the older adults with chronic conditions. One study also mentioned the difficulty of administering such risk-based strategies at the population level.[305] While several of the studies included year-round immunisation programmes, these were not prioritised for inclusion in this HTA given that the majority of the data available relate to seasonal administration or administration close to the start of the RSV season.

5.5.3 Intervention characteristics

All of the studies derived the intervention efficacy data from published trials. Due to the recent implementation of population-based immunisation programmes, real world evidence on the effectiveness of vaccines and monoclonal antibodies was not available at the time these economic studies were conducted. The majority of studies reported on intervention efficacy parameters against multiple outcomes related to health service usage such as protection against primary care visits, ED visits, hospitalisation and ICU admissions, although there was some variability between studies. Of the 11 studies that reported on immunisation against RSV in infants, three studies reported specific efficacy estimates for different risk groups, such as the term status of the infant.[294, 306, 307] Among older adults, across studies, efficacy was not assumed to vary by age or chronic medical condition status.

For infants, modelled efficacy was typically in line with their authorised indications of up to 150 days for nirsevimab and 180 days for maternal vaccination, assuming 0% efficacy thereafter or linear waning to 0% by 9 or 10 months after birth. Among older adults, each of the five studies reported vaccine efficacy for both RSVPreF3 and RSVpreF over a maximum of two years, although they differed in their approach to waning immunity. The approach to waning immunity was noted to influence the cost effectiveness findings, with studies typically reporting higher PPDs at which strategies were cost-effective with linear waning.[300, 308]

Assumed vaccine coverage rates varied across the studies. The majority of the studies were undertaken prior to the implementation of population-level vaccination programmes, requiring them to make assumptions based on other existing vaccination or preventative care programmes. The modelled coverage rates for maternal vaccine ranged from 60% to 100%, and for nirsevimab ranged from 71% to 100%. For vaccination of older adults, modelled coverage rates varied from 20% to 100%. One study assumed different coverage rates based on age and the presence of at least one chronic condition.[309] Another study assumed different

coverage rates among long-term care home residents and community dwelling adults.[308] Variability across the studies is expected as the coverage rates adopted should be country-specific. In Ireland, the RSV Immunisation Pathfinder Programme was implemented for the 2024/2025 RSV season, offering nirsevimab to all infants born between 1 September 2024 and 28 February 2025, and was subsequently extended to include a catch-up programme for the 2025/26 season for infants aged less than six months entering their first RSV season.[11] The cumulative national uptake rate of the programme for the 2024/25 season was 83%.

Costs and effects

The type of direct medical costs associated with RSV that were included was largely consistent across studies and reflected the health states of the models. GP visits and hospitalisations were the most frequently reported direct costs, though some studies also considered a separate ED cost in addition to inpatient care. The additional cost of the medical ventilation for ICU patients was considered by few studies only.[308] Four studies included costs related to long-term complications (for example, recurrent wheezing, asthma).[295, 298, 299, 307] Three studies included the costs of vaccine-related adverse events.[301, 305, 309] Direct medical costs pertaining to vaccine acquisition were consistently included in all studies. Eleven studies also included direct costs associated with vaccine administration.[294-296, 298, 299, 302-306, 308, 309] Only three studies included the cost related to vaccine wastage.[294, 303, 309] Direct costs to the patient, including transport and medication, were considered in four studies.[299, 301, 303, 309] Productivity losses associated with RSV infections were included where appropriate, that is, where the societal perspective was adopted.[295, 297-300, 303, 305, 306, 308, 309] Seven studies included a productivity loss for carers, [295, 297-299, 303, 306, 309] of which one study was for older adult vaccination.[309] Six studies included productivity loss due to premature death, of which two were among infants,[299, 303] and four were among older adults.[300, 308, 309]

Outcome measures included in studies generally included RSV cases, ED visits, ICU admissions, hospitalisations and RSV-related deaths. Only three studies included non-medically attended cases as outcomes.[297, 304, 307] Four studies also considered long-term complications such as recurrent wheezing and asthma in the model.[295, 298, 299, 307] Only three studies considered vaccine-related adverse events as an outcome in their analysis.[301, 305, 309] Health outcomes were measured in QALYs in all studies. Studies reported a range of disutility values and QALY losses associated with the health outcomes. However, the disutility values were generally poorly reported across studies, particularly in studies in infants.

5.5.4 Author's conclusion

Across the included studies that evaluated the cost effectiveness of immunising infants against RSV, the cost effectiveness estimates were strongly influenced by the assumed PPD/CPPA. The likelihood of a given strategy being optimal was influenced by the relative prices. Assumptions regarding costs differed substantially across studies, ranging from €50 to CAD $1,065 for nirsevimab and from €50 to CAD $230 for the maternal vaccination. In general, replacing palivizumab with nirsevimab for infants at high risk of severe disease was concluded to be cost effective or cost saving from the chosen perspective. Similarly, nirsevimab and the maternal vaccine were deemed cost effective at various combination of prices; however, cost effectiveness was typically highly sensitive to the assumed unit price (or price per dose delivered) of these interventions and frequently at a significant reduction relative to their list price. Moreover, where strategies were compared, the relative price of the vaccines was influential in conclusions regarding the optimal strategy. In terms the timing of administration, seasonal-based strategies were generally concluded to be cost effective compared with year-round strategies. This was likely influenced by the assumptions regarding waning immunity and the risk that infants would not be protected for the duration of the RSV season if immunised several months earlier. Of the three studies that evaluated the cost effectiveness of a combined strategy with maternal vaccination provided as first line and a monoclonal antibody provided to infants unprotected from maternal vaccination, two studies concluded that the cost effectiveness of the strategy was dependent on the PPDs while the third study concluded the strategy was not cost effective compared to other standalone programmes.[299, 303, 306]

All the studies that evaluated the cost effectiveness of older adult vaccines were non-industry funded. Four studies concluded that a single dose vaccination strategy for adults aged 60 years and older or 65 years and older could be cost effective compared with no vaccination if there is a substantial reduction in vaccine price[300, 301, 305, 308] or if the protection from vaccination extends to a second RSV season. Only one study compared the cost effectiveness of universal age-based vaccination to a risk-based vaccination approach.[305] The study concluded the universal age-based vaccination is not cost effective compared with a risk-based strategy of offering vaccination to those aged 70 years and older with at least one chronic condition.[309]

5.5.5 Comparison with the previous systematic review

This rapid review was developed based on the structure of a previous systematic review published in 2021 that contained searches up until October 2020, prior to the authorisation of recently licensed forms of RSV immunisation against RSV.[289] While the current review excluded studies that only provided epidemiological outcomes of the RSV intervention, the 2021 systematic review included both epidemiological

studies (n=11 studies) and economic evaluations (n=11 studies) including two cost analyses. Additionally, the 2021 systematic review also included studies from low- and middle-income countries unlike the rapid review. Nine out of the eleven included economic evaluations assessed infant immunisation and the remaining two studies evaluated the vaccination of older adults. The costs of the interventions used in the individual studies were not reported in the review. Most of the studies reported economic outcomes in terms of cost per gained health outcome such as QALY and cost per averted healthcare service. As the 2021 systematic review was limited to studies that assessed the effectiveness and cost effectiveness of potential or hypothetical RSV vaccines and mAbs based on assumed product characteristics (dose, effectiveness, duration of protection) in the absence of clinical evidence, the findings are of limited relevance. Nevertheless, the systematic review was informative to develop the structure of the current review.

5.6 Conclusion

The objective of this rapid review was to examine the approaches taken to modelling the expected costs and benefits of RSV immunisation among infants and older adults in high income countries and to use the findings to inform the economic modelling of RSV immunisation in Ireland. The review identified a number of important features to be considered in the economic modelling of RSV immunisation strategies. Static decision-tree models were the most common model choice across the included studies. While dynamic transmission models capture the direct and indirect effects associated with a communicable disease control programme, they were less commonly used, likely reflecting a lack of available data, parameter uncertainty and insufficient evidence indicating that the target groups for immunisation are epidemiologically influential for onward transmission. Alternate immunisation strategies were modelled especially for the infant population. Nearly half of the studies adopted dual perspectives, considering both the payer and societal perspectives. Overall, the quality appraisal of the included studies did not raise major concerns. While included studies found immunisation of infants to be cost effective or cost saving, this was typically highly sensitive to the assumed unit price (or price per dose delivered) of these interventions and frequently at a significant reduction relative to their list price. Moreover, the optimal strategy (maternal vaccination or EHL-mAb) was influenced by their relative prices. Similarly, the cost effectiveness of offering vaccination toolder adults was found to be largely dependent on the PPD of the vaccines, and was cost effective typically only at a significant reduction relative to the vaccine list price. All of the features highlighted above will be considered when developing the de novo economic model of RSV immunisation specific to Ireland.

6 Economic Evaluation

Key points

- A Markov model was developed to characterise the incidence of medically attended cases of respiratory syncytial virus (RSV) in Ireland and estimate the cost effectiveness and budget impact of both an infant- and adult-based RSV immunisation programme. The budget impact of RSV immunisation for a cohort of adults aged 60 years and older with additional risk factors for severe disease was also estimated.
- Five alternative infant-based RSV immunisation strategies were assessed:
  - an extended half-life monoclonal antibody (EHL-mAb) offered seasonally at birth to infants born during the RSV season – strategy 1 (S1)
  - an EHL-mAb offered both seasonally at birth to infants born during the RSV season and as catch-up in the first month of the season to infants born prior to their first RSV season - strategy 2 (S2)
  - a maternal vaccine offered seasonally to pregnant women between 24 and 36 weeks' gestation where the estimated due date falls during the RSV season - strategy 3 (S3)
  - a combination of a maternal vaccine offered seasonally to pregnant women between 24 and 36 weeks' gestation where the estimated due date falls during the RSV season, and an EHL-mAb offered seasonally at birth to infants born during the RSV season who are not protected by maternal vaccination - strategy 4 (S4)
  - a combination of a maternal vaccine offered seasonally to pregnant women between 24 and 36 weeks' gestation where the estimated due date falls during the RSV season, and an EHL-mAb offered seasonally at birth to infants born during the RSV season who are not protected by maternal vaccination, and an EHL-mAb offered as catch-up in the first month of the season to infants born prior to their first RSV season - strategy 5 (S5).
- Four alternative adult-based RSV immunisation strategies were assessed with immunisation offered to those aged:
  - 65 to 69 years in year one of the programme and those aged 65 years only in subsequent years – strategy 6 (S6)
  - 70 to 74 years in year one of the programme and those aged 70 years only in subsequent years – strategy 7 (S7)
  - 75 to 79 years in year one of the programme and those aged 75 years only in subsequent years – strategy 8 (S8)

  - 80 years and older in year one of the programme and those aged 80 years only in subsequent years – strategy 9 (S9).

- Model parameters including but not limited to disease incidence, hospitalisation and mortality rates, EHL-mAb and vaccine efficacy, transition probabilities, costs and utility values were estimated from a variety of published sources and national datasets for Ireland.

- Compared with no immunisation, the epidemiological analysis indicated that:
  - For the infant-based strategies, the estimated reduction in the annual number of medically attended RSV cases in those aged up to one year, ranged from 43.2% for S2 (coverage rates of 82.6% and 76.0% for seasonal and catch-up EHL-mAb, respectively) to 11.6% for S3 (coverage rate of 62%). The highest reductions in medically attended RSV cases were reported in the 0- to 2-month-old age group, at 52.8% and 22.6% for S2 and S3, respectively.
  - The estimated reduction in the annual number of hospitalised cases in those aged up to one year ranged from 52.1% for S2 to 12.2% for S3. The highest reductions in hospitalised cases were reported in the 0- to 2-month-old age group, at 62.5% and 23.3% for S2 and S3, respectively.
  - For the adult-based strategies, the estimated reduction (compared with no immunisation) in the total number of medically attended RSV cases in the immunised age group over the five years of the model, ranged from 41.9% for S8 (coverage rate of 88.4%) to 28.2% for S6 (coverage rate of 60.1%).

- From both the payer and societal perspectives, the base-case incremental cost-effectiveness ratios (ICERs) for all infant- and adult-based RSV immunisation strategies assessed, exceeded willingness-to-pay (WTP) thresholds of €20,000 and €45,000 per quality-adjusted life-year (QALY) gained.
  - At assumed prices of €301 and €165 (ex VAT) for the EHL-mAb and maternal vaccine, respectively, the ICERs for the infant-based strategies were €210,000 per QALY for S5 compared with no immunisation, and €310,000 per QALY for S2 compared to S5. All other infant-based strategies were eliminated in the incremental analysis. Sensitivity analysis demonstrated that at a price of €166 or less (ex VAT) for the EHL-mAb and a price of at least €90 for the maternal vaccine, S2 would be cost effective compared with no immunisation at a WTP threshold of €45,000 per QALY. At a price of €47 or less (ex VAT) for the maternal vaccine and a price of at least €190 for the EHL-mAb, S3 would be cost

effective compared with no immunisation at a WTP threshold of €45,000 per QALY.
  - At a price of €165 (ex VAT) for the adult vaccine, S9 dominated (less costly and generated more QALYs) all other adult-based RSV immunisation strategies. The ICER for S9 was €232,576 per QALY compared with no immunisation. Sensitivity analysis demonstrated that at a vaccine price of €20 or less (ex VAT), that is an 88% reduction from base case, S9 would be cost effective compared with no immunisation at a WTP threshold of €45,000 per QALY.

- In terms of budget impact:
  - Assuming a price of €301 + VAT for an EHL-mAb (a seasonal coverage rate of 82.6% and catch-up coverage rate of 76%) and a price of €165 + VAT for the maternal vaccine (coverage rate of 62%), the five-year incremental budget impact for the infant-based strategies ranged from €15.6 million for S3 to €58.5 million for S2.
  - Assuming a price of €165 + VAT for the adult vaccine and coverage rates ranging from 60.1% (S6) to 88.4% (S8 and S9), the five-year incremental budget impact for the adult-based immunisation strategies ranged from €70.6 million for S9 to €73.7 million for S6.

- Based on a coverage rate of 97.8%, the total budget impact over five years for the full cohort of adults aged 60 years and over with additional risk factors for severe disease due to comorbidity or who are resident in a long-term care facility (LTCF) was estimated at €93.4 million. Of this figure, €7.9 million related to vaccine procurement, administration and pick and pack for those resident in a LTCF.

- All models are subject to limitations due to both the quantity and quality of data available to populate the models. The applicability of the findings is dependent on the underlying assumptions that underpin the model structure and the chosen parameter values. Despite these limitations, the infant-based model outputs broadly align with those reported by the HSE for the 2024/25 Pathfinder RSV immunisation programme. Based on extensive scenario and sensitivity analyses, the findings of the economic evaluations presented are largely robust to data and structural assumptions with the exception of the uncertainty over the price of EHL-mAbs and vaccines.

- Based on the analyses presented, RSV immunisation would be associated with significant reductions in medically attended cases and RSV hospitalisations, with the greatest impact seen in the paediatric setting due to the higher burden of disease in this cohort. However, these benefits would come at a high

financial cost. Considerable reductions in the estimated current vaccine and EHL-mAb prices would be required for either an infant- or adult-based RSV immunisation programme to represent an efficient use of healthcare resources in Ireland. As such, policy decision-making regarding the potential introduction of an RSV immunisation programme in Ireland should consider both the price and the relative prices of EHL-mAbs and RSV vaccines that can be achieved in the tendering process.

6.1 Introduction

An economic model of respiratory syncytial virus (RSV) immunisation for both infants aged up to one year and the general population aged 65 years and older in Ireland were developed as part of this HTA. This chapter describes the cost-utility analysis (CUA) and budget impact analysis (BIA) for both the infant and adult RSV immunisation programmes under consideration. It also considers a BIA for adults aged 60 years and over with additional risk factors for severe disease due to comorbidity or who are resident in a long-term care facility (LTCF).

6.2 Methods

The analyses described in this chapter were conducted in line with national HTA guidelines,[317, 319] reported in accordance with the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) statement,[320] and undertaken in Microsoft Excel® 2016.

6.2.1 Study objective

The purpose of this economic analysis was to estimate the cost effectiveness and budget impact of RSV immunisation programmes for infants aged up to one year and the general population aged 65 years and older in Ireland. The CUA estimates the costs and outcomes of an RSV immunisation programme, comparing immunisation strategies with no immunisation and or alternative strategies, while the BIA provides a means to predict the potential financial impact of introducing an RSV immunisation programme.

6.2.2 Intervention

The economic model for an immunisation programme for infants aged up to one year assessed the following five alternative immunisation strategies, offered either seasonally (during the RSV season from September to February inclusive each year) or seasonally and as a catch-up:

- an extended half-life monoclonal antibody (EHL-mAb) offered seasonally at birth to infants born during the RSV season – strategy 1 (S1)
- an EHL-mAb offered both seasonally at birth to infants born during the RSV season and as catch-up in the first month of the season to infants born prior to their first RSV season - strategy 2 (S2)
- a maternal vaccine offered seasonally to pregnant women between 24 and 36 weeks' gestation where the estimated due date falls during the RSV season - strategy 3 (S3)
- a combination of a maternal vaccine offered seasonally to pregnant women between 24 and 36 weeks' gestation where the estimated due date falls during the RSV season, and an EHL-mAb offered seasonally at birth to infants born during the RSV season who are not protected by maternal vaccination - strategy 4 (S4)
- a combination of a maternal vaccine offered seasonally to pregnant women between 24 and 36 weeks' gestation where the estimated due date falls during the RSV season, and an EHL-mAb offered seasonally at birth to infants born during the RSV season who are not protected by maternal vaccination, and an EHL-mAb offered as catch-up in the first month of the season to infants born prior to their first RSV season - strategy 5 (S5).

For the purpose of costing the infant immunisation strategies, the following assumptions were made regarding the administration of an EHL-mAb and a maternal vaccine:

- an EHL-mAb offered to those born during the RSV season would be administered in maternity hospitals
- an EHL-mAb offered to those born outside the RSV season would be administered in a primary care setting
- a maternal vaccine would be administered in a primary care setting.

The economic model for an immunisation programme for the general population aged 65 years and older assessed four single-dose (once-off) immunisation strategies where a vaccine would be offered in the six weeks prior to the anticipated onset of the RSV season. Eligibility for these four immunisation strategies included individuals:

- aged 65 to 69 years in year one of the programme and those aged 65 years only in subsequent years – strategy 6 (S6)
- aged 70 to 74 years in year one of the programme and those aged 70 years only in subsequent years – strategy 7 (S7)
- aged 75 to 79 years in year one of the programme and those aged 75 years only in subsequent years – strategy 8 (S8)
- aged 80 years and over in year one of the programme and those aged 80 years only in subsequent years – strategy 9 (S9).

For the purpose of costing the immunisation strategies for the general population aged 65 years and older, it was assumed that the vaccine would be administered in the primary care setting.

6.2.3 Target population

A population of approximately 5.4 million people was stratified into age cohorts based on the current population distribution in Ireland,[321] with the following age groups included in the models:

- Infant model
  - 0 to 2 months
  - 3 to 5 months
  - 6 to 11 months
  - 1 to 2 years
- Adult model
  - 65 to 69 years
  - 70 to 74 years
  - 75 to 79 years
  - 80 years and older.

6.2.4 Study design

Two CUAs were undertaken to estimate the incremental cost and health benefits associated with RSV immunisation for infants and adults, comparing immunisation to no immunisation and or alternative immunisation strategies. The analysis was undertaken within a decision-analytic framework that simulated the costs and patient outcomes associated with RSV over a five-year time period. Health benefits were expressed in terms of quality-adjusted life-years (QALYs), which reflect the impact of the intervention on individual patients' quality and quantity of life. The BIA estimated the five-year incremental cost to the Health Service Executive of implementing RSV immunisation programmes for infants aged up to one year, adults in the general population aged 65 years and older, and separately adults aged 60 years and older with additional risk factors for severe disease.

6.2.5 Model overview

A probabilistic, age-structured Markov model of RSV was developed for Ireland. The model structure was informed by a review of economic models published for high-income countries (Chapter 5). The model, developed in Microsoft Excel® 2016, describes the transmission and incidence of medically attended RSV in the general population in Ireland. RSV is a notifiable disease in Ireland and data on notified cases are published by the Health Protection Surveillance Centre (HPSC) and publicly available.[322] It is accepted that notification data underestimate the true incidence of

medically attended RSV in Ireland as not all suspected cases are laboratory confirmed. In order to estimate the incidence of medically attended RSV in Ireland, a multiplier was applied to the notified case data. This multiplier was estimated based on the difference between the incidence of medically attended RSV reported in the international literature and incidence based on the notified case data for Ireland.[112, 113, 323]

6.2.6 Model structure

A Markov chain simulation model was developed to include the costs (in Irish Euro) and outcomes (QALYs) with and without immunisation. The model comprised the following health states:

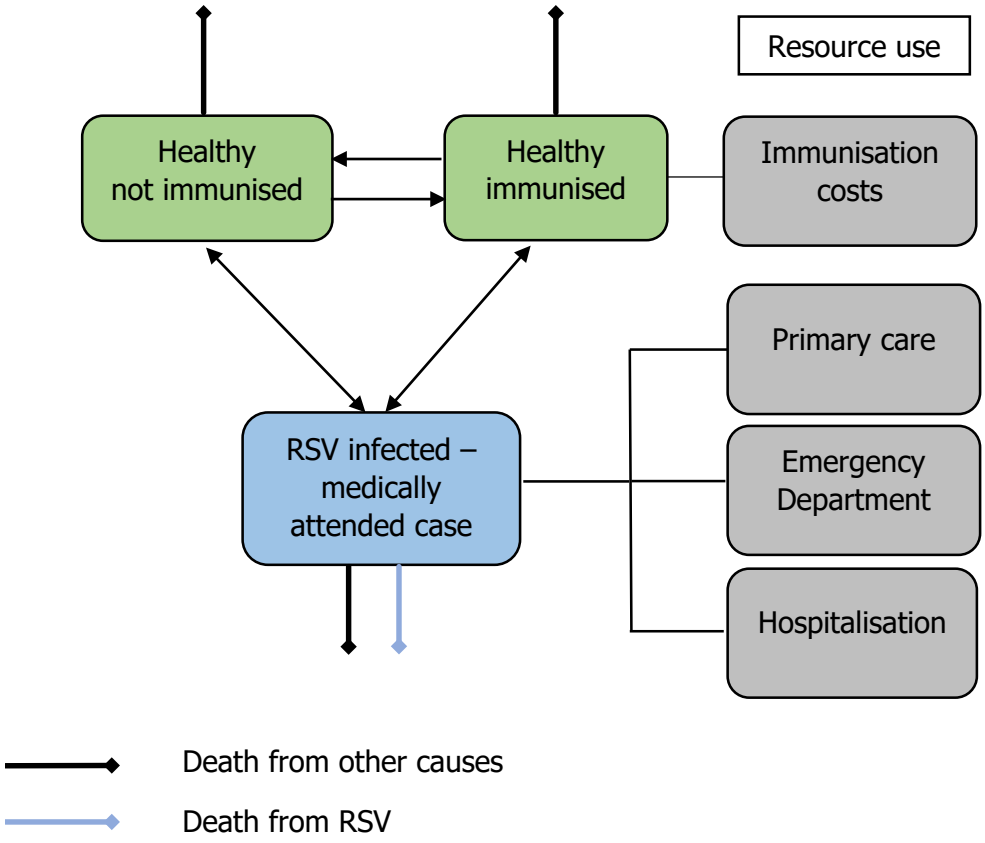
- healthy – not immunised
- healthy – immunised
- medically attended RSV (including primary care visit, presentation at the emergency department (ED) and hospitalisation)
- RSV-related death
- all-cause death.

The cohort enter the model in the *healthy - not immunised* state after which individuals move through the model in weekly cycles. A schematic of the Markov model is presented in Figure 6.1. Given that the model was built based on medically attended cases, for costing purposes it was assumed that all individuals infected with RSV, and who move to the *RSV infected* state, attend their GP at least once during the course of their illness, with a proportion requiring an ED visit and or hospitalisation which may include a period in intensive care. Following RSV infection, individuals who have not died due to RSV or another cause return to the *healthy - not immunised* state. If immunised, an individual moves to the *healthy – immunised* state, where susceptibility to RSV is reduced in line with monoclonal antibody or vaccine effectiveness as appropriate. As above, it was assumed that all immunised individuals infected with RSV, and who move to the *RSV infected* state, attend their GP, with a proportion requiring an ED visit and or hospitalisation. Following RSV infection, individuals who have not died due to RSV or another cause return to the *healthy - not immunised* state. Individuals move from *the healthy – immunised* state back to the *healthy – not immunised* state based on waning immunity.

For the economic evaluation, costs and QALYs were assigned to health outcomes in the absence of, and with an RSV immunisation programme, enabling the calculation of the incremental costs and incremental QALYs associated with alternative RSV immunisation strategies. The BIA model included cost savings (primary care and hospitalisation) as a result of immunisation. The net budget impact per annum and

total budget impact over five years were estimated, defined as the difference in average annual costs between immunisation and no immunisation.

Figure 6.1 Schematic representation of model structure



Key: RSV – respiratory syncytial virus.

6.2.7 Perspective, time horizon and discounting

In the base-case analysis, the CUA adopted the perspective of the Irish publicly funded health and social care system (that is, the payer), namely the HSE. In line with recommended good practice guidelines for the economic analysis of vaccination programmes and given the expected impact on productivity, a societal perspective was also adopted.[324] For the payer perspective, only direct medical costs to the HSE were incorporated. For the societal perspective, direct medical costs to the HSE, indirect costs such as productivity losses associated with morbidity for individuals with the disease, out-of-pocket expenses incurred by individuals for GP visits and medication, and opportunity costs associated with publicly funded GP care, were included in the analysis.

Costs and outcomes were estimated over a five-year time horizon except for the QALY and productivity losses associated with RSV-related death which were

estimated based on a lifetime time horizon. For those who recovered from RSV infection, we assumed no long-term sequelae (Chapter 3, Section 3.2). All costs and outcomes were discounted at a rate of 4% as specified in national guidelines.[317] Discounting reflects a societal preference for benefits to be realised in the present and costs to be experienced in the future. In the BIAs, the incremental costs associated with introducing an RSV immunisation programme were estimated over a five-year time horizon. To reflect the actual cost to the HSE in each year reported, and ensure consistency with national guidelines,[319] no discounting was applied in the BIAs.

6.2.8 Model input parameters

Incidence rates, probabilities, costs and utility values were estimated from a variety of published sources and national datasets for Ireland, including those published by the Central Statistics Office (CSO), the Healthcare Pricing Office (HPO) (for Hospital InPatient Enquiry [HIPE] data), and the HPSC. These sources were also supplemented by input provided by experts where necessary. Additionally, the National Immunisation Office (NIO) provided input and advice relating to immunisation programme costs relevant for Ireland.

Model inputs were selected with consideration to the hierarchy of evidence, as well as generalisability to the Irish context. Inputs for the BIAs were consistent with those used in the CUA with the exception of the addition of VAT (where applicable). In line with national guidelines, only direct costs were included and indirect costs, such as productivity gains associated with reduced morbidity arising from immunisation, were excluded from the BIAs.[319] All economic model input parameters are provided in Appendix A 6.1.

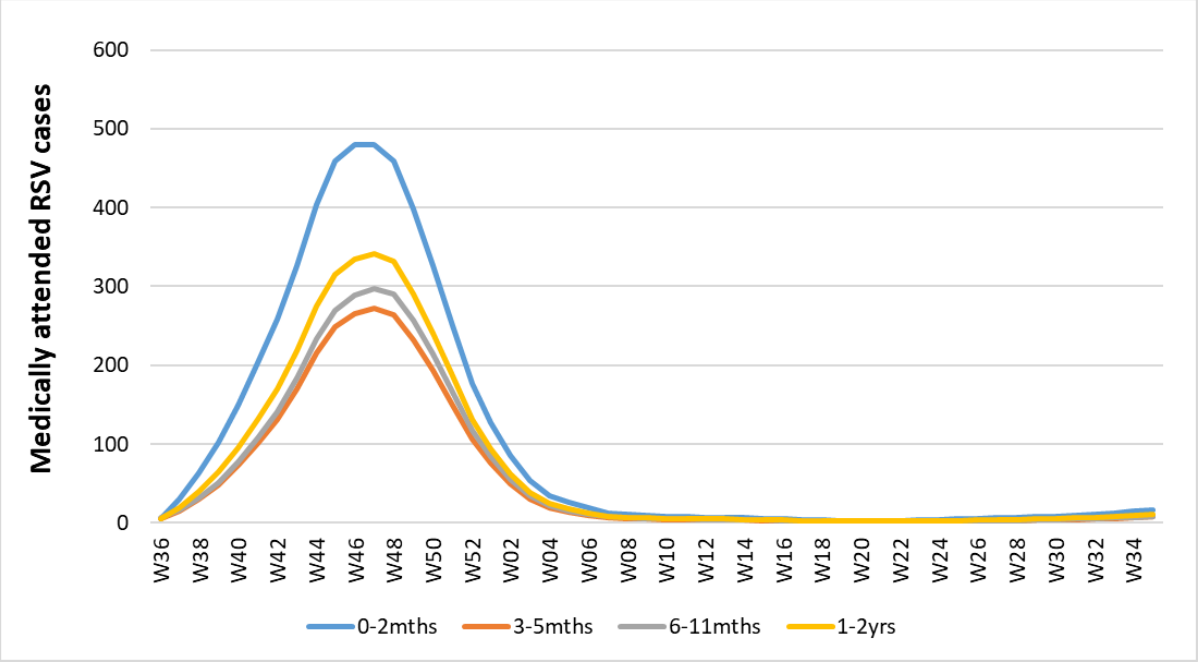
6.2.8.1 Health outcomes – medically attended RSV

The model was built using Irish demographic data and epidemiological data of notified RSV cases sourced from the HPSC.[322] As testing for RSV is not conducted on all suspected cases, the notified case data do not fully reflect the incidence of medically attended RSV. As such, to estimate the incidence of medically attended RSV, a multiplier of four was applied to the notified case data. That is, for every notified case, it was assumed that three more RSV cases (that are not confirmed through testing) present for medical attention. This multiplier was estimated based on the difference between the incidence of medically attended RSV reported in the international literature and incidence based on the notified case data for Ireland.[112, 113, 323]

To establish the base-case scenario without RSV immunisation, the model was developed based on an average RSV season in Ireland using observed notified RSV

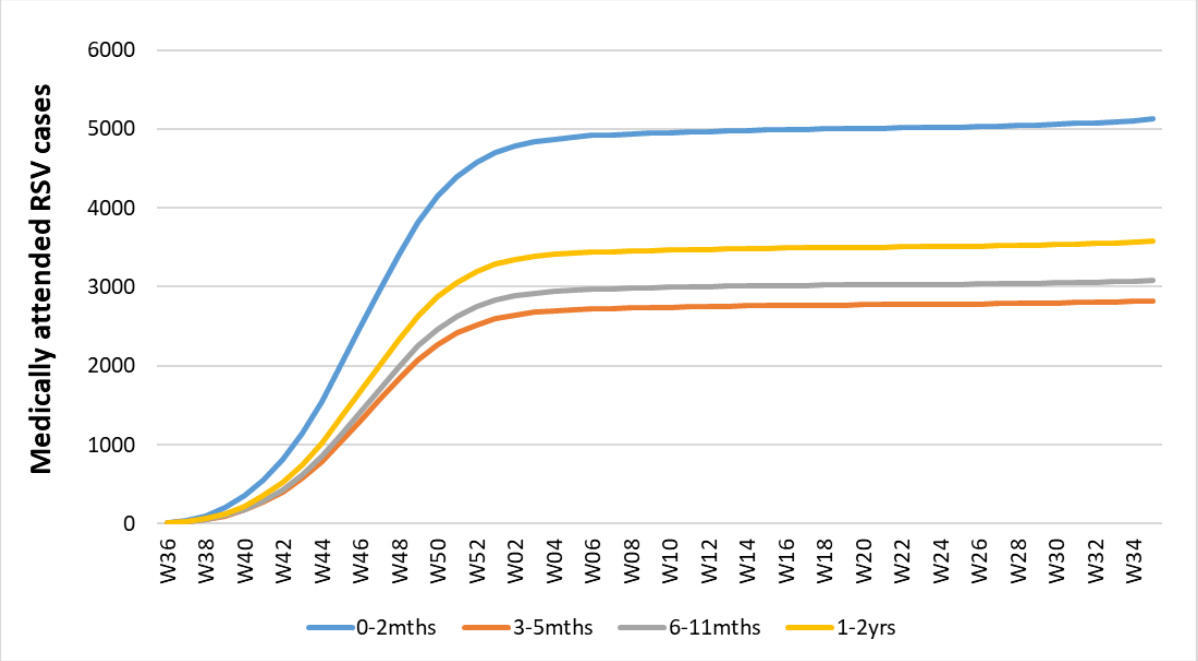
case data and then adjusted using the multiplier as described above. For those aged up to and including two years, case data from the most recent three RSV seasons (2021/22, 2022/23 and 2023/24) before the introduction of the HSE Pathfinder pilot RSV immunisation programme, were used (Figure 6.2 and Figure 6.3). For those aged 65 years and above, case data from the most recent three RSV seasons (2022/23, 2023/24 and 2024/25) were used (Figure 6.4 and Figure 6.5). The LOESS method was used to smooth the RSV incidence data. RSV-related mortality in Ireland (Chapter 3, section 3.5.3) was also incorporated into the model. In the Markov model, movement between health states (that is, disease progression) was governed by transition probabilities. As the model uses a one-week cycle length, annual transition probabilities and instantaneous event rates from published literature sources were converted to one-week probabilities of event occurrence. This method assumes that the event rate is constant over time.[325]

Figure 6.2 Average number of medically attended RSV cases each week in Ireland by age group up to 2 years of age



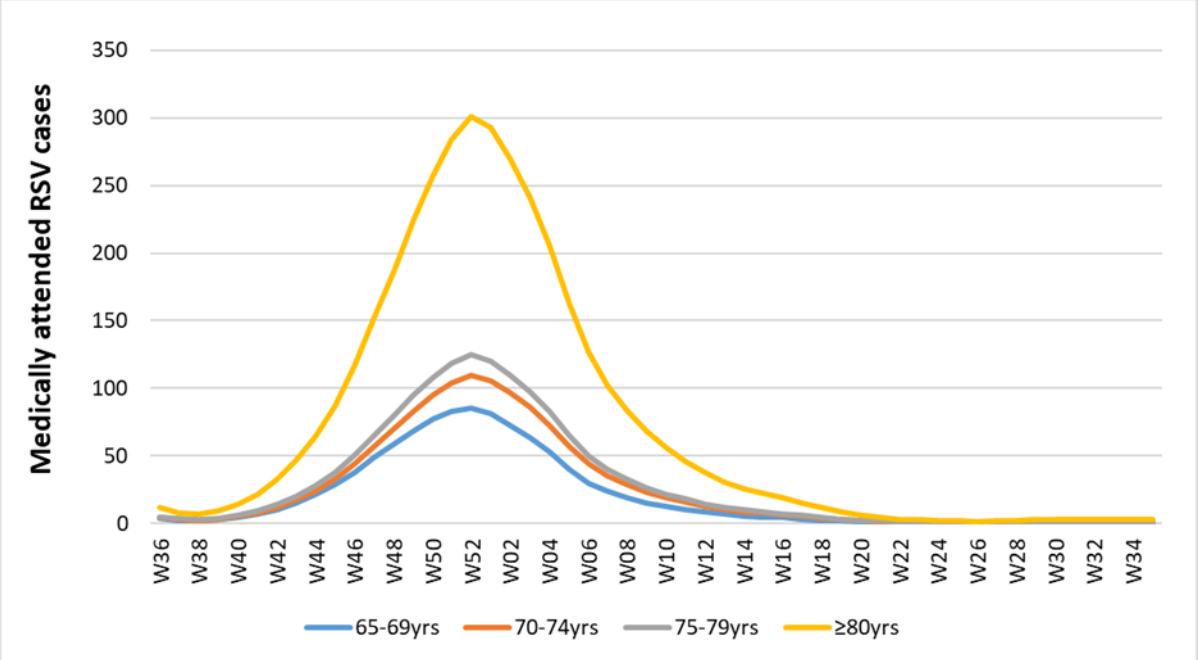
Note: Average based on HPSC notified case data from 2021/22 to 2023/24 and with a multiplier of four applied.

Figure 6.3 Average cumulative number of medically attended RSV cases each week in Ireland by age group up to 2 years of age



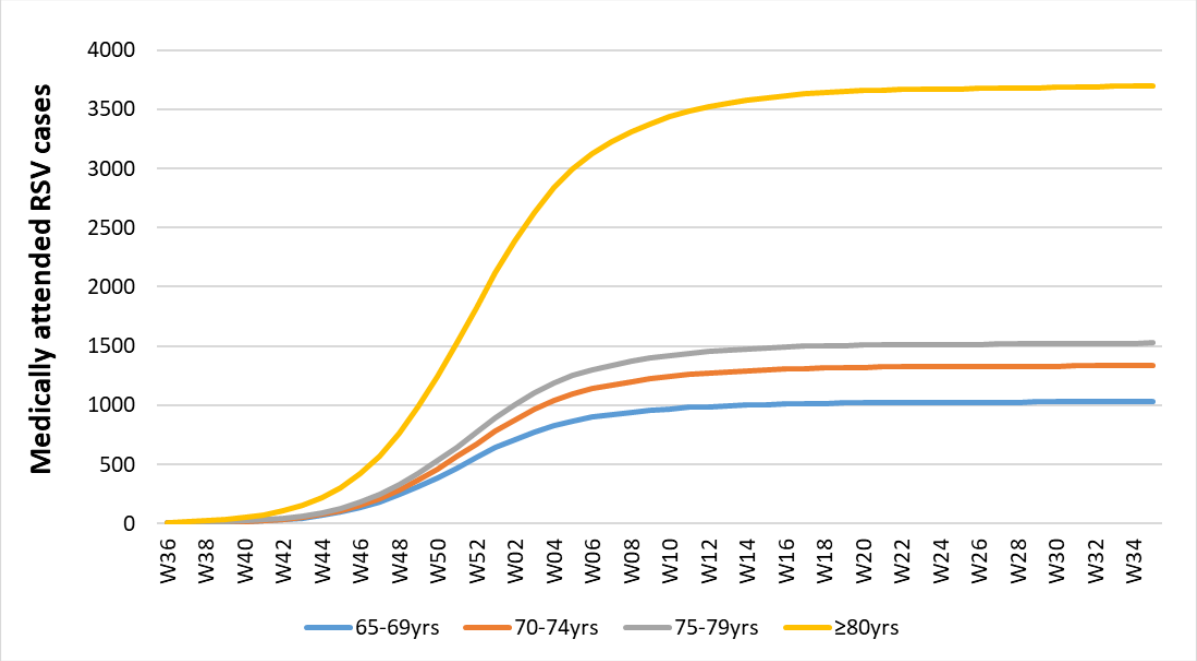
Note: Average based on HPSC notified case data from 2021/22 to 2023/24 and with a multiplier of four applied.

Figure 6.4 Average number of medically attended RSV cases each week in Ireland by age group from 65 years of age



Note: Average based on HPSC notified case data from 2022/23 to 2024/25 and with a multiplier of four applied.

Figure 6.5 Average cumulative number of medically attended RSV cases each week in Ireland by age group from 65 years of age



Note: Average based on HPSC notified case data from 2022/23 to 2024/25 and with a multiplier of four applied.

The total number of medically attended RSV cases (by age group, week and year) for each of the immunisation strategies was obtained from the Markov model output. As noted, it was assumed that all medically attended RSV cases attend primary care at least once during the acute illness episode, that a proportion attend the ED and that a proportion develop severe disease requiring hospitalisation. The probability of medically attended RSV cases attending the ED and requiring hospitalisation (Table 6.1) was estimated from the medically attended RSV case data described above and data provided by the HPSC which detailed the number of notified RSV cases that presented at the ED and the number of notified RSV cases hospitalised (Chapter 3, Section 3.5).

Table 6.1 Estimated probability of emergency department visits and hospitalisation among medically attended RSV cases

Age group	Estimated probability of ED visit for medically attended RSV case			Estimated probability of hospitalisation for medically attended RSV case		
	Mean (%)	Minimum (%)	Maximum (%)	Mean (%)	Minimum (%)	Maximum (%)
0-2 months	10.3	8.7	11.6	13.1	12.2	14.8
3-5 months	11.4	10.8	11.8	11.7	11.3	11.9
6-11 months	11.5	10.8	12.1	11.0	10.6	11.3
1-2 years	10.9	11.1	12.4	11.7	10.5	12.6
65-69 years	7.5	7.4	7.6	8.0	7.4	8.4
70-74 years	6.1	1.8	9.0	9.1	7.9	10.1
75-79 years	7.4	7.1	7.5	9.2	8.4	10.2
≥80 years	6.4	6.1	6.9	9.1	8.2	10.2

Source: Estimated based on HPSC notified case data and HIPE data.[322, 326]

Chapter 4 presented the results relating to medically attended RSV-associated lower respiratory tract illness (LRTI) or lower respiratory tract disease (LRTD) and RSV-associated hospitalisation. The reported efficacy against hospitalisation represented the risk ratio across all trial participants. For the purposes of modelling, the risk ratio for hospitalisation was expressed conditional on having RSV as it is only applied to medically attended RSV cases. On this basis, the following were applied in the model:

- Passive immunisation of infants and young children through EHL-mAbs reduces medically attended RSV-associated LRTI over one season, with an estimated efficacy of 69% ((95% CI: 60% to 75%) pooled data from three RCTs; high certainty of evidence).
- Conditional on having RSV, passive immunisation of infants and young children through EHL-mAbs reduces RSV-associated hospitalisation, over one season, with an estimated efficacy of 46% ((95% CI: -47% to 81%) pooled data from three RCTs; high certainty of evidence).
- Passive immunisation of infants and young children through maternal vaccination reduces medically attended RSV-associated LRTD over 180 days,

with an estimated efficacy of 49% ((95% CI: 32% to 62%) one RCT; moderate certainty of evidence).

- Conditional on having RSV, passive immunisation of infants and young children through maternal vaccination reduces RSV-associated hospitalisation over 180 days, with an estimated efficacy of 12% ((95% CI: -34% to 42%) one RCT; moderate certainty of evidence).
- Active immunisation of older adults through vaccination reduces medically attended RSV-related LRTD, with an estimated efficacy of 78% ((95% CI: 51% to 90%) pooled data from two RCTs) in year one and 53% ((95% CI: 28% to 70%) pooled data from two RCTs) in year two. Based on data from one RCT, the efficacy in year three was assumed to be the same as that in year two.
- For older adults, there was an absence of evidence to confirm efficacy against hospitalisation over and above a reduction in medically attended RSV. A pro-rata reduction in hospitalisation was applied for this cohort in line with the reduction in medically attended RSV.

In summary, efficacy data relating to medically attended RSV were applied in both the infant- and adult-based models. In addition to applying pro-rata reductions in ED presentations and hospitalisations (due to the reduction in medically attended RSV cases with immunisation) in both models, efficacy data relating to hospitalisation conditional on having RSV were also applied for the EHL-mAbs and maternal vaccine in the infant-based model.

6.2.8.2 Health outcomes – safety of enhanced half-life monoclonal antibodies and vaccines for protection against RSV

With respect to adverse events, the assessment of the safety of EHL-mAbs, the maternal vaccine and RSV vaccination of older adults (Chapter 4) demonstrated an increased risk of solicited adverse events in the older adult cohort only. Specifically, in older adults, compared with placebo, an increased risk (RR 1.30 (95% CI: 1.26 to 1.34)) of any unsolicited adverse event within one month following vaccination and an increased risk of solicited adverse events (RR 1.81 (95% CI: 1.77 to 1.85)) following vaccination were reported. Among older adults, the frequencies of severe solicited adverse reactions (Grade 3 or 4 reactions) among vaccine recipients compared with placebo recipients were: ≤0.7% vs. ≤0.7% (RSV mRNA), 4.1% vs 0.9% (RSVPreF3) and 6.2% vs 4.1% (RSVpreF). An increased risk of severe (Grade 3 or 4) solicited adverse reactions among older adult vaccine recipients and the associated impact on quality of life was incorporated into the model.

While there is some uncertainty relating to potential serious adverse events associated with RSV immunisation in older adults such as Guillain-Barré syndrome (GBS), the evidence suggests that these events are rare (Chapter 4). Given the uncertainty and lack of data to support the cost and QALY impact of GBS on adults who receive the RSV vaccine, it has not been incorporated into the model.

6.2.8.3 Quality of life estimates

In the model, health benefits are expressed in terms of quality-adjusted life years (QALYs) gained. QALYs reflect the impact of an intervention on patients' quality and length of life, estimated using self-reported utilities or health-related quality of life. For both infant and adult cohorts, a comprehensive search was conducted to identify original studies that elicited health state utility values (HSUV) or disutilities associated with medically attended RSV. Preference was given to utility values measured using generic preference-based measures such as the EQ-5D. Where HSUVs were not identified or it was not possible to estimate QALY losses derived from HSUVs, reported QALY losses for RSV were considered and used, where appropriate in the CUA.

For the infant cohort, in the absence of baseline and health state utility values associated with RSV, QALY losses were assigned based on data from the international literature (Table 6.2). The adult cohort was assigned Irish baseline utility values (by age group) at the outset of the model.[327] The baseline and health state utility values used to estimate QALYs for adults in the CUA are presented in Table 6.2. For the purpose of the adult cohort model, it was assumed that notified cases of RSV experience seven days' utility loss due to RSV. For those attending the ED, it was assumed that the duration of utility loss for each group is the sum of the duration of utility loss for non-hospitalised cases (seven days) plus half the duration (in days) of length of stay for those hospitalised with RSV. For those hospitalised due to RSV, it was assumed that the duration of utility loss is the sum of the duration of utility loss for non-hospitalised cases (seven days) and the duration (in days) of their stay in hospital (ranging from three days for those aged six months to two years, to 12 days for those aged 80 years and older). It was assumed that adult vaccine recipients who experience severe solicited adverse reactions experience non-hospitalised RSV-related utility loss for two days. Quality-adjusted life year loss due to RSV-related mortality was estimated over the life course using published life tables for Ireland.[328]

Table 6.2 Quality-adjusted life year losses for medically attended RSV

Age group	Primary care	ED attendance	Hospitalisation
0-2 months	0.006301	0.008219	0.010137
3-5 months	0.006301	0.008219	0.010137
6-11 months	0.006301	0.008219	0.010137
1-2 years	0.003811	0.003811	0.003811

Source: Mao et al. 2023[329], Hodgson et al. 2020[330]

Table 6.3 Baseline and health state utility values for medically attended RSV

Age group	Baseline*	Primary care and ED attendance	Hospitalisation
65-69 years	0.8790	0.74	0.46
70-74 years	0.8790	0.74	0.46
75-79 years	0.8410	0.74	0.46
≥80 years	0.8410	0.74	0.46

*Source: Irish baseline utility values – Hobbins et al. 2018.[327] Health state utility values – Chapter 5.

6.2.8.4 Immunisation programme inputs

Immunisation coverage for the infant-based RSV immunisation strategies was informed by:

- the uptake rate for the EHL-mAb under the HSE Pathfinder pilot programme for RSV immunisation in Ireland for those born during the 2024/25 RSV season[331]
- published international uptake rates for an EHL-mAb offered as part of a catch-up programme (Chapter 3)
- the uptake rate for maternal vaccines in Ireland.[332]

It is acknowledged that the uptake rate (76% - Table 6.4) assumed for an EHL-mAb as part of a catch-up programme is higher than the uptake rate achieved during the initial clinics (September 2025 to first week of October 2025) provided for this cohort under the HSE Pathfinder 2 pilot RSV immunisation programme for 2025/26 in Ireland. However, there was a limited period of time for this catch-up programme to be designed and implemented in Ireland, which in turn limited the opportunity to conduct stakeholder engagement, particularly to provide prenatal advice to mothers and to engage with them early after their child was born. Due to these challenges,

additional clinics are being offered for this cohort. The format of the catch-up programme under the HSE Pathfinder 2 pilot programme (dedicated immunisation clinics) does not reflect the likely implementation approach should a catch-up programme be rolled out as part of a long-term infant-based RSV immunisation programme. As such, the initial uptake of the catch-up programme under the HSE Pathfinder 2 pilot programme was considered a significant underestimate of potential uptake, and therefore our assumption has been informed by uptake rates from international programmes.

Estimated coverage rates for the infant-based RSV immunisation strategies are assumed to be unaffected when interventions are combined in strategies. For example, the coverage rate for S3 (seasonal maternal) is assumed to be 62%. In S4 (seasonal maternal and EHL-mAb) and S5 (seasonal maternal and EHL-mAb plus catch-up EHL-mAb), where interventions are combined, the coverage rate for the maternal vaccine is also assumed to be 62%. While knowledge that there are options that could impact uptake of each intervention, we have no basis for predicting how behaviour might change. Coverage for the adult-based RSV immunisation strategies was informed by uptake of the influenza vaccine in older adults in Ireland.[333] All coverage rates used in the models are summarised in Table 6.4 below.

Table 6.4 Assumed fixed coverage rates for RSV immunisation strategies

Immunisation strategy	Coverage (%)
S1 - seasonal EHL-mAb	82.6
S2 - seasonal EHL-mAb plus catch-up EHL-mAb	82.6 (seasonal EHL-mAb) and 76.0 (catch-up EHL-mAb)
S3 - seasonal maternal vaccine	62.0
S4 - seasonal maternal vaccine and EHL-mAb	62.0 (seasonal maternal vaccine) and 54.2 (seasonal EHL-mAb) 82.6 overall seasonal
S5 - seasonal maternal vaccine and EHL-mAb plus catch-up EHL-mAb	62.0 (seasonal maternal vaccine) and 54.2 (seasonal EHL-mAb) 82.6 overall seasonal 76.0 (catch-up EHL-mAb)
S6 - adult vaccine for those aged 65 to 69 years in year one and those aged 65 years each year thereafter	60.1
S7 - adult vaccine for those aged 70 to 74 years in year one and those aged 70 years each year thereafter	73.0
S8 - adult vaccine for those 75 to 79 years in year one and those aged 75 years each year thereafter	88.4

Immunisation strategy	Coverage (%)
S9 - adult vaccine for those aged 80 years and older in year one and those aged 80 years each year thereafter	88.4

Key: S1 - Strategy 1; S2 - Strategy 2; S3 - Strategy 3; S4 - Strategy 4; S5 - Strategy 5; S6 - Strategy 6; S7 - Strategy 7; S8 - Strategy 8; S9 - Strategy 9.

With respect to costs, the immunisation strategies under consideration in this economic analysis consider:

- product (RSV vaccine or monoclonal antibody) procurement costs
- administration costs (administration fee or a labour cost to reflect administration within the secondary care system)
- pharmaceutical technician costs to support delivery of a seasonal monoclonal antibody programme in maternity units
- HSE National Cold Chain Service (NCCS) 'pick and pack' costs calculated per unit of product
- costs relating to additional storage and distribution agreements for the HSE National Cold Chain Service (NCCS) for a new immunisation strategy
- the cost of a public health information campaign (year one only)
- the cost of development of a training module (year one only)
- a programme management cost to update IT and data systems to accommodate the addition of a new vaccine / immunisation agent to the immunisation schedule (year one only)
- the ongoing cost of a national programme manager to oversee implementation and operation of the programme.

The immunisation product, administration and pick and pack costs are variable and are influenced by the size of the eligible population for each strategy and uptake. All other costs are once-off implementation costs which would likely apply similarly with the introduction of any new programme(s). These costs would apply irrespective of the target populations considered and do not vary with immunisation uptake.

Included costs were informed by:

- the list price of products currently marketed in Ireland and information provided by the health technology developers in submitted dossiers

- international published contract prices for products not currently marketed in Ireland
- current payments to primary care contractors for the administration of vaccines
- HSE Consolidated Salary Scales[334]
- discussions with the National Immunisation Office (NIO) and those involved in the implementation of the HSE Pathfinder 2024/25 pilot programme for RSV immunisation in Ireland.

Table 6.5 Immunisation programme costs – base-case analysis

Cost item	Unit Cost (ex VAT)	Units
EHL-mAb	€301.12	Dependent on uptake
Maternal vaccine	€165.00	
Adult vaccine	€165.00	
EHL-mAb administration - seasonal programme Registered midwife (staff nurse) - per 15 minute consultation	€11.32	
EHL-mAb administration - catch-up programme	€19.73	
Vaccine administration - maternal vaccine	€25.00	
Vaccine administration - adult vaccine	€25.00	
Pick and pack (per single dose pack)	€1.39	
Storage and distribution (per annum)	€600,000	1
Pharmacy technician† (per annum)	€73,909	4.5 x WTEs
Programme manager (Grade VIII clerical) (per annum)	€137,488	1 x WTE
Once-off immunisation programme implementation costs		
Public health information campaign (infant programme)	€500,000	1
Public health information campaign (adult programme)	€500,000	1
Development of training module	€50,000	1
Programme management (IT system upgrade)	€1,000,000	1

Key: EHL-mAb - extended half-life monoclonal antibody; VAT: value-added tax; WTE – whole-time equivalent.

†To support seasonal EHL-mAb RSV immunisation programmes in maternity units only (resource requirement advised by the National Immunisation Office is equivalent to 4.5 whole-time equivalents).

6.2.8.5 Cost inputs

In accordance with national HTA guidelines, all costs are presented in 2025 Euro (€).[317, 319] All costs were derived from Irish sources; those from years prior to 2025 were adjusted using the Consumer Price Index for health and relevant sub-indices.[335] In the CUA, the costs associated with notified RSV from the payer perspective included the cost of GP visits for those with a GP visit or medical card, the cost of prescription medication for those with a medical card, and the cost of hospitalisation. The proportion of people with a GP visit and or medical card was sourced from HSE - Primary Care Reimbursement Service (PCRS) eligibility data as of July 2025.[336]

Table 6.6 Estimated proportion of the population assessed as eligible for a GP visit card or a medical card

Age group	Proportion of population eligible for GP visit card (%)	Proportion of population eligible for medical card (%)
0-2 months*	69.3	20.6
3-5 months*	69.3	20.6
6-11 months*	69.3	20.6
1-2 years*	69.3	20.6
65-69 years	3.8	36.5
70-74 years*	38.6	53.4
75-79 years	26.9†	73.1
≥80 years	26.9†	73.1

Source: Health Service Executive[336]
*All individuals in these age groups are eligible to apply for a GP visit card. As such, the rows should sum to 100%. Where they do not sum to 100%, the discrepancy may be due to the fact that those who are entitled to apply for a GP visit card may not have done so as yet or they may not have been able to register with a GP who holds a General Medical Service (GMS) Scheme contract.
†This figure was adjusted from 29.4% to ensure that the total proportion of the population eligible for a GP visit card or medical card in these age groups did not exceed 100%.

It was assumed that all of those with notified RSV would attend their GP. In the absence of Irish-specific data, the frequency of GP visits related to medically attended cases of RSV and the probability of a prescription being issued were

sourced from a number of international studies and expert opinion from Ireland (Table 6.7).[329, 337, 338] The average cost of a GP consultation for a public patient (€53.04) was sourced from a study that estimated unit costs for non-acute medical care in Ireland.[339]

HSE prescribing guidelines and recommended treatment courses for upper and lower respiratory tract infections were used to identify treatment items for RSV.[340] Cost data for these items were sourced from the PCRS (https://www.sspcrs.ie/druglist/pub). Estimates of the proportion of patients prescribed different medication classes were sourced from the literature.[337],[329] The average cost of prescription medication was estimated using relevant published guidelines.[341] While it is recognised that antibiotics are not effective for treating RSV, it was assumed that some of those presenting to their GP with RSV-like symptoms may be treated with antibiotics as symptoms may be clinically similar to bacterial respiratory tract infections. Details of the items included in estimating the average cost of prescription medication for RSV for both children and adults are included in Appendix A 6.2.

Table 6.7 Average number of GP visits per medically attended RSV case and probability prescription issued

Age group	Mean number of GP visits for notified case of RSV	Probability prescription issued for RSV (%)
0-2 months	2.7*	49.7*
3-5 months	2.7*	49.7*
6-11 months	2.7*	49.7*
1-2 years	2.1*	61.7*
65-69 years	2.0†	36.0‡
70-74 years	2.0†	36.0‡
75-79 years	4.0†	36.0‡
≥80 years	4.0†	36.0‡

Source:*Hak et al. 2025,[337] †Expert opinion; ‡ Mao et al. 2023[329]

Table 6.8 Estimated average cost of medication for individuals presenting with RSV

Age group	Prescription		Over-the-counter
	Public patient*	Private patient†	All patients†
Infants (≤1 year)	€5.70	€7.87	€9.14
1-2 years	€8.23	€11.23	€8.82
≥65 years	€8.11	€10.31	€19.87

*Used for payer perspective – see Appendix A 6.2 and Appendix A 6.3 for details of items included in estimate.
†Used for societal perspective – see Appendix A 6.3 for details of items included in estimate.
Note: Value-added tax was added where relevant for inclusion in the budget impact analysis.

The average cost of an ED visit provided by the HSE Healthcare Pricing Office (HPO) was estimated at €474.(326) The average cost of an RSV-related hospitalisation by age group was estimated based on cost data from HIPE (provided by the HPO for the period from 2018 to 2024) relating to hospitalisations with one of the following principal diagnoses:

- B97.4 (RSV as the cause of disease classified elsewhere)
- J12.1 (RSV pneumonia)
- J20.5 (acute bronchitis due to RSV)
- J21.0 (acute bronchiolitis due to RSV).

These cost data were adjusted for each age group based on the proportion of hospitalisations within each group that included an ICU stay (supplied by the HPSC). The costs provided in Table 6.9 are estimated average costs; individual cases could incur higher or lower costs depending on the underlying diagnosis, intensity of treatment and length of stay.

Table 6.9 Estimated cost of an RSV-related hospitalisation

Age group	Estimated average hospitalisation cost for a notified case of RSV* (€)
0-2 months	13,142
3-5 months	9,351
6-11 months	9,058
1-2 years	8,850
65-69 years	9,661

Age group	Estimated average hospitalisation cost for a notified case of RSV* (€)
70-74 years	9,177
75-79 years	9,105
≥80 years	8,530

*Source: Estimated based on data supplied by the Healthcare Pricing Office from the Hospital Inpatient Enquiry (HIPE) System[326]

In addition to the costs included in the payer perspective (described above), the societal perspective also included the following costs associated with medically attended RSV:

- Out-of-pocket expenses for those not eligible for a GP visit or medical card and who therefore incur GP consultation and prescription medication costs (transportation costs incurred to attend the GP were not included).
- Out-of-pocket expenses for over-the-counter medications to alleviate symptoms of RSV.
- Productivity loss of paid work, due to absenteeism, for those ill with medically attended RSV and those who are caring for children who are ill. The proportion of the population not eligible for a GP visit or medical card (and therefore considered private patients) was determined based on scheme eligibility data published by the HSE (Table 6.6). The average cost of a GP consultation for private patients (€58.67) was sourced from the literature.[339] The average cost of prescription medication issued to private patients was estimated as above for public patients and based on an average of three values: the estimated cost under the Drugs Payment Scheme; an estimated cost that included 20% mark-up and a €5 fee per item for the pharmacy; and an estimated cost that included no mark-up and a €10 fee for the pharmacy. The average cost of over-the-counter medication for RSV was estimated using current retail prices (assuming a five-day course) and data from international studies that estimate the proportion of people taking each medicine class.[337] Details of the items included in estimating the average cost of over-the-counter medication for RSV for both children and adults are included in Appendix A6.6

Estimates of the productivity loss to society due to absence from paid work for those ill with medically attended RSV and those caring for children who are ill, were valued using the Human Capital Approach by multiplying the days lost to health problems by median daily earnings.[342] The average number of work days lost per medically attended RSV case that did not present to the ED or was not hospitalised was

assumed to be five. This equates to the number of days of utility loss due to medically attended RSV without ED presentation or hospitalisation (n=7), minus two non-working days per week. For those presenting to the ED, it was assumed that the average number of work days lost was five (as above for those who only attend primary care) plus half the duration (in days) of length of stay for those hospitalised with RSV. For those hospitalised due to RSV, it was assumed that the average number of work days lost was five plus the duration (in days) of length of stay in hospital (ranging from three days for those aged six to 11 months, to 12 days for those aged 80 years and older).

Labour force data published by the Central Statistics Office (CSO) were used to estimate the proportion of the population in paid employment for each age group of the adult cohort model.[343] Census Data from 2022 include data on the number of children under 15 years of age in Ireland in childcare.[344] These data were used to estimate the proportion of the population in paid employment and caring for those aged up to one year with medically attended RSV (56%); this estimate assumes 0% in paid employment for those caring for infants aged less than six months, due to the availability of statutory maternity leave.[344] Earnings analysis data, published by the CSO, were used to estimate median daily earnings by age group (Table 6.10).[345] Based on the average age of mothers of newborns in Ireland being 33 years, it was assumed that caregivers for those aged up to one year with medically attended RSV would be in the 30–39-year-old age group.

Estimates of the productivity loss to society as a result of medically attended RSV-related mortality were also valued using the Human Capital Approach[342] and calculated using life tables, labour force and earnings data.[343-345]

Table 6.10 Proportion of the adult population in paid employment and estimate of median daily earnings by age group

Age group	Proportion of the population working (%)	Estimate of median daily earnings (€)
30-39 years	N/A*	169.25
65-69 years	28.4	129.79
70-74 years	17.2	129.79
75-79 years	0.08	129.79
≥80 years	0.03	129.79

Source: Central Statistics Office (CSO)[343-345]

N/A – not applicable. Note: While median earnings for this age group are relevant for estimating productivity losses for caregivers of children with medically attended RSV, the proportion in paid employment is not relevant. The relevant proportion for this calculation is the proportion of children

aged up to one year with medically attended RSV that require care from someone in paid employment (56%).

6.2.9 Model outputs

In the CUA, incremental costs and QALYs were estimated and then used to calculate a cost-effectiveness ratio — the incremental cost per QALY gained. In the first instance, immunisation strategies were compared with no immunisation to estimate an average cost-effectiveness ratio (ACER). The strategies were then ordered by increasing cost and compared with the previous least costly alternative to estimate an incremental cost-effectiveness ratio (ICER). In accordance with national HTA guidelines, the ICERs were reported relative to willingness-to-pay (WTP) thresholds of €20,000 and €45,000 per QALY gained.[317] For the BIA, incremental costs associated with, and costs averted as result of the introduction of an immunisation programme, were estimated and used to calculate the budget impact over five years.

6.2.10 Assessment and quantification of uncertainty

Probabilistic and deterministic sensitivity analyses (PSA and DSA, respectively) were conducted to test the robustness of the economic model outputs.

Sensitivity analysis for cost-utility analysis and budget impact analysis

Parameter uncertainty was assessed using a Monte Carlo simulation with 10,000 iterations. Each model parameter was defined by a statistical distribution to represent uncertainty in the mean parameter value. For each parameter, an appropriate statistical distribution was selected (for example, a beta distribution for a probability). Parameter values were then drawn as random variates from their specified distributions and the total costs and benefits were recalculated. The total costs and QALYs for each simulation were recorded and used to quantify the proportion of simulations that were considered cost effective with respect to an illustrative WTP threshold (that is, €45,000 per QALY). The output was presented on a cost-effectiveness plane. While there is no specific guidance available on the optimal number of simulations necessary to reach convergence,[346] model convergence was assessed after 10,000 simulations.

One-way sensitivity analysis (OWSA) for each immunisation strategy was conducted by fixing each parameter in turn at its upper and lower bounds, while all other parameters were held at their mean. The impact of extreme variation in single-input parameters on the model outputs was presented on tornado plots. This provides a visual representation of the sensitivity of the model to the uncertainty associated with individual parameters.

Threshold analysis for cost-utility analysis

A threshold analysis estimates the conditions above or below which the model output may become cost effective, by substituting the point estimate for a wide sequence of values and recording the variation in model outputs. Given the uncertainty around the price the HSE would have to pay for the EHL-mAbs and the maternal and adult vaccines, a threshold analysis was used to explore the impact on cost effectiveness of different prices for the products.

6.2.11 Model validation and calibration

Internal validation of model was conducted in accordance with HIQA's Internal Quality Assurance Framework. All model inputs, calculations, and model outputs were reviewed by a second economic modeller.

6.3 Results

6.3.1 Epidemiological analysis for infant-based RSV immunisation strategies

Based on estimated prices for the EHL-mAbs and maternal vaccine, coverage rates reported in Table 6.4 and intervention efficacy data reported in Section 6.2.8.1, the annual model output for the impact of infant-based immunisation strategies on the number of medically attended RSV cases and RSV-associated hospitalisations is reported in Table 6.11, Table 6.12, Figure 6.6 and Figure 6.8.

For the infant-based strategies, S2 (seasonal EHL-mAb plus catch-up EHL-mAb) demonstrated the largest reduction (43.2%) in the total annual number of medically attended RSV cases in those aged less than one year compared with a scenario where no immunisation is offered to infants in the general population. Within this strategy, the largest reduction (52.8%) was in the 0- to 2-month-old age group while the smallest overall reduction (11.6%) was seen with Strategy 3 (seasonal maternal vaccine). Within this strategy, there was a 22.6% reduction in medically attended RSV cases in the 0- to 2-month-old age group. Differences in the size of the reduction in the total number of annual cases reflect differences in the size of the cohort to whom immunisation is offered, differences in uptake and intervention effectiveness.

S2 (seasonal EHL-mAb plus catch-up EHL-mAb) demonstrated the largest reduction (52.1%) in the annual number of RSV-associated hospitalisations compared with no immunisation. Within this strategy, the largest reduction (62.5%) in RSV-associated hospitalisations was in the 0- to 2-month-old age group. S3 (seasonal maternal vaccine) demonstrated the smallest overall reduction (12.2%) in the annual number of RSV-associated hospitalisations compared with no immunisation. Within this strategy, there was a 23.3% reduction in RSV-associated hospitalisations in the 0- to 2-month-old age group.

Given that a pro-rata reduction (based on intervention efficacy) was applied to medically attended RSV cases that present at the ED, the same percentage reductions apply to ED cases (Figure 6.7).

Table 6.11 Annual number of medically attended RSV cases (% reduction compared with no immunisation) by immunisation strategy and age group

Strategy \ Age group	0-2mths	3-5mths	6-11mths	Total
No immunisation	5,125	2,827	3,082	11,034
S1 - seasonal EHL-mAb	3,008 (41.3)	2,669 (5.6)	3,059 (0.7)	8,736 (20.8)
S2 - seasonal EHL-mAb plus catch-up EHL-mAb	2,417 (52.8)	1,376 (51.3)	2,475 (19.7)	6,269 (43.2)
S3 - seasonal maternal vaccine	3,965 (22.6)	2,725 (3.6)	3,059 (0.7)	9,750 (11.6)
S4 - seasonal maternal vaccine and EHL-mAb	3,461 (32.5)	2,695 (4.6)	3,059 (0.8)	9,216 (16.5)
S5 - seasonal maternal vaccine and EHL-mAb plus EHL-mAb catch-up	2,881 (43.8)	1,403 (50.4)	2,475 (19.7)	6,759 (38.7)

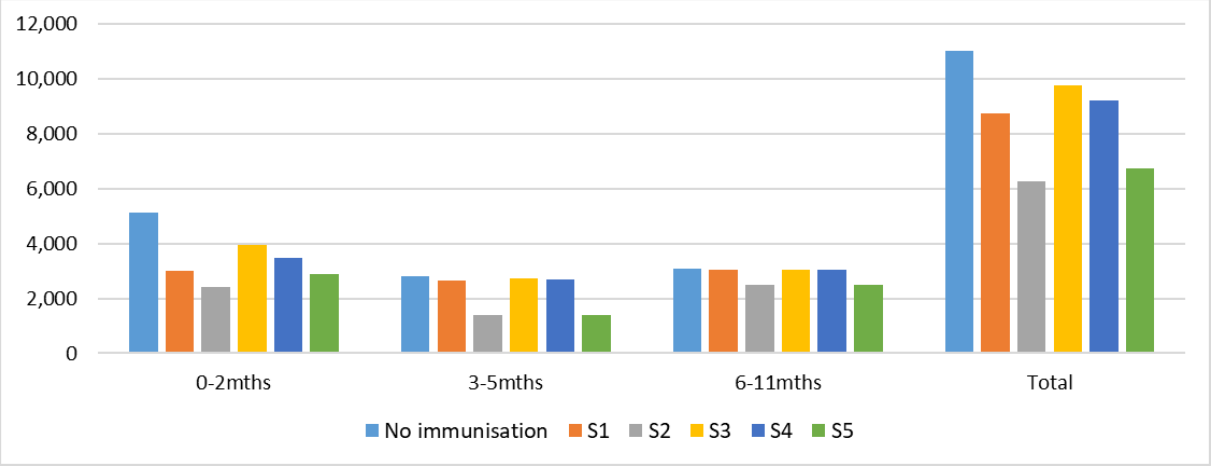
Key: EHL-mAb – extended half-life monoclonal antibody; S1 - Strategy 1; S2 - Strategy 2; S3 - Strategy 3; S4 - Strategy 4; S5 - Strategy 5.

Table 6.12 Annual number of hospitalised RSV cases (% reduction compared with no immunisation) by immunisation strategy and age group

Strategy \ Age group	0-2mths	3-5mths	6-11mths	Total
No immunisation	657	326	336	1,319
S1 - seasonal EHL-mAb	340 (48.2)	309 (5.2)	336 (0.0)	985 (25.3)
S2 - seasonal EHL-mAb plus catch-up EHL-mAb	246 (62.5)	126 (61.2)	259 (23.1)	631 (52.1)
S3 - seasonal maternal vaccine	504 (23.3)	318 (2.6)	336 (0.0)	1,158 (12.2)
S4 - seasonal maternal vaccine and EHL-mAb	419 (36.2)	313 (4.0)	336 (0.0)	1,068 (19.0)
S5 - seasonal maternal vaccine and EHL-mAb plus EHL-mAb catch-up	326 (50.3)	130 (60.0)	259 (23.1)	716 (45.7)

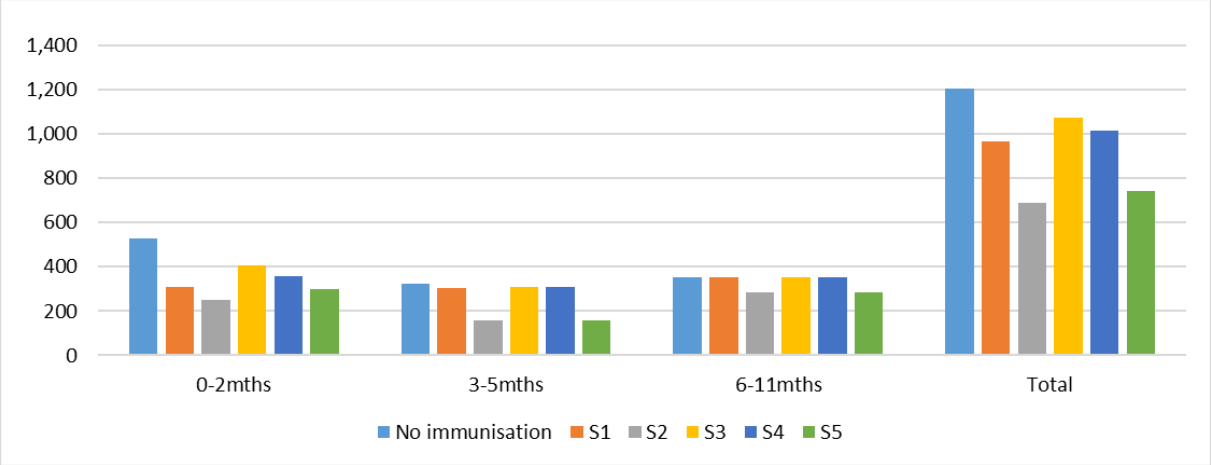
Key: EHL-mAb – extended half-life monoclonal antibody; S1 - Strategy 1; S2 - Strategy 2; S3 - Strategy 3; S4 - Strategy 4; S5 - Strategy 5.

Figure 6.6 Estimated annual number of medically attended RSV cases by immunisation strategy and age group



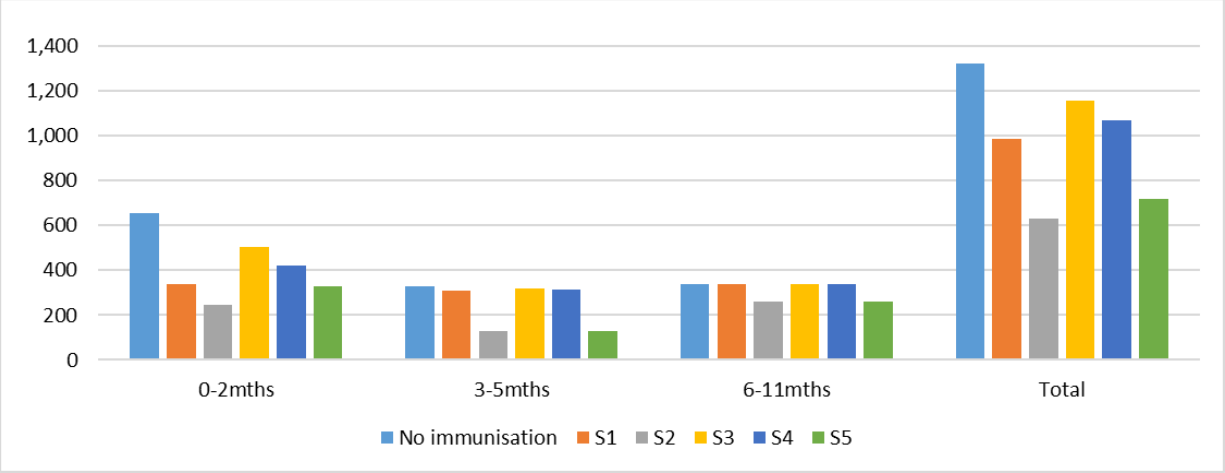
Key: S1 - Strategy 1; S2 - Strategy 2; S3 - Strategy 3; S4 - Strategy 4; S5 - Strategy 5.

Figure 6.7 Estimated annual number of medically attended RSV cases attending the ED by immunisation strategy and age group



Key: S1 - Strategy 1; S2 - Strategy 2; S3 - Strategy 3; S4 - Strategy 4; S5 - Strategy 5.

Figure 6.8 Estimated annual number of medically attended RSV cases hospitalised by immunisation strategy and age group



Key: S1 - Strategy 1; S2 - Strategy 2; S3 - Strategy 3; S4 - Strategy 4; S5 - Strategy 5.

6.3.2 Cost-utility analysis for infant-based RSV immunisation strategies

Base-case analysis

The reported incremental cost-effectiveness ratio (ICER) reflects the mean ICER obtained by PSA with 10,000 simulations. Convergence testing indicated that the number of simulations was sufficient to provide a stable result. For the immunisation strategies under consideration, a stable estimate of the ICER was achieved after approximately 2,500 simulations (Appendix A 6.4).

Overall, from the payer perspective and over a five-year time horizon, all five infant-based immunisation strategies were both more costly and more effective (generating incremental QALY gains) than no immunisation. While S3 (seasonal maternal vaccine) generated the smallest incremental costs compared with no immunisation, it also generated the smallest incremental QALY gains. S2 (seasonal EHL-mAb plus catch-up EHL-mAb) generated both the largest incremental costs and largest incremental QALYs compared with no immunisation. The average cost-effectiveness ratios (ACERs), which compare each of the five infant-based immunisation strategies with no immunisation, are detailed in Table 6.13. From the payer perspective, over a five-year time horizon S5 (seasonal maternal vaccine and EHL-mAb with catch-up EHL-mAb) had the lowest ACER at €209,670 per QALY gained, while S3 (seasonal maternal vaccine) had the highest ACER at €296,938 per QALY gained.

Table 6.13 Average cost-effectiveness ratios for infant immunisation strategies against medically attended RSV

Intervention	Total costs €, millions	Total QALYs	Incremental costs €, millions	Incremental QALYs	ACERs (€/QALY)*
No immunisation	92.3	779,028	-	-	-
S1 - seasonal EHL-mAb	114.4	779,102	21.8	74	296,056
S2 - seasonal EHL-mAb plus catch-up EHL-mAb	128.5	779,193	36.2	164	220,374
S3 - seasonal maternal vaccine	103.6	779,066	11.2	38	296,938
S4 - seasonal maternal vaccine and EHL-mAb	108.3	779,086	16.0	57	278,426
S5 - seasonal maternal vaccine and EHL-mAb plus catch-up EHL-mAb	123.1	779,175	30.8	147	209,670

Key: ACER - average cost-effectiveness ratio; EHL-mAb - extended half-life monoclonal antibody; QALYs - quality-adjusted life years.
*ACER compares each immunisation strategy with no immunisation.

Given that there are five immunisation strategies under consideration and the goal is to maximise health gain, it is necessary to conduct an incremental analysis comparing all mutually exclusive strategies directly. As policy decisions are subject to a budget constraint, ICERs were estimated by ordering the immunisation strategies by increasing cost and comparing each strategy with the preceding least costly strategy. In the incremental analysis, S1 (seasonal EHL-mAb), S3 (seasonal maternal vaccine) and S4 (seasonal maternal vaccine and EHL-mAb) were extended dominated (with higher ICERs than strategies that followed) and were therefore eliminated from any further comparison in the analysis. In the absence of a budget constraint, S5 (seasonal maternal vaccine and EHL-mAb plus catch-up EHL-mAb) had the lowest ICER of €209,670 per QALY gained, versus no immunisation, followed by S2 (seasonal EHL-mAb plus catch-up EHL-mAb) with an ICER of €310,050 per QALY gained, compared with S5 (Table 6.14). The results were plotted on the cost-effectiveness plane (Figure 6.9), which clearly illustrates the relative positions of each of the immunisation strategies under consideration on the cost-effectiveness frontier. Based on the results of the incremental analysis, none of the

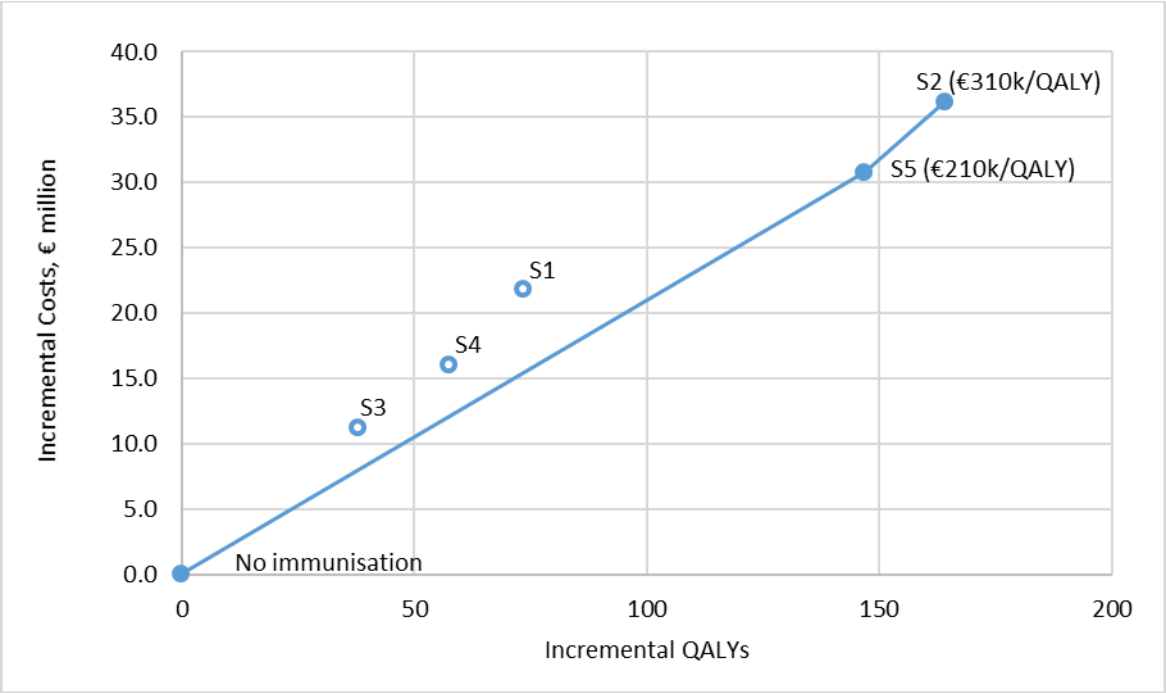
infant-based immunisation strategies would be deemed cost effective at a willingness-to-pay (WTP) threshold of €45,000 per QALY.

Table 6.14 Incremental cost-effectiveness ratios for infant-based immunisation strategies against medically attended RSV

Intervention*	Total costs €, million	Total QALYs	Incremental costs €, million (95% CI)	Incremental QALYs (95% CI)	ICER† (€/QALY)
No immunisation	92.3	779,028	-	-	-
S3 - seasonal maternal vaccine	103.6	779,066	-	-	Extended dominated‡
S4 - seasonal maternal vaccine and EHL-mAb	108.3	779,086	-	-	Extended dominated‡
S1 - seasonal EHL-mAb	114.1	779,102	-	-	Extended dominated‡
S5 - seasonal maternal vaccine and EHL-mAb plus catch-up EHL-mAb	123.1	779,175	30.8 (17.9 – 43.0)	147 (116 – 181)	209,670††
S2 - seasonal EHL-mAb plus catch-up EHL-mAb	128.5	779,193	5.4 (-1.3 – 12.5)	18 (4 – 33)	310,050‡‡

Key: EHL-mAb – extended half-life monoclonal antibody; ICER – incremental cost-effectiveness ratio; QALYs – quality-adjusted life-years; S1 - Strategy 1; S2 - Strategy 2; S3 - Strategy 3; S4 - Strategy 4; S5 - Strategy 5.
*Ordered from least costly to most costly immunisation strategy.
†ICER compares each immunisation strategy with the previous least costly strategy.
‡This strategy is classified as extended dominated as the ICER is greater than a subsequent strategy and it is eliminated from ICER calculations.
††Compared with no immunisation as the previous immunisation strategies are eliminated.
‡‡Compared with Strategy 5.

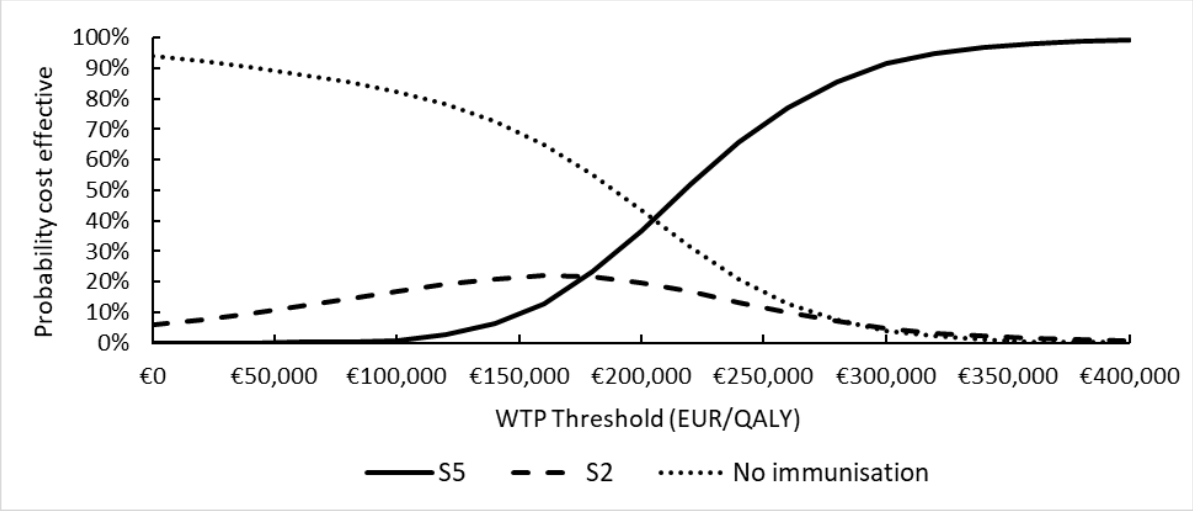
Figure 6.9 Cost-effectiveness frontier for RSV infant-based immunisation strategies



Key: QALYs - quality-adjusted life years; S1 - Strategy 1; S2 - Strategy 2; S3 - Strategy 3; S4 - Strategy 4; S5 - Strategy 5.

The cost-effectiveness acceptability curve (CEAC) summarises the uncertainty in the results of the economic evaluation. It plots the proportion of times that each of the alternative strategies under consideration has the greatest net monetary benefit (that is, the intervention's value in monetary terms) across a range of WTP thresholds. At a WTP threshold of €45,000 per QALY, the probability of any of the infant-based immunisation strategies being cost effective was less than 5%. At a WTP threshold of €220,000 per QALY, the probability of S5 (seasonal maternal vaccine and EHL-mAb plus catch-up EHL-mAb) being cost effective was 52.1% (Figure 6.7). The probability of S2 (seasonal EHL-mAb plus catch-up EHL-mAb), which was the only other strategy on the cost-effectiveness frontier, being cost effective was never greater than 22.3%.

Figure 6.10 Cost-effectiveness acceptability curves for infant-based RSV immunisation strategies 5 and 2



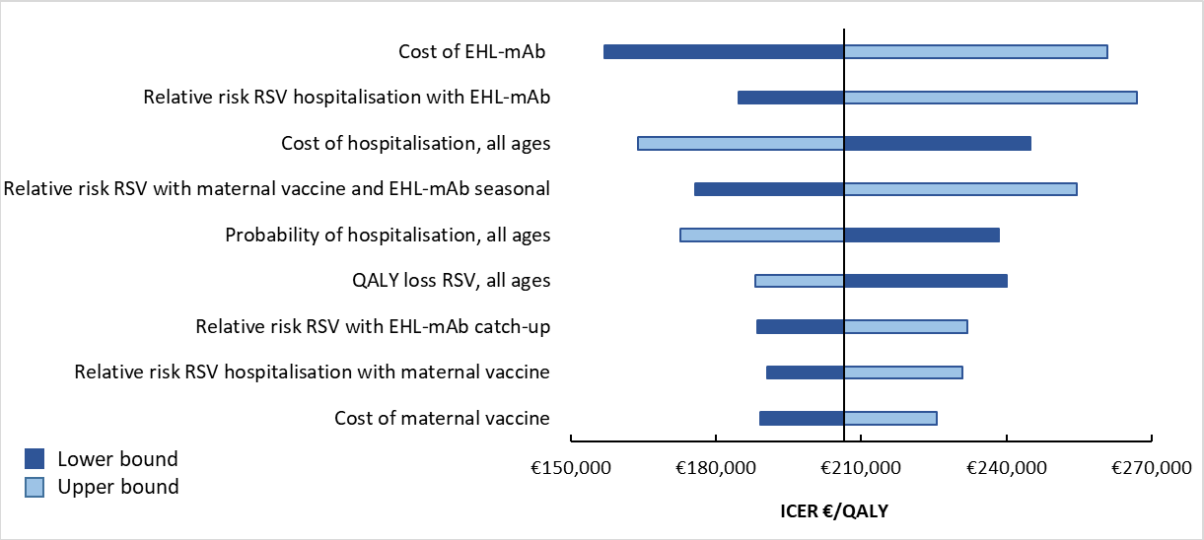
Key: QALYs - quality-adjusted life years; S2 - Strategy 2; S5 - Strategy 5; WTP - willingness-to-pay.

From the societal perspective, which included productivity losses associated with absence from paid work for caregivers of those with medically attended RSV and primary care costs for those without a medical card or GP visit card, all five immunisation strategies were both more costly and more effective (generate greater QALYs) than no immunisation. For the incremental analysis, where each strategy was compared to the previous least expensive strategy, the ICERs for all strategies exceeded €45,000 per QALY. Therefore, from the societal perspective, none of the RSV immunisation strategies would be considered cost effective compared with no immunisation or the previous least expensive strategy, at a WTP threshold of €45,000 per QALY. The ICERs estimated from the payer and societal perspectives did not differ markedly due to current statutory maternity leave benefit, which is payable for 26 weeks, and increasing eligibility for a GP visit card or medical card.

Univariate sensitivity analysis

When conducting OWSA, all input parameters are varied individually and ranked in order of increasing influence on the uncertainty in the ICER. To demonstrate the impact of parameter uncertainty, a deterministic OWSA was conducted from the payer perspective comparing the intervention with the lowest ICER, S5 (seasonal maternal vaccine and EHL-mAb plus catch-up EHL-mAb) with no immunisation. Although all parameters were varied in the analysis, only those that resulted in a ≥10% fluctuation from the mean ICER are presented. The OWSA conducted on the cost of the EHL-mAb resulted in the greatest fluctuation from the mean ICER (ranging from €157,000 per QALY to €261,000 per QALY). None of the OWSA conducted resulted in an ICER below a WTP threshold of €45,000 per QALY (Figure 6.11).

Figure 6.11 Tornado plot of univariate sensitivity analysis for ICER for Strategy 5 (seasonal maternal vaccine and EHL-mAb plus catch-up EHL-mAb) versus no immunisation



Key: EHL-mAb – extended half-life monoclonal antibody; ICER – incremental cost-effectiveness ratio; QALY – quality-adjusted life year; RSV – respiratory syncytial virus.

Two-way sensitivity analysis and threshold analysis

Given the uncertainty around the cost of both the EHL-mAbs and the maternal vaccine, a deterministic threshold analysis was conducted to assess the impact of a lower EHL-mAb price and maternal vaccine price (beyond the reduction used in the OWSA) on the cost effectiveness of RSV immunisation. All other parameters were held at their mean value during the analysis. The price of the EHL-mAb was varied in €50 increments at levels ranging from €100 to €250 (wholesale price ex VAT) while the price of the maternal vaccine was varied in €20 increments at levels ranging from €80 to €140 (wholesale price ex VAT). The incremental analysis was repeated with the ICER results (Table 6.15) as follows:

- At a price of €100 for the EHL-mAb and prices ranging from €80 to €140 for the maternal vaccine, S2 (seasonal EHL-mAb plus catch-up EHL-mAb) was the dominant strategy, being less costly and more effective than all other strategies and the no immunisation option.
- At a price of €150 for the EHL-mAb and prices ranging from €80 to €140 for the maternal vaccine, S2 (seasonal EHL-mAb plus catch-up EHL-mAb) was the most cost-effective strategy with an ICER of €24,550 per QALY, compared with no immunisation. This strategy would be considered cost effective at a WTP threshold of €45,000 per QALY.
- At a price of €200 for the EHL-mAb and prices ranging from €80 to €100 for the maternal vaccine, the most cost effective strategy, compared with no

immunisation, was S5 (seasonal maternal vaccine and EHL-mAb plus catch-up EHL-mAb), with the ICERs above a WTP threshold of €45,000 per QALY (Table 6.15). When the price of the maternal vaccine increased to between €120 and €140, S2 was the most cost effective strategy compared with no immunisation, with the ICERs also above a WTP threshold of €45,000 per QALY (Table 6.15).

- At a price of €250 for the EHL-mAb and a price of €80 for the maternal vaccine, the most cost effective strategy, compared with no immunisation, was S3 (seasonal maternal vaccine), with the ICER above a WTP threshold of €45,000 per QALY (Table 6.15). At a price of €250 for the EHL-mAb and a price of at least €100 for the maternal vaccine, the most cost effective strategy, compared with no immunisation, was S5 (seasonal maternal vaccine and EHl-mAb plus EHL-mAb catch-up), with the ICER also above a WTP threshold of €45,000 per QALY (Table 6.15).

The threshold analysis demonstrated that:

- At a price of €166 for the EHL-mAb and a price of €165 (base-case price) for the maternal vaccine, S2 (seasonal EHL-mAb plus catch-up EHL-mAb) was the most cost effective strategy compared with no immunisation and resulted in the ICER falling to €44,836 per QALY (Table 6.15).

- At a price of €47 for the maternal vaccine and a price of €301 (base-case price) for the EHL-mAb, S3 (seasonal maternal vaccine) was the most cost effective strategy compared with no immunisation, with an ICER of €44,251 per QALY.

Table 6.15 Results of two-way sensitivity analysis and threshold analysis for the price of the EHL-mAb and maternal vaccine

Wholesale price of EHL-mAb (ex VAT)	Wholesale price of maternal vaccine (ex VAT)	Most cost-effective strategy	ICER (€/QALY)
€100	€80 to €140	S2	Dominant*
€150	€80 to €140	S2	€24,550†
€200	€80	S5	€72,139†
€200	€100	S5	€83,213†
€200	€120 to €140	S2	€87,943†
€250	€80	S3	€114,791†
€250	€100	S5	€126,348†

€250	€120	S5	€137,422[†]
€250	€140	S5	€148,496[†]
€166	€165 (base-case)	S2	€44,836[†]
€301 (base-case)	€47	S3	€44,251[†]

Note: The row colour change reflects a change in the price of the EHL-mAb.
[*] "Dominant" indicates that a strategy is less costly and more effective (generating more QALYs) than alternative strategies.
[†]Compared with no immunisation
Key: EHL-mAb – extended half-life monoclonal antibody; ICER – incremental cost-effectiveness ratio; QALY – quality-adjusted life year; VAT – value-added tax; S2 – Strategy 2 (seasonal EHL-mAb plus catch-up EHL-mAb); S5 – Strategy 5 (seasonal maternal vaccine and EHL-mAb plus catch-up EHL-mAb).

6.3.3 Budget impact analysis – infant-based RSV immunisation strategies

The BIA for each of the immunisation strategies is presented relative to no immunisation. The budget impact is conducted from the payer perspective and is limited to the immunisation programme costs (Section 6.2.8.4) and the costs averted as a result of a decrease in incidence of medically attended RSV associated with the introduction of an immunisation programme. In line with national guidelines,[(319)] VAT is included in the BIA. VAT on non-oral drugs (such as injectables) is standard rated[(347)] (23% as of October 2025), while services delivered by a recognised medical professional for the purpose of protecting health (for example, vaccine administration) are VAT exempt.[(348)] Potential organisational issues associated with the introduction of an infant-based RSV immunisation programme are described in Chapter 7.

Base-case analysis

Assuming a price of €301 + VAT for an EHL-mAb, a price of €165 + VAT for the maternal vaccine and coverage rates as outlined in Table 6.4, the five-year incremental budget impact ranged from €15.6 million for S3 (seasonal maternal) to €58.5 million for S2 (seasonal EHL-mAb plus catch-up EHL-mAb). The five-year incremental budget impact for each of the infant-based immunisation strategies is presented in Table 6.16 and Figure 6.12.

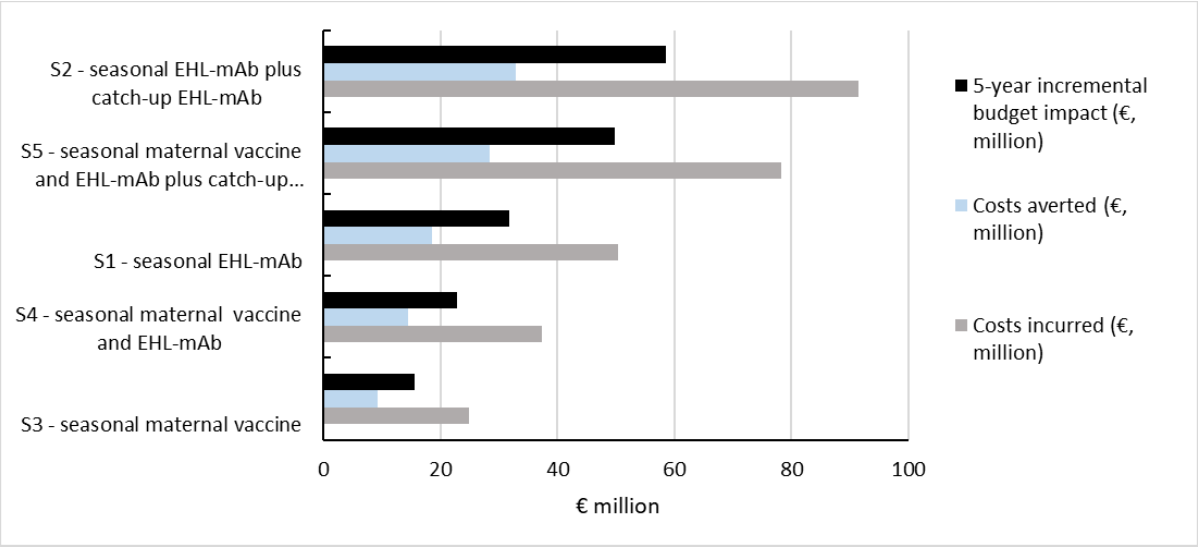
Table 6.16 Results of base-case analysis for five-year incremental budget impact for infant-based RSV immunisation strategies versus no immunisation

Strategy	Number Eligible (per annum)	Number Immunised (per annum)	Total costs incurred €, million (95% CI)	Total costs averted €, million (95% CI)	5 year incremental budget impact €, million*
S1 - seasonal EHL-mAb	27,586	22,786	50.5 (42.4 - 59.4)	18.6 (12.7 - 25.6)	31.8
S2 - seasonal EHL-mAb plus catch-up EHL-mAb	55,172	43,751	91.5 (76.0 - 108.6)	33.0 (23.1 - 44.2)	58.5
S3 - seasonal maternal vaccine	27,586	17,103	24.9 (21.5- 28.5)	9.2 (5.5 - 13.8)	15.6
S4 - seasonal maternal vaccine and EHL-mAb	27,586	22,786	37.3 (33.3 - 41.5)	14.5 (9.7 - 20.2)	22.8
S5 - seasonal maternal vaccine and EHL-mAb plus catch-up EHL-mAb	55,172	43,751	78.4 (68.3 - 89.4)	28.5 (20.3 - 37.9)	49.9

*Compared with no immunisation.

Key: CI – confidence interval; EHL-mAb – extended half-life monoclonal antibody; RSV – respiratory syncytial virus; S1 – Strategy 1; S2 – Strategy 2; S3 – Strategy 3; S4 – Strategy 4; S5 – Strategy 5.

Figure 6.12 Five-year incremental budget impact of infant-based RSV immunisation strategies versus no immunisation



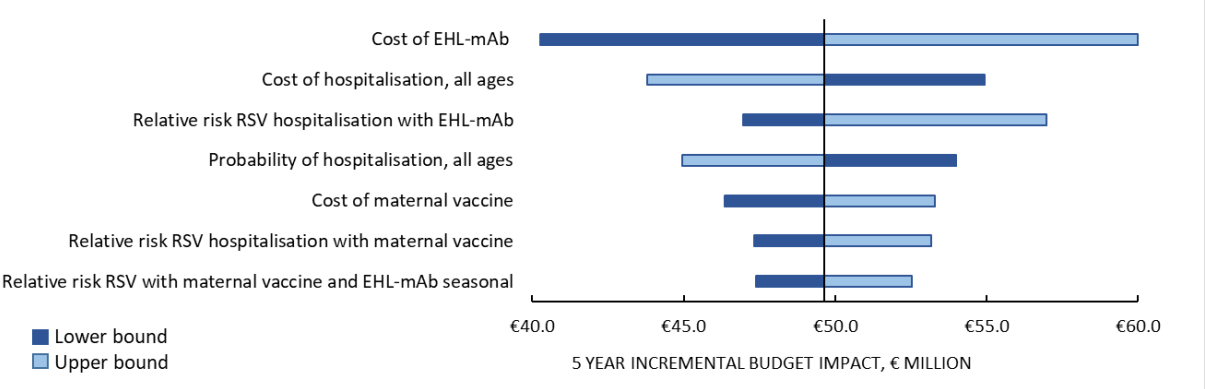
Key: EHL-mAb – extended half-life monoclonal antibody; S1 – Strategy 1; S2 – Strategy 2; S3 – Strategy 3; S4 – Strategy 4; S5 – Strategy 5.

The majority of costs incurred for all five immunisation strategies over the five-year time horizon related to vaccine procurement (approximately 70% to 88%), with the highest rates incurred by S2 and S5 which include a catch-up programme. The second largest cost item was administration of the EHL-mAb and or maternal vaccine (5% to 11%), followed by cold storage and distribution (3% to 12%). As a percentage of total costs incurred, total cost offsets ranged from 37% to 39% for the five strategies. For all immunisation strategies, at least 97% of costs averted related to hospitalisations.

Univariate sensitivity analysis

To demonstrate the impact of parameter uncertainty, a deterministic OWSA was conducted from the payer perspective comparing the intervention with the lowest ICER from the base-case cost-utility analysis above, which was S5 (seasonal maternal vaccine and EHL-mAb plus catch-up EHL-mAb), with no immunisation. Although all parameters were varied in the analysis, only those that resulted in a ≥10% fluctuation from the mean incremental budget impact are presented (Figure 6.13). The OWSA conducted on the cost of the EHL-mAb resulted in the greatest fluctuation from the mean incremental budget impact (ranging from €40.3 million to €60.0 million).

Figure 6.13 Tornado plot of univariate sensitivity analysis for BIA for RSV immunisation strategy 5 (seasonal maternal vaccine and EHL-mAb plus catch-up EHL-mAb) versus no immunisation



Key: EHL-mAb – extended half-life monoclonal antibody; RSV – respiratory syncytial virus; S1 – Strategy 1; S2 – Strategy 2; S3 – Strategy 3; S4 – Strategy 4; S5 – Strategy 5.

At a price of €166 + VAT for the EHL-mAb (the price in the threshold analysis at which S2 (seasonal EHL-mAb plus catch-up EHL-mAb) had an ICER of approximately €45,000 per QALY compared with no immunisation), the estimated five-year incremental budget impact for S2 was €21.6 million. At a price of €47 + VAT for the maternal vaccine (the price in the threshold analysis at which S3 (seasonal maternal vaccine) had an ICER of approximately €45,000 per QALY compared with no immunisation), the estimated five-year incremental budget impact for S3 was €3.3 million.

6.3.4 Epidemiological analysis for adult-based RSV immunisation strategies

Based on coverage rates reported in Table 6.4 and intervention efficacy data reported in Section 6.2.8.1, the annual model output for the impact of adult-based immunisation strategies on medically attended RSV case numbers is reported in Table 6.17. For the adult-based strategies and over the five years of the model, the largest reduction (41.9%) in the total number of medically attended RSV cases (compared with no immunisation) within the immunised age group was reported for S8 (adults aged 75 to 79 years in year one and aged 75 years thereafter). The smallest reduction (28.2%) in the overall number of medically attended RSV cases (compared with no immunisation) within the immunised age group over five years was reported for S6 (adults aged 65 to 69 years in year one and aged 65 years thereafter). Given that a pro-rata reduction (based on intervention efficacy) was applied to medically attended RSV cases that present at the ED and those that are hospitalised, the same percentage reductions apply to ED and hospitalised cases.

Table 6.17 Model output of number of medically attended RSV cases in the immunised age group (% reduction compared with no immunisation) by immunisation strategy and year

Year / Strategy	Year 1	Year 2	Year 3	Year 4	Year 5	Total
S6 – adults aged 65 to 69 years in year one and aged 65 years thereafter	615 (41.6)	744 (32.7)	776 (32.5)	967 (18.4)	996 (17.8)	4,098 (28.2)
S7 – adults aged 70 to 74 years in year one and aged 70 years thereafter	654 (51.3)	829 (39.6)	856 (39.3)	1,135 (21.8)	1,167 (21.8)	4,641 (34.4)
S8 – adults aged 75 to 79 years in year one and aged 75 years thereafter	583 (61.9)	809 (48.0)	830 (47.6)	1,183 (26.8)	1,209 (26.8)	4,615 (41.9)
S9 – adults aged 80 years and over in year one and aged 80 years thereafter	1,409 (62.7)	2,116 (47.2)	2,249 (46.8)	3,588 (19.2)	3,777 (18.7)	13,139 (37.7)

Key: S6 - Strategy 6; S7 - Strategy 7; S8 - Strategy 8; S9 - Strategy 9.

With respect to mortality, the largest reduction (27%) in the number of RSV-related deaths over the five years of the model was observed with S9 (adults aged 80 years and over in year one and aged 80 years thereafter).

Table 6.18 Model output of number of RSV-related deaths by immunisation strategy and age group over five years

Age group / Strategy	65-69yrs	70-74yrs	75-79yrs	≥80yrs	Total	Reduction (%)
No immunisation	21	17	37	190	265	N/A
S6 – adults aged 65 to 69 years in year one and aged 65 years thereafter	15	17	37	190	259	6 (2.6)
S7 – adults aged 70 to 74 years in year one and aged 70 years thereafter	21	11	35	190	257	8 (3.1)
S8 – adults aged 75 to 79 years in year one and aged 75 years thereafter	21	17	22	181	242	23 (8.9)

Strategy \ Age group	65-69yrs	70-74yrs	75-79yrs	≥80yrs	Total	Reduction (%)
S9 – adults aged 80 years and over in year one and aged 80 years thereafter	21	17	37	118	194	71 (27.0)

Key: N/A – not applicable; S6 - Strategy 6; S7 - Strategy 7; S8 - Strategy 8; S9 - Strategy 9.

6.3.5 Cost-utility analysis for adult-based RSV immunisation strategies

The reported ICER reflects the mean ICER obtained by PSA with 10,000 simulations. Convergence testing indicated that the number of simulations was sufficient to provide a stable result. For all adult-based immunisation strategies under consideration, a stable estimate of the ICER was achieved after approximately 2,000 simulations (Appendix A 6.5)

This assessment considered the four adult-based strategies as mutually exclusive alternatives and that only one strategy would be selected in the context of policy decision-making. As such it is appropriate to compare the immunisation strategies with each other.

Base-case analysis

Overall, from the payer perspective and over a five-year time horizon, all four adult-based immunisation strategies were both more costly and more effective (generating incremental QALY gains), than no immunisation. S9 (adults aged 80 years and over in year one and aged 80 years thereafter), generated the smallest incremental costs compared with no immunisation, but also generated the largest incremental QALY gains. The ACERs, which compare each of the four adult-based immunisation strategies with no immunisation, are detailed in Table 6.19. From the payer perspective over a five-year time horizon, S9 (adults aged 80 years and over in year one and aged 80 years thereafter) had the lowest ACER at €232,287 per QALY gained, while S6 (adults aged 65 to 69 years in year one and aged 65 years thereafter) had the highest ACER at €829,186 per QALY gained.

Table 6.19 Average cost-effectiveness ratios for adult-based immunisation strategies against medically attended RSV

Intervention	Total costs €, millions	Total QALYs	Incremental costs €, millions	Incremental QALYs	ACERs (€/QALY)*
No immunisation	39.6	3,813,408	-	-	
S6 – adults aged 65 to 69 years in year one and aged 65 years thereafter	99.8	3,813,481	60.2	73	€829,186
S7 – adults aged 70 to 74 years in year one and aged 70 years thereafter	98.1	3,813,482	58.5	74	€789,867
S8 – adults aged 75 to 79 years in year one and aged 75 years thereafter	95.4	3,813,551	55.8	143	€390,668
S9 – adults aged 80 years and over in year one and aged 80 years thereafter	93.6	3,813,640	54.0	233	€232,287

Key: ACER - average cost-effectiveness ratio; QALYs - quality-adjusted life years.
*ACER compares each immunisation strategy with no immunisation.

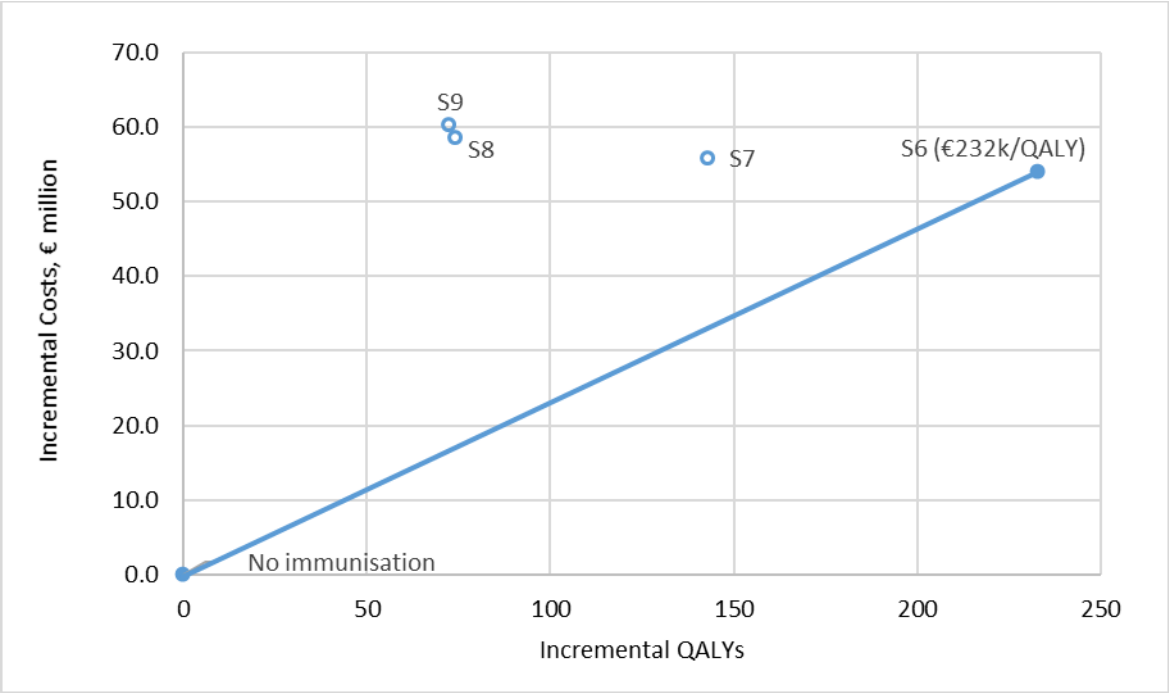
Given that there are four immunisation strategies under consideration and the goal is to maximise health gain, it is necessary to conduct an incremental analysis comparing all mutually exclusive strategies directly. As policy decisions are subject to a budget constraint, ICERs were estimated by ordering the immunisation strategies by increasing cost and comparing each strategy with the preceding least costly strategy. In the incremental analysis, S9 (adults aged 80 years and over in year one and aged 80 years thereafter) dominated all other strategies as it was less costly and more effective (generating more QALY gains). Strategies 6, 7 and 8 were therefore eliminated from any further comparison in the analysis. (Table 6.20). The results were also plotted on the cost-effectiveness plane (Figure 6.14), which clearly illustrates the relative positions of each of the four immunisation strategies under consideration on the cost-effectiveness frontier. Based on the results of the incremental analysis, none of the adult-based immunisation strategies would be deemed cost effective at a WTP threshold of €45,000 per QALY.

Table 6.20 Incremental cost-effectiveness ratios for adult-based immunisation strategies against medically attended RSV

Intervention*	Total costs €, million	Total QALYs	Incremental costs €, million (95% CI)	Incremental QALYs (95% CI)	ICER† (€/QALY)
No immunisation	39.6	3,813,408	-	-	-
S9 – adults aged 80 years and over in year one and aged 80 years thereafter	93.6	3,813,640	54.0 (43.9 – 64.8)	233 (138 –289)	€232,287
S8 – adults aged 75 to 79 years in year one and aged 75 years thereafter	95.4	3,813,551	1.8	-90	Dominated‡
S7 – adults aged 70 to 74 years in year one and aged 70 years thereafter	98.1	3,813,482	2.7	-69	Dominated‡
S6 – adults aged 65 to 69 years in year one and aged 65 years thereafter	99.8	3,813,481	1.7	-1	Dominated‡

Key: CI – confidence interval; ICER – incremental cost-effectiveness ratio; QALYs – quality-adjusted life-years; S6 - Strategy 6; S7 - Strategy 7; S8 - Strategy 8; S9 - Strategy 9.
*Ordered from least costly to most costly immunisation strategy.
†ICER compares each immunisation strategy with the previous least costly strategy.
‡This strategy is classified as dominated as a preceding strategy generates more QALYs at a lower cost and it is eliminated from ICER calculations.

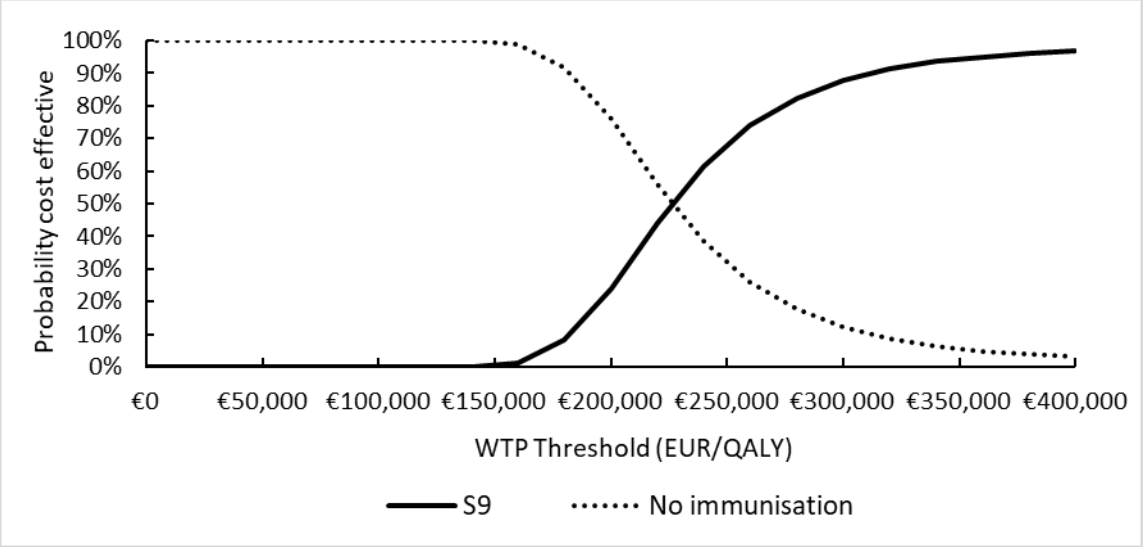
Figure 6.14 Cost-effectiveness frontier for adult-based immunisation strategies



Key: QALYs - quality-adjusted life years; S6 - Strategy 6; S7 - Strategy 7; S8 - Strategy 8; S9 - Strategy 9.

The cost-effectiveness acceptability curve (CEAC) demonstrates that at a WTP threshold of €45,000 per QALY, the probability of S9 (adults aged 80 years and over in year one and aged 80 years thereafter) being cost effective was 0%. At a WTP threshold of €240,000 per QALY, the probability of S9 (adults aged 80 years and over in year one and aged 80 years thereafter) being cost effective was 61.5% (Figure 6.15).

Figure 6.15 Cost-effectiveness acceptability curves for adult-based RSV Immunisation Strategy 9



Key: QALYs - quality-adjusted life years; S9 - Strategy 9; WTP - willingness-to-pay.

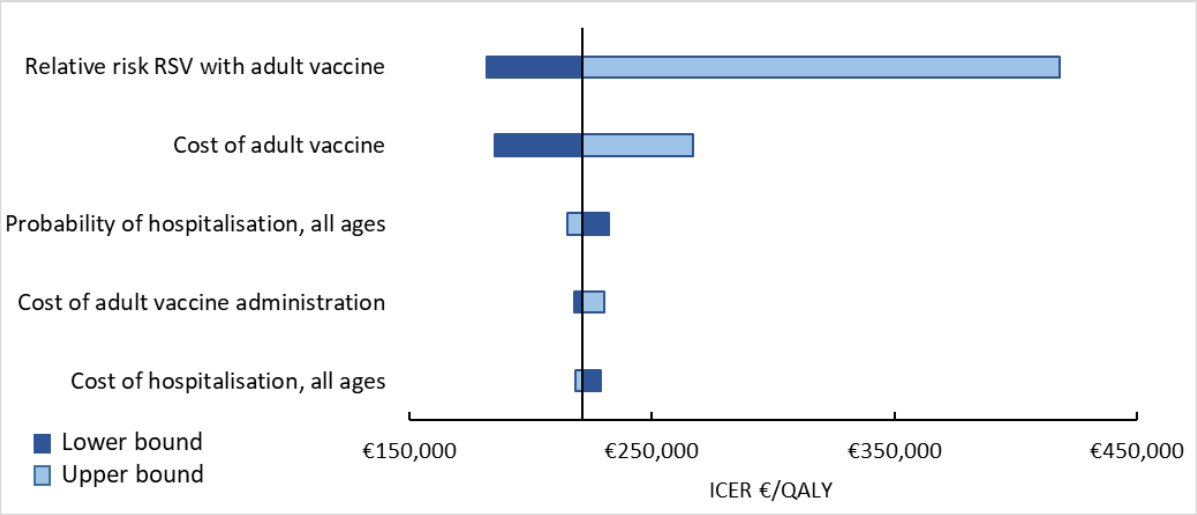
From the societal perspective, which included productivity losses associated with absence from paid work for those with medically attended RSV and primary care costs for those who have not registered for a medical card or GP visit card (or who are not registered with a GP who has a GMS contract), all four adult-based immunisation strategies were both more costly and more effective (generated greater QALYs) relative to no immunisation. For the incremental analysis, where each strategy was compared to the previous least expensive strategy, the ICERs for all strategies exceeded €45,000 per QALY. Therefore, from the societal perspective, none of the adult-based RSV immunisation strategies would be considered cost effective compared with no immunisation or the previous least expensive strategy, at a WTP threshold of €45,000 per QALY. The ICERs estimated from the payer and societal perspectives did not differ markedly due to the low workforce participation rates in the age groups under consideration for immunisation and increasing eligibility for a GP visit card or medical card.

Univariate sensitivity analysis

To demonstrate the impact of parameter uncertainty, a deterministic OWSA was conducted from the payer perspective comparing the intervention with the lowest ICER, which was S9 (adults aged 80 years and over in year one and aged 80 years thereafter), with no immunisation. Although all parameters were varied in the analysis, only those that resulted in a ≥5% fluctuation from the mean ICER are presented. The OWSA conducted on the relative risk of RSV with the adult vaccine resulted in the greatest fluctuation from the mean ICER (ranging from €182,000 per

QALY to €418,201 per QALY). None of the OWSA conducted resulted in an ICER below a WTP threshold of €45,000 per QALY (Figure 6.16).

Figure 6.16 Tornado plot of univariate sensitivity analysis for ICER for Strategy 9 (adults aged 80 years and over in year one and aged 80 years each year thereafter) versus no immunisation



Key: ICER – incremental cost-effectiveness ratio; QALY – quality-adjusted life year; RSV – respiratory syncytial virus.

Threshold analysis

Given the uncertainty around the cost of the vaccine, a deterministic threshold analysis was conducted to assess the impact of a lower vaccine price (beyond the reduction used in the OWSA) on the cost effectiveness of RSV immunisation. All other parameters were held at their mean value during the analysis. The price of the vaccine was varied in €20 increments at levels ranging from €80 to €140 (wholesale price ex VAT). The incremental analysis was repeated with the ICER results reported in Table 6.21. All ICERs exceeded €100,000 per QALY. The price of the vaccine would need to fall to approximately €20 before the ICER is below a WTP threshold of €45,000 per QALY.

Table 6.21 Results of threshold analysis for the price of the adult vaccine

Wholesale price of adult vaccine (ex VAT)	Most cost-effective strategy	ICER (€/QALY)*
€80	S9	€119,170
€100	S9	€143,876
€120	S9	€168,582
€140	S9	€193,288

*Compared with no immunisation.
Key: ICER – incremental cost-effectiveness ratio; QALY – quality-adjusted life year; S9 - Strategy 9; VAT – value-added tax.

6.3.6 Budget impact analysis – adult-based RSV immunisation strategies

The BIA for each of the adult-based immunisation strategies is presented relative to no immunisation. The budget impact is conducted from the payer perspective and is limited to the immunisation programme costs (Section 6.2.8.4) and the costs averted as a result of a decrease in incidence of medically attended RSV associated with the introduction of an immunisation programme. Potential organisational issues associated with the introduction of an adult-based RSV immunisation programme are described in Chapter 7.

Base-case analysis

Assuming a price of €165.00 + VAT per dose for the vaccine and coverage rates as outlined in Table 6.4, the five-year incremental budget impact ranged from €70.6 million for S9 (adults aged 80 years and over in year one and aged 80 years thereafter) to €73.7 million for S6 (adults aged 65 to 69 years in year one and aged 65 years thereafter). The five-year incremental budget impact for each of the adult-based RSV immunisation strategies is presented in Table 6.22 and Figure 6.17.

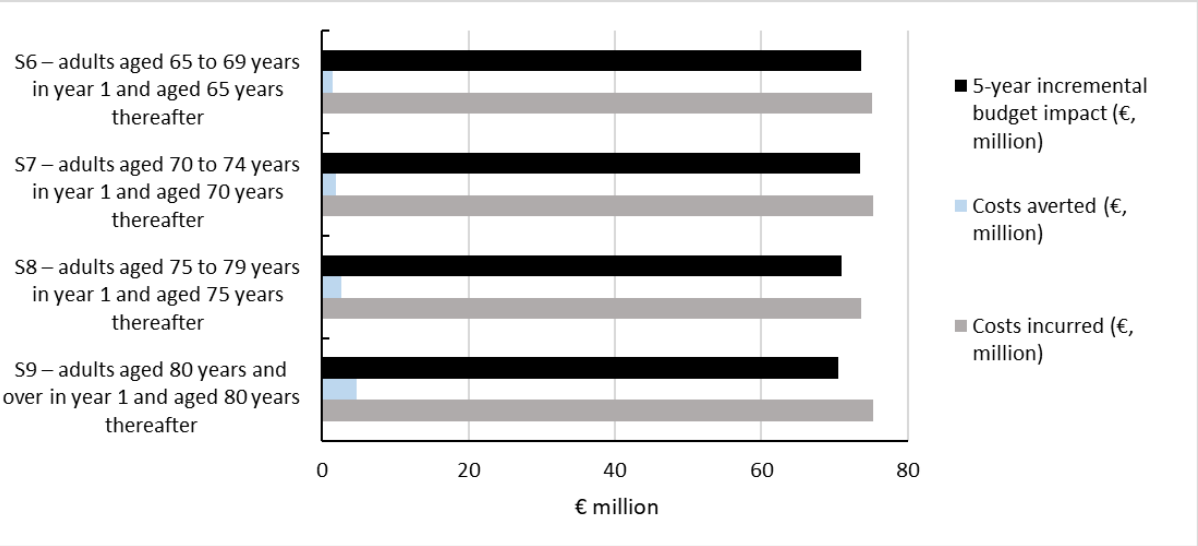
Table 6.22 Results of base-case analysis for five-year incremental budget impact for adult-based RSV immunisation strategies

Strategy	Number Eligible in Year 1	Number Immunised in Year 1	Total costs incurred €, million (95% CI)	Total costs averted €, million (95% CI)	5 year incremental budget impact €, million*
S6 – adults aged 65 to 69 years in year one and aged 65 years thereafter	257,176	154,563	75.1 (63.1 – 88.3)	1.4 (0.8 – 2.0)	73.7
S7 – adults aged 70 to 74 years in year one and aged 70 years thereafter	219,283	160,077	75.3 (63.4 – 88.6)	1.9 (1.0 – 2.8)	73.4
S8 – adults aged 75 to 79 years in year one and aged 75 years thereafter	176,206	155,766	73.7 (62.0 – 86.6)	2.7 (1.4 – 3.8)	71.0
S9 – adults aged 80 years and over in year	208,431	184,253	75.2 (63.3 – 88.5)	4.7 (2.5 – 6.7)	70.6

one and aged 80 years thereafter					

*Compared with no immunisation.
Key: CI – confidence interval; S6 – Strategy 6; S7 – Strategy 7; S8 – Strategy 8; S9 – Strategy 9.

Figure 6.17 Five-year incremental budget impact of adult-based RSV immunisation strategies versus no immunisation



Key: S6 – Strategy 6; S7 – Strategy 7; S8 – Strategy 8; S9 – Strategy 9.

The majority of costs incurred for all four adult-based immunisation strategies over the five-year time horizon related to vaccine procurement (82%). The second largest cost item was administration of the vaccine (10%), followed by cold storage and distribution (4%). As a percentage of total costs incurred, total cost offsets were 7% for each of the four adult-based immunisation strategies. The majority (94%) of cost offsets for all four strategies related to hospitalisations averted.

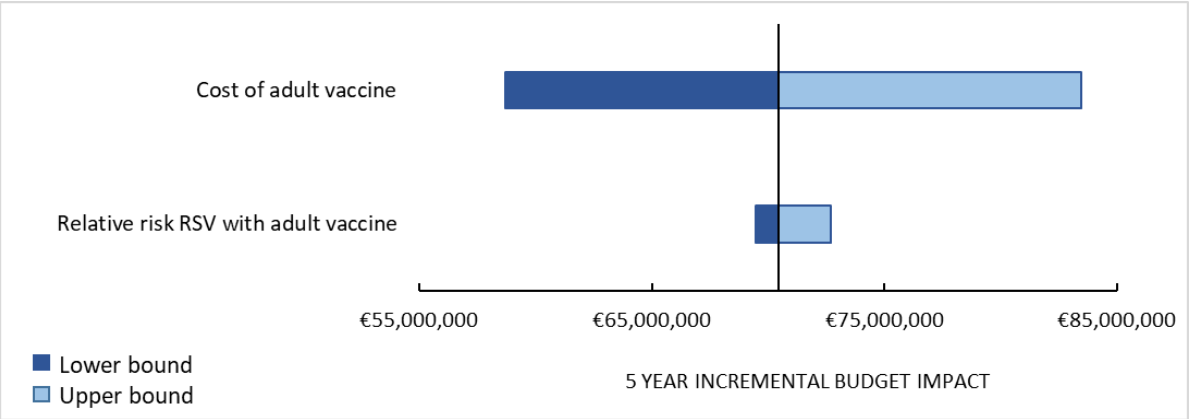
Univariate sensitivity analysis

To demonstrate the impact of parameter uncertainty, a deterministic OWSA was conducted from the payer perspective comparing the intervention with the lowest ICER from the base-case cost-utility analysis above, which was S9 (adults aged 80 years and over in year one and aged 80 years thereafter), with no immunisation. Although all parameters were varied in the analysis, only those that resulted in a ≥5% fluctuation from the mean incremental budget impact are presented (Figure 6.18). The OWSA conducted on the cost of the adult vaccine resulted in the greatest fluctuation from the mean incremental budget impact (ranging from €58.7 million to €83.5 million).

In a sensitivity analysis where the vaccine price was set at €80 (the lowest value applied in the cost-utility analysis) + VAT, the five-year incremental budget impact

for S9 (adults aged 80 years and over in year one and aged 80 years thereafter) fell to €38.6 million.

Figure 6.18 Tornado plot of univariate sensitivity analysis for BIA for RSV immunisation strategy 9 (≥80 years in year one and 80 years old each year thereafter) versus no immunisation



Key: RSV – respiratory syncytial virus; S9 – Strategy 9.

6.3.7 Budget impact analysis – RSV immunisation for adults aged 60 years and over with additional risk factors for severe disease due to comorbidity or who are resident in a long-term care facility

This BIA additionally considered an eligible population of adults aged 60 years and over with additional risk factors for severe disease due to comorbidity or who are resident in a long-term care facility (LTCF). Only costs incurred were estimated in the analysis, with no cost offsets included due to a lack of relevant data. The total eligible population in year one, based on the number of people aged 60 years and over enrolled in the Chronic Disease Management (CDM) Treatment Programme and the number of those aged 60 years and over resident in LTCFs, is provided in Table 6.23 and detailed further in Chapter 3 Section 3.6.4.

Table 6.23 Number of adults aged 60 years and over with additional risk factors for severe RSV due to comorbidity or who are resident in a long-term care facility

Age groups (Years)	Eligible for RSV immunisation
60-64	28,155
65-69	37,569
70-74	75,168
75-79	80,287
80-84	59,605
85-89	36,659
90 and over	16,315
60 and over and resident in a LTCF	28,750
Total 60 and over	**333,758**
60-74	140,982
75 and over	192,866
60 and over and living in LTCF	28,750

Key: LTCF – long-term care facility; RSV – respiratory syncytial virus.

In years two to five of the BIA, it was assumed that the eligible population in the cohort aged 60 to 74 years with additional risk factors for severe disease would be a proportion of the number ageing into the age group. Based on current data, 9.3% of the adult population aged 60 to 64 years is enrolled in the CDM Treatment Programme. This proportion was applied to the number ageing into the cohort each year, with estimates of the eligible population in the group aged 60 to 74 years ranging from 5,871 in year two to 6,156 in year five of the BIA. Similarly, for those aged 60 years and over and resident in a LTCF, it was assumed that the eligible population in years two to five of the BIA would be a proportion of the number ageing into the cohort. Based on current data, 2.4% of the adult population aged 60 years and over are resident in a LTCF. This proportion (which is conservative for the purpose of estimating budget impact) was applied to the number ageing into the cohort each year, with estimates of the eligible population aged 60 years and over and living in LTCFs ranging from 3,781 in year two to 3,965 in year five of the BIA. It was assumed that vaccination would only be offered to those aged 75 years and over with additional risk factors for severe disease in year one of a programme.

An immunisation coverage rate of 97.8% was assumed based on uptake of the seasonal influenza vaccine for those enrolled in the CDM Treatment Programme.[189] All cost inputs for the BIA are the same as those detailed previously in the chapter and listed in Table 6.5.

Based on a coverage rate of 97.8%, the total budget impact over five years for the full cohort of adults aged 60 years and over with additional risk factors for severe

disease due to comorbidity or who are resident in a LTCF was estimated at €93.4 million (95% CI: €78.3 million to €110.0 million). The total cost of vaccine procurement represents 83% of the total budget impact, followed by vaccine administration at 10%, and cold storage and distribution at 3%. The variable costs of vaccine procurement and administration for the different cohorts within the eligible population are detailed in Table 6.24 below.

Table 6.24 Variable costs of vaccine procurement and administration by cohort

	Adults aged 60 to 74 years with additional risk factors for severe disease (€, million)	Adults aged 75 years and over with additional risk factors for severe disease (€, million)	Adults aged 60 years and over and resident in LTCFs (€, million)	Total (€, million)
Vaccine procurement	€32.7	€38.3	€6.9	€78.0
Vaccine administration	€4.0	€4.7	€0.9	€9.6

Key: LTCF – long-term care facility

A sensitivity analysis was conducted whereby the immunisation coverage rates were set at lower rates based on those used in the analysis for the general adult population (Table 6.4). Using rates of 64.4% for those aged 60 to 74 years with additional risk factors for severe disease and 88.4% for both those aged 75 years and over with additional risk factors for severe disease and those aged 60 years and over and resident in LTCFs, the total budget impact over five years was estimated at €75.8 million (95% CI: €63.8 million to €89.2 million).

6.4 Discussion

A de novo Markov model was developed to characterise the incidence of medically attended RSV cases in an average RSV season in Ireland and assess the impact of both an infant- and adult-based RSV immunisation programme. The model was used to estimate the cost effectiveness and incremental budget impact of infant- and adult-based RSV immunisation programmes in Ireland. The analysis of cost effectiveness was conducted from both the payer (HSE) and societal perspectives over five years, while the BIAs estimated the incremental cost to the HSE also over a five-year period.

6.4.1 Main findings

Infant-based RSV immunisation strategies

Results from the epidemiological analysis indicate that the annual incidence of medically attended RSV in those aged up to one year is expected to fall after the introduction of an RSV immunisation programme. The absolute size of the reduction

is influenced by the size of the cohort to whom immunisation is offered (those born during the RSV season or all infants entering their first RSV season), and differences in the uptake and effectiveness of the different strategies. S2 (seasonal EHL-mAb plus catch-up EHL-mAb) demonstrated the greatest reduction (43.2%) in the annual number of medically attended RSV cases, followed by S5 (seasonal maternal vaccine and EHL-mAb plus catch-up EHL-mAb) at 38.7%. Similarly, S2 (seasonal EHL-mAb plus catch-up EHL-mAb) demonstrated the greatest reduction (52.1%) in the annual number of RSV-associated hospitalisations, with the largest reduction (62.5%) observed in the 0- to 2-month-old age group. These modelled data broadly align with those reported by the HSE in the 2024/25 Pathfinder RSV immunisation programme which offered immunisation to those born between 1 September 2024 and 28 February 2025. As outlined in Chapter 3, the HSE reported the percentage reduction in notified cases, RSV-associated ED presentations and RSV-associated hospitalisations by comparing outcomes for those born between September and February for the periods 2023/24 and 2024/25. In the HIQA analysis, the data in the base case were instead based on the most recent three RSV seasons (2021/22, 2022/23 and 2023/24). Comparing the 2024/25 numbers with this three-year average would have generated somewhat smaller reductions than those reported for notified cases (59% versus 65%) and for RSV-associated hospitalisations (69% versus 76%). Moreover, the HSE reported outcomes specifically for the cohort eligible for immunisation rather than the total population aged less than 12 months.

In terms of cost effectiveness, in the base-case analysis from the payer perspective, none of the immunisation strategies were estimated to be cost effective, relative to no immunisation, or the previous least costly strategy at a WTP threshold of €45,000 per QALY. The ICERs ranged from €209,670 per QALY for S5 (seasonal maternal vaccine and EHL-mAb plus catch-up EHL-mAb) compared with no immunisation, to €310,050 per QALY for S2 compared with S5.

Sensitivity analysis demonstrated how sensitive the results of the cost-effectiveness analyses were to changes in the prices of the EHL-mAb and maternal vaccine and to the relative price of the two products. Assuming all other parameters are set at their base-case values, the price of the EHL-mAb would need to fall by approximately 45% (from €301 used in the base case analysis to €166) before the ICER for S2 (seasonal EHL-mAb plus catch-up EHL-mAb), compared with no immunisation, falls below a WTP threshold of €45,000 per QALY. Similarly, assuming all other parameters are set at their base-case values, the price of the maternal vaccine would need to fall by approximately 72% (from €165 used in the base case analysis to €47) before the ICER for S3 (seasonal maternal vaccine), compared with no immunisation, falls below a WTP threshold of €45,000 per QALY.

In the base-case analysis, and assuming a price of €301 (ex VAT) for the EHL-mAb and €165 (ex VAT) for the maternal vaccine, S3 (seasonal maternal vaccine) had the lowest five-year incremental budget impact at €15.6 million while S2 (seasonal EHL-mAb plus catch-up EHL-mAb) had the highest five-year incremental budget impact at €58.5 million. In a sensitivity analysis, where the price of the EHL-mAb was set at €166 (ex VAT) (that is, the price at which S2 (seasonal EHL-mAb plus catch-up EHL-mAb) was the most cost effective strategy and had an ICER of approximately €45,000 per QALY compared with no immunisation), the estimated five-year incremental budget impact for S2 fell to €21.6 million. Similarly, in a sensitivity analysis where the price of the maternal vaccine was set at €47 (ex VAT), the price at which S3 (seasonal maternal vaccine) was the most cost effective strategy compared with no immunisation and had an ICER of approximately €45,000 per QALY, the estimated five-year incremental budget impact for S3 fell to €3.3 million.

Adult-based RSV immunisation strategies

Results from the epidemiological analysis indicate that annual incidence of medically attended RSV is expected to fall after the introduction of an adult-based RSV immunisation programme. Over the five years of the model, S8 (adults aged 75 to 79 years in year one and aged 75 years thereafter) demonstrated the largest reduction (41.9%) in the overall number of medically attended RSV cases (compared with no immunisation) within the immunised age group. S6 (adults aged 75 to 79 years in year one and aged 75 years thereafter), demonstrated the smallest reduction (28.2%) in the overall number of medically attended RSV cases (compared with no immunisation) within the immunised age group over five years. In terms of RSV-related mortality, S9 (adults aged 80 years and over in year one and aged 80 years thereafter) demonstrated the largest reduction (27%) in the number of deaths (from 265 to 194) deaths over the five years of the model.

In terms of cost effectiveness, in the base-case analysis none of the immunisation strategies were estimated to be cost effective from the payer perspective relative to no immunisation or the previous least costly strategy, at a WTP threshold of €45,000 per QALY. S9 (adults aged 80 years and over in year one and aged 80 years thereafter) dominated all other immunisation strategies and the probabilistic ICER for S9 compared with no immunisation was €232,287 per QALY.

Sensitivity analysis demonstrated that with at least a 50% reduction in the price of the adult vaccine to €80 (ex VAT), the ICER for S9 (adults aged 80 years and over in year one and aged 80 years thereafter) compared with no immunisation was still greater than €100,000 per QALY. At a vaccine price of €20 (ex VAT), the ICER fell below a WTP threshold of €45,000 per QALY.

In the base-case analysis, and assuming a price of €165 (ex VAT) for the adult vaccine, the five-year incremental budget impact ranged from €70.6 million for S9 (adults aged 80 years and over in year one and aged 80 years thereafter) to €73.7 million for S6 (adults aged 65 to 69 years in year one and aged 65 years thereafter). In a sensitivity analysis where the vaccine price was set at €80 (ex VAT) (the lowest value applied in the cost-utility analysis), the five-year incremental budget impact for S9 (adults aged 80 years and over in year one and aged 80 years thereafter) fell to €38.6 million.

Risk-based RSV immunisation strategy

Assuming a coverage rate of 97.8%, the total budget impact (incorporating incurred costs only) over five years for the full cohort of adults aged 60 years and over with additional risk factors for severe disease due to comorbidity or who are resident in a LTCF was estimated at €93.4 million. The total cost of vaccine procurement represents 83% of the total budget impact, followed by vaccine administration at 10%, and cold storage and distribution at 3%.

6.4.2 Limitations

As with any economic modelling exercise, the certainty of the results is limited by the choice of model, the underlying assumptions that underpin the model structure, the availability of data to populate the model and the chosen parameter values.

This study employed a static rather than a dynamic model which does not account for indirect effects of immunisation including herd immunity and therefore potentially underestimates the benefits of an RSV immunisation programme. Given that the eligible target group (0- to 6-month-olds) for infant-based RSV immunisation does not include an epidemiologically influential group for transmission, the impact of using a static model for this group is likely to be limited. The approach adopted is also consistent with that seen in the international literature (Chapter 5), the majority of which (13 out of 16 studies) employed a static modelling approach. Additionally, a recent model comparison study examining the cost effectiveness of RSV-preventive interventions in children using static and dynamic models reported similar outcomes for medically attended RSV cases.[349]

The incidence of RSV in Ireland is highly uncertain. While RSV has been a notifiable disease in Ireland since 2012 and testing capacity has increased over time, the notified case data are likely an underestimate of the total burden, and particularly the burden in primary care, as not all RSV cases are laboratory confirmed and some discharges may not be coded (Chapter 3). As the model sought to incorporate the total economic burden and QALY loss associated with medically attended RSV, the notified case data were used as a starting point to estimate the incidence of

medically attended RSV, with a multiplier, which was based on relevant international data, subsequently applied. This multiplier was not applied to ED and hospitalisation rates among notified cases and given that not at all of those who attend the ED are tested for RSV, the incidence of RSV-associated ED attendance is therefore likely underestimated in the model. While acknowledging this underestimate, it is noted that given the cost of ED attendance, higher rates of attendance than those used in the sensitivity analysis would not materially alter the overall results of the economic evaluation. While uncertainty remains around incidence of medically attended RSV, using international data to estimate incidence also presents a limitation. Testing regimes differ between countries and people may present with RSV in different ways due to the underlying nature of the relevant healthcare system. The challenges with estimating incidence of RSV are widely recognised and are not limited to a single country or region so the uncertainty remains. Additionally, although the incidence rates used in this analysis endeavour to capture a significant portion of the economic burden and QALY losses associated with RSV in Ireland (in the form of medically attended cases), they do not capture the burden associated with non-medically attended RSV. However, by definition, it would be assumed that there are no financial costs to the health and social care system (payer) for non-medically attended RSV cases, although it could be argued that there are associated QALY losses.

A number of the parameter values used in the economic model are highly uncertain. While there are list prices for two of the vaccines marketed in Ireland, there are no published price data for the third vaccine (the mRNA vaccine, mResvia) or for the EHL-mAbs. Moreover, while published list price data may be available for products, nationally and or internationally, the cost is unknown given the confidential nature of negotiations between payers, including the HSE, and manufacturers. Therefore, for the purpose of this HTA, prices of €301 and €165 (excluding VAT; storage, distribution and pick and pack fees; and administration fees) for the EHL-mAb and vaccine (maternal and adult), respectively, were assumed in the economic analysis. The sensitivity analyses conducted for the CUAs and BIAs for both the infant- and adult- based RSV immunisation programmes highlight the considerable impact of the uncertainty associated with these prices and the scale of the price reductions required to improve cost effectiveness. Where multiple products for protection against RSV are available, the potential to negotiate substantial price reductions, as part of a competitive tender, may be possible.

The duration of protection against RSV offered by the EHL-mAbs and vaccines was based on the available data as reported in Chapter 4. For infants it was assumed to be limited to a single RSV season after which they were assumed to have no protection. For older adults it was assumed to be a maximum duration of three years, with evidence of waning immunity between years one and two. While

immunity likely persists for longer than assumed in the model and declines over the course of the following months, the approach adopted is conservative. In time, availability of longer-term follow-up data may support a longer duration of protection which may lead to these interventions becoming more cost effective. However, unless very long-term effectiveness is demonstrated, it would not result in these interventions being cost effective at typical WTP thresholds in Ireland.

Health state utility values associated with RSV and used to calculate QALY losses, particularly for adults, are highly uncertain due to a lack of published studies. Additionally, national Irish data were not identified to populate a number of parameter values relating to primary care resource use for RSV. Therefore, international data on the probability of a prescription being issued and the composition of the prescription were used in the analysis. Similarly, while it was assumed that all medically attended RSV cases result in a GP visit, international data and expert opinion were used to inform the frequency of GP visits (that is, to include return visits for the same episode of RSV) that should be used in the analysis. While using international data presents a limitation and the uncertainty around all parameter values impacts the certainty of the results, a probabilistic model was used and extensive sensitivity analyses were conducted which confirmed the overall results of the economic evaluation.

Health outcomes associated with RSV used in the model were limited to those involving medical attendance, including attendance at a GP, presentation at an ED, hospitalisation and death. Long-term sequelae associated with RSV, such as asthma and wheezing, were not included in the infant-based strategies as the causal links are not yet established (Chapter 3). It is likely that the model underestimates the impact of RSV immunisation when these outcomes are excluded. Additionally, the analysis did not include knock-on outcomes associated with a reduction in medically attended RSV cases that require hospitalisation. It is acknowledged that a reduction in RSV-related hospitalisations could be associated with a reduction in ambulance transfers and associated costs. In the absence of robust data these costs have not been incorporated into the models. However, given the likely cost associated with an ambulance transfer and the potential number of cases involved, its inclusion would not alter the overall result of the economic analysis. In the case of older adults who are hospitalised with RSV, a proportion of individuals may need step-down care following discharge from an acute hospital. This may include some combination of post-acute inpatient rehabilitation and or support from community-based services to aid recuperation and maximise functional outcomes. The cost of providing this care is not captured within the HIPE system and is not readily quantifiable. Moreover, the impact on quality of life during the period of step-down care is unclear. As such, this outcome has not been incorporated into the model.

This analysis included assumptions regarding the administration fees payable to primary care contractors (that is, GPs and community pharmacies) per dose administered. These fees were estimated based on existing HSE contractor payment agreements for vaccine administration. Any agreements regarding administration fees payable may be subject to negotiation with professional representative groups and may differ from the values assumed in this analysis. Additionally, the administration of RSV vaccines by HSE Vaccination Teams to eligible adults resident in LTCFs was not costed separately. Instead, the same administration cost (€25) was applied in the base case to all RSV adult-based immunisation strategies. While recognising that costs in the LTCF setting may differ and that an administration fee would not be paid as vaccination would be undertaken by HSE staff, it is noted that the uncertainty around the cost of administration was not an influential parameter in terms of cost effectiveness or budget impact of the immunisation strategies.

The economic analysis conducted from the societal perspective included the productivity loss associated with absence from paid work for both parents caring for children with RSV and for individuals of working age sick with RSV. The analysis did not include the productivity loss associated with absence from paid work for those adults caring for adults sick with RSV. In the absence of relevant data, this cost is difficult to quantify and is noted as a limitation. Although its inclusion would improve the cost effectiveness of an adult-based RSV immunisation programme, the effect is likely to be such that it would not impact the overall result of the economic evaluation.

6.5 Conclusion

RSV places a significant burden on young children, older adults and secondary healthcare services, with the highest burden seen in children aged less than two years. The base-case results of this economic evaluation suggest potentially large reductions in incidence and hospitalisations associated with an RSV immunisation programme, as well as a large reduction in RSV-related mortality with an adult-based programme for those aged 80 years and over. The infant-based model outputs broadly align with those reported by the HSE for the 2024/25 Pathfinder RSV immunisation programme. However, based on the analyses presented, and acknowledging the limitations of the models and substantial uncertainty in relation to the prices of EHL-mAbs and vaccines for RSV that could be achieved as part of a competitive contract, the current evidence suggests that neither an infant- or adult-based RSV immunisation programme in Ireland would represent an efficient use of healthcare resources at the modelled product prices.

The outcome of both the infant- and adult-based CUA is highly sensitive to the assumed unit price of the EHL-mAb and or vaccine. The analysis identified that at a

price of €166 for the EHL-mAb the ICER for the infant-based S2 (seasonal EHL-mAb plus catch-up EHL-mAb) would fall below a WTP threshold of €45,000 per QALY. Similarly, the analysis identified that at a price of €47 for the maternal vaccine, the ICER for the infant-based S3 (seasonal maternal vaccine) would fall below a WTP threshold of €45,000 per QALY. For the adult-based RSV immunisation programme, the analysis identified that at a vaccine price of approximately €20, the ICER for S9 (adults aged 80 years and over in year one and 80 years thereafter) would fall below a WTP threshold of €45,000 per QALY. The potential benefits of RSV immunisation have been demonstrated through this modelling work and economic analysis. However, given the results of the CUAs and BIAs, policy decision-making regarding the potential introduction of an RSV immunisation programme in Ireland should consider both the price and the relative prices of EHL-mAbs and RSV vaccines that can be achieved in the tendering process.

7 Organisational issues

Key points

Passive immunisation of infants

- Five infant strategies were considered involving immunisation with an extended half-life monoclonal antibody (EHL-mAb) or maternal vaccine:
  - seasonal EHL-mAb
  - seasonal plus catch up EHL-mAb
  - seasonal maternal vaccination
  - combination seasonal
  - combination seasonal plus catch up.
- Approximately 27,500 infants would be eligible for immunisation per year with a seasonal programme, increasing to over 55,000 infants if a catch-up programme is also provided.
- For seasonal EHL-mAb strategies, hospital-based administration after birth in the maternity unit/hospital would be consistent with the approach adopted in the HSE Pathfinder Programme, and which achieved high uptake (83% overall in the 2024/25 RSV season).
- For the seasonal maternal vaccination strategy, the vaccine would be offered between 24 and 36 weeks' gestation and where the estimated due date falls during the RSV season — this would correspond with the maternal vaccine being offered between approximately May until late January.
  - Administration in primary care would be consistent with the approach for other vaccines recommended in pregnancy.
  - Timing of RSV immunisation to coincide with a scheduled antenatal visit may be possible in some instances and would reduce the burden on patients and providers.
  - Co-administration with influenza vaccine and COVID-19 vaccine is possible, but a minimum interval of two weeks is recommended between administration of RSVpreF and (pertussis) Tdap vaccines.
  - Consideration may be needed for maternity unit-based vaccination for individuals without a GP.
- For a catch-up programme, provision in GP practice settings would be consistent with the approach for vaccines on the Primary Childhood Immunisation Schedule. Complexities include the large number of infants involved and the aim for them to be immunised as close to the start of the RSV season as possible.

- Timing of RSV immunisation to coincide with a scheduled visit (for example, post-natal examination at 2 or 6 weeks; or the 2-, 4- or 6-month vaccination visit) may be possible in some instances and would reduce the burden on parents and providers.
- While co-administration with scheduled vaccines is possible, there may be a preference to limit the number of vaccines/injections for which consent is sought at a single visit, as the 2-month visit currently includes three injections, while the 4- and 6-month visits currently include two injections each.

Vaccination of older adults

- The RSV vaccine is a one-dose vaccine; the need for a booster has not been established. Given waning immunity, vaccination will have most impact if administered just before the RSV season.
- Providing vaccination for all cohorts identified in the 2025 NIAC recommendations within the first year of a programme would likely prove challenging given the large number of individuals (over 550,000) involved, the substantial budget impact, and considering the commitments for these cohorts under existing immunisation programmes.
- Provision of RSV vaccination through GP practices and community pharmacies, supported by mobile vaccination teams for residents of long-term care facilities, would be consistent with the approach for other vaccines in the adult programme.
- Currently, three vaccines are funded for older adults in Ireland, two annual seasonal vaccines (influenza and COVID-19) for those aged 60 years and older, and once-off pneumococcal vaccination offered at 65 years of age or older. If implemented, the RSV vaccine would represent a third seasonal vaccine. While co-administration would reduce the number of vaccine-related healthcare visits, challenges include:
  - the potential for increased side effects, which could impact future uptake of the other seasonal vaccines
  - potential decreased immune responses to certain influenza strains, when co-administered with influenza vaccine, the clinical significance of which is unknown
  - a reluctance to administer three (or potentially) four vaccines at a single visit.

General organisational considerations

- Each year, RSV has a substantial and predictable seasonal impact on the healthcare system, particularly on paediatric services due to the

disproportionate burden in young children, particularly those aged less than one year. This can affect the delivery of other scheduled and unscheduled care, increase pressure on staff, increase the risk of hospital-acquired infections, and challenge the ability to provide safe and effective care.

- A decision to fund RSV immunisation could have considerable financial and logistical implications depending on the population group for whom the programme of immunisation is funded.
- The likely uptake of RSV immunisation is uncertain and may differ depending on the immunisation approach (for example, maternal vaccination or EHL-mAB) and or the population group for whom the programme is offered.
- As with other immunisation interventions, all RSV interventions have stringent storage and handling requirements. Given existing seasonal influenza and COVID-19 vaccination programmes, providers may need to manage large amounts of stock in the autumn period to meet demand.
- If a decision were made to fund RSV vaccination, resource considerations would include:
  - the appropriate recruitment, provision and training of healthcare workers (including but not limited to nurses, midwives, doctors, and pharmacists)
  - an information campaign and materials to clearly communicate the benefits, risks and eligibility regarding RSV immunisation, including engagement of representatives of typically under-represented or hard to reach groups
  - monitoring and evaluation of the programme, including monitoring uptake in target populations.

7.1 Introduction

The aim of this chapter is to provide an overview of the potential organisational issues associated with different RSV immunisation programme options in Ireland. This includes consideration of aspects relating to the passive immunisation of infants against RSV through maternal vaccination or direct administration of an extended half-life monoclonal antibody (EHL-mAb). It also provides an overview of the potential organisational issues associated with the vaccination of those aged 65 years and older against RSV in Ireland and also the vaccination of adults aged 60 years and older with additional risk factors for severe disease due to comorbidities and or residing in a long-term care facility.

7.2 Organisational implications of RSV immunisation strategies

The assessment considered the organisational implications of each immunisation strategy for infants and older adults included in the economic evaluation, as presented in Chapter 6. For infants, the focus was on the general population of infants.

7.2.1 Immunisation of infants

The five infant immunisation strategies that were modelled in Chapter 6 were:

- seasonal EHL-mAb
- seasonal plus catch up EHL-mAb
- seasonal maternal vaccination
- combination seasonal (maternal vaccination and EHL-mAb)
- combination seasonal plus catch up (maternal vaccination and EHL-mAb).

The organisational implications of these strategies are considered below in the context of the existing immunisation programmes offered to infants in Ireland with the resource implications further discussed in Section 7.3.

Ireland currently has a nationally-funded childhood immunisation programme that commenced in the 1930s. This programme was most recently updated in October 2024 and includes the primary childhood immunisation programme for children aged 2 to 13 months inclusive, which is administered in GP practices.[350] In addition, as outlined in Chapter 2, as a temporary measure for the 2024/25 and 2025/26 RSV seasons, the HSE has implemented publicly-funded RSV Immunisation Pathfinder Programmes which offers immunisation with the EHL-mAb nirsevimab.[31] Eligibility for these programmes were informed by recommendations from the National Immunisation Advisory Committee (NIAC).[351] For the 2025/26 RSV season, those eligible include:[31, 352]

- all infants born during the RSV season, from September to end of February inclusive (the birth cohort)
- infants aged six months or less at the start of the RSV season (catch-up cohort)
- all high-risk infants aged 12 months or younger at the start of their first RSV season (high-risk cohort)
- all ex-preterm children aged less than 24 months of age with chronic lung disease in their second RSV season, and severely immunocompromised children less than 24 months during the RSV season for whom nirsevimab is deemed necessary in consultation with their treating specialist (high-risk cohort).

The settings in which immunisation is being offered include maternity hospitals (birth cohort); HSE clinics (catch-up cohort); and by Children's Health Ireland (CHI) and contracted nurse-led services for eligible infants in hospital and the community, respectively (high-risk cohort). The immunisation clinics for the catch-up cohort ran from the end of August to the beginning of October 2025, with additional clinics offered from 17 November to 12 December 2025; access to nirsevimab is available for eligible infants through pre-booked appointments.[352] To date, nirsevimab has not been administered in GP settings, but it has been noted that this approach is a consideration for future seasons.[353]

As discussed in Chapter 3, overall uptake was high in this programme during the 2024/25 season, at 83% (range 69% to 91%) in maternity hospitals, and 96% in CHI. Uptake in the high-risk cohort who were offered immunisation in the community through a contracted nurse-led service was 99%.[31, 351] These data suggest high uptake is achievable for a seasonal EHL-mAb programme and indicates a willingness among parents and guardians to protect newborns and infants against RSV through immunisation. Attitudes and perceptions towards immunisation, including results from this Irish programme, are discussed in Chapter 8, section 8.2.3. Preliminary evaluation data, as reported by NIAC in March 2025, also reported that groups associated with declining to receive nirsevimab immunisation included ethnic minority groups such as Irish Traveller or Eastern European, non-native English language speakers and those concerned about side effects.[351]

Monoclonal antibody strategies

It was assumed that a strategy involving the administration of nirsevimab or another EHL-mAb from the 2026/27 RSV season onwards would build on the existing approach to the delivery of the primary childhood immunisation programme and the learnings from the 2024/25 and 2025/26 RSV Immunisation Pathfinder Programmes. Based on this assumption, delivery of the immunisation programme would likely include some combination of maternity hospitals, paediatric care services such as CHI, GP practices, and potentially HSE mobile vaccination teams.

<u>Seasonal monoclonal antibody and seasonal plus catch-up monoclonal antibody strategies</u>

The adoption of a monoclonal antibody-based strategy, using an EHL-mAb, would mean the age at which infants receive their first immunisation would lower from two months of age to within days of birth for those born during the RSV season. Hospital-based administration after birth in the maternity unit/hospital would be consistent with the approach adopted in the Pathfinder Programme and by other countries that have implemented RSV immunisation for those born during the RSV season (see Chapter 2, section 2.4.4). Additionally, it is noted that almost all births

in Ireland occur in hospital settings. Data from the Central Statistics Office (CSO) indicate that domiciliary or home births accounted for only 0.6% (n=300) of total births in 2022.[354] While alternative arrangements would be required for this small subset, hospital-based administration for infants born during the RSV season would reduce the burden on parents as it would not necessitate an additional healthcare visit, likely leading to higher uptake. Other interventions infants receive at birth include intramuscular vitamin K (phytomenadione). Nirsevimab can be administered at the same time, provided administration occurs into a different limb.[31]

According to the economic evaluation in Chapter 6, under a seasonal EHL-mAb strategy that offers immunisation to those born during the RSV season there would be an estimated 27,586 infants that would be eligible for immunisation per year. The inclusion of catch-up for infants aged less than six months old born at the start of the RSV season would effectively double the eligible infant population to 55,172 per year. While the 2024/25 Pathfinder programme demonstrated the ability to achieve high uptake rates for those born during the RSV season, there are complexities with delivering a catch-up programme given the large number of infants involved and the aim for them to be immunised as close to the start of the RSV season as possible. While the 2025/26 Pathfinder Programme is relying on HSE immunisation clinics specifically convened to support delivery of the catch-up programme, the alternative is for immunisation of these infants with an EHL-mAb to occur in GP practices along with the other scheduled items on the primary childhood immunisation programme.

To minimise the burden on parents and providers of an additional healthcare visit, one option is that, where possible, infants would receive their RSV immunisation at the same time as their scheduled vaccines in the primary childhood immunisation programme at age two, four or six months, with the choice of visit likely whichever is closest to the start of the RSV season. While evidence is limited, it is not expected that administration of an EHL-mAb would interfere with the active immune response to co-administered vaccines. For example, current guidance states that nirsevimab can be given concomitantly with childhood vaccines and that the safety and reactogenicity profile of nirsevimab co-administered with childhood vaccines is similar to that of the childhood vaccines given alone.[255] However, it is noted that infants are already scheduled to receive multiple vaccines (with some given as combination products, such as the 6 in 1 vaccine) at these visits. Specifically, infants receive three injections at the two-month visit, and two injections at each of the four- and six-month visits; this is in addition to an oral vaccine at the two- and four-month visits. There may be a reluctance by parents and or providers for the child to receive an additional injection at one of these visits. Moreover, if solely offered in the context of one of these existing scheduled visits, there is a potential risk that parents, and potentially healthcare professionals, would either delay their appointment to coincide with the interval in which RSV immunisation is being offered

for the catch-up cohort, or to prioritise RSV immunisation ahead of the other scheduled vaccinations.

The Maternity and Infant Care Scheme, which is described in further detail below, provides for two post-natal visits to the GP at which the baby is examined, at two and six weeks. Depending on the age of the baby at the start of the RSV season, it may be possible to schedule immunisation of some infants in the catch-up cohort to coincide with one of these scheduled post-natal checks. Assuming on average 1,050 infants are born each week, then approximately 6,300 infants born within the six weeks immediately prior to the start of a catch-up programme would be due a scheduled 2-week or 6-week postnatal check within the first four weeks of the programme.

In certain circumstances, timing of RSV immunisation to coincide with a scheduled visit could result in RSV immunisation taking place after the start of the RSV season, raising the risk that the infant would be exposed to and experience adverse outcomes from RSV in the interim. Where it is not possible, or not desirable to schedule RSV immunisation for infants in the catch-up cohort to coincide with an existing visit, then an additional visit would be required, placing an additional burden on the parent and the GP practice. Staffing resources associated with the alternative approaches to providing immunisation are discussed in Section 7.3.1.

Maternal vaccination strategies

The maternal vaccination strategy considered in Chapter 6 involved a seasonal approach, whereby the maternal vaccine is offered to pregnant women between 24 and 36 weeks' gestation and where the estimated due date falls during the RSV season. This would correspond with maternal vaccines being offered between about May until late January (the approximate period encompassing estimated due dates falling between September and the end of February). The estimated number of infants eligible for immunisation under a seasonal maternal vaccination strategy is 27,586, as described in Chapter 6. If a seasonal maternal vaccination strategy is chosen, a decision will need to be made as to whether this would be offered in primary or secondary care, with a primary care-based approach modelled in the economic evaluation (Chapter 6).

All pregnant women who are ordinarily resident in Ireland are entitled to free medical care relating to their pregnancy under the Maternity and Infant Care Scheme.[355] As part of this scheme, pregnant women receive combined medical services from their GP and a hospital obstetrician, and may be expected to attend approximately six examinations with their GP prior to birth, one ideally before 12 weeks and a further five examinations during the pregnancy, which are alternated with the visits to the maternity unit/hospital. Where comorbidities or risk factors are

present, pregnant women may attend their maternity unit more regularly than usual, depending on their need for specialist care. It was noted in the rapid HTA on RSV that, in such circumstances, pregnant women may attend primary care appointments less frequently, which could challenge opportunities to provide the maternal vaccine via primary care.[10]

In Ireland, there are two vaccines currently recommended during pregnancy: influenza and pertussis vaccination.[356, 357] Pertussis vaccine (provided as Tdap, a combined low dose booster vaccine to protect against tetanus [T], diptheria [d] and acellular pertussis [ap] — whooping cough) is administered between 16 and 36 weeks' gestation.[356] Tdap vaccine is provided free of charge from the National Cold Chain Service; however, within primary care, administration is free to the patient only if provided in a GP setting (GPs can obtain an outbreak code from their local department of public health to claim an administration fee).[356, 358] The influenza vaccine can be administered at any time during pregnancy and is recommended for women who are pregnant between October and April.[357] The vaccine and its administration is funded for individuals who are pregnant, among others, as part of the HSE's Seasonal Influenza Vaccination programme.[359] Additionally, COVID-19 vaccination is available on an individual basis for pregnant women who, following a discussion with a healthcare provider, may choose to receive a vaccine.[151] Although these three vaccines, COVID-19, influenza and Tdap vaccines can be co-administered, a minimum interval of two weeks is recommended between administration of RSVpreF and Tdap vaccines.[7] While there are no safety concerns when RSVpreF is co-administered with Tdap in healthy non-pregnant women, immune responses to the pertussis component are noted to be lower compared with separate administration, and non-inferiority has not been demonstrated for the pertussis component. RSVpreF can be co-administered with seasonal influenza vaccines (standard dose adjuvanted or high dose unadjuvanted). Additionally, RSVpreF can be given at the same time as COVID-19 mRNA vaccines, with or without concomitant high dose unadjuvanted influenza vaccination. However, for pregnant women scheduled to receive COVID-19, influenza and Tdap in addition to the RSV vaccine, a second appointment will be required given the minimum recommended two-week interval between the administration of RSVpreF and Tdap vaccines.

Regarding the timing of vaccination, a decision between year-round vaccination or seasonal vaccination would impact the number of individuals eligible to be vaccinated each year. In the context of this HTA, maternal vaccination strategies focused on a seasonal approach, whereby the maternal vaccine is offered to pregnant women between 24 and 36 weeks' gestation where the estimated due date falls during the RSV season. A seasonal maternal vaccination strategy would require

careful planning and management, with clear communication to pregnant women and healthcare providers regarding who is eligible for the vaccine, and when.

Any immunisation programme targeting pregnant women should consider how best to ensure optimal uptake rates. Vaccine uptake of other maternal vaccines in Ireland, and RSV maternal vaccination internationally, is discussed in Chapter 3. Factors related to an individual's perceptions towards vaccination are explored in Chapter 8.2.3. As reported by NIAC, preliminary results from the RSV Immunisation Pathfinder Programme Evaluation Group found that the most common group to refuse nirsevimab were those who did not receive information antenatally.[351] This suggests early antenatal information provision and dedicated follow-up should be considered as important factors for timely immunisation and uptake of RSV immunisation. For those availing of the Maternity and Infant Care Scheme, there would be opportunities for the GP to discuss maternal vaccination at one or more of the scheduled examinations and to organise for the vaccine to be administered during an appointment that would coincide with another of the scheduled visits. This approach of providing the maternal vaccine in a GP practice setting would potentially be the most convenient for pregnant women, since for the majority of uncomplicated pregnancies, the woman will be scheduled to attend their GP for a routine medical examination within the specific vaccination window. Alternatively, the foetal anatomy scan, typically scheduled at 20 gestational weeks, may provide an opportunity for an obstetrician or midwife to initially discuss maternal vaccination against RSV with pregnant women. Information relating to the timing of the vaccination window could be explained, and pregnant women could be encouraged to engage with their primary care services for additional information and, if agreeable, to make an appointment with their GP to receive the vaccine. Delivery of maternal vaccination through maternity units and or hospitals is another option, which may need to be considered for individuals without a GP. However, this would require pregnant women to return within the appropriate vaccination window for an additional appointment, which may be inconvenient for the pregnant woman and may present logistical challenges for maternity services. Finally, as for other vaccines recommended during pregnancy, the maternal vaccine could also be provided in community pharmacies. This approach has been adopted in the UK, with a limited number of pharmacies initially commissioned to provide the maternal vaccine alongside GP practices as part of their nationally-funded programme. However, consideration would be required as to how to support adherence to the timing restrictions (between 24 and 36 weeks' gestation where the estimated due date falls during the RSV season) in this setting.

As described in Chapter 2, seven countries have decided to fund both RSV maternal vaccination and older adult RSV vaccine strategies. In such circumstances, a decision-maker may have a preference to choose a vaccine that is licensed for both

indications, as this may have operational advantages (for example, reducing the risk of administering the wrong vaccine to a patient) or potential cost savings (if ordering larger amounts of product). For example, the UK, which has implemented a maternal vaccination and an older adult programme, is funding only RSVpreF (which is authorised for both populations). To-date, the other six countries with both strategies in place have not preferentially funded the same vaccine for older adults as used for maternal vaccination. In addition, this HTA considered a seasonal maternal vaccination strategy only. However, other countries, such as the UK, have adopted year-round maternal vaccination.[360] While year-round maternal vaccination may be considered more straightforward from an operational perspective, the duration of protection against RSV offered by maternal vaccination is approximately 180 days after birth, as discussed in Chapter 4. This means those born outside of the RSV season may not be adequately protected against RSV during their first RSV season, under a year-round strategy.

Finally, adoption of a maternal vaccination strategy would require consideration of how immunisation would be handled in subsequent pregnancies of previously vaccinated individuals. According to the EMA's European Public Assessment Report for RSVpreF, the need for revaccination in subsequent pregnancies has not been established.[7] There are differences in approaches internationally. The US CDC does not currently recommend use of RSVpreF in subsequent pregnancies, instead advising an EHL-mAb for such newborns.[361] The UK, however, has noted that RSVpreF will be offered for subsequent pregnancies to maintain consistent coverage and protection.[165] Given that a number of maternal vaccination programmes have been implemented internationally since the 2024/25 RSV season, it is likely that additional data will become available over time to establish the effectiveness of re-vaccination.

Combination strategies

The fourth and fifth strategies considered in Chapter 6 related to combination seasonal strategies. In these strategies, seasonal maternal vaccination is offered as described in the previous section. In Strategy 4, the combination seasonal strategy, an EHL-mAb is additionally offered to infants born during the RSV season who are not protected by maternal vaccination (that is, infants born to mothers for whom there is either no record of maternal vaccination or who are born within two weeks of maternal vaccination). The estimated number of infants that would be eligible to receive immunisation under this strategy is 27,856 per year. Strategy 5, combination seasonal plus catch up, comprises strategy 4 with the addition of an EHL-mAb also offered to those infants born prior to the RSV season according to the seasonal plus catch-up monoclonal antibody strategy described previously. As for Strategy 2, the

addition of a catch-up cohort increases the number of infants eligible for immunisation to 55,172 per year.

While all immunisation strategies require careful consideration and planning, combination strategies present an additional layer of complexity as they involve multiple health technologies for different groups at different times. With respect to maternal vaccination, pregnant women would be eligible from about May until late January (the approximate period encompassing estimated due dates falling between September and end of February). Robust data collection practices would be essential to ensure the appropriate timing of vaccination and identification of newborns and infants not considered protected and requiring EHL-mAb administration.

7.2.2 Immunisation of older adults

Single dose RSV vaccination of older adults

If RSV vaccination is funded for older adults, a decision will be needed as to what age group will be eligible to receive the vaccine, informed by the findings of this HTA, as it is unlikely to be feasible or affordable to offer RSV vaccination to everyone over the age of 65 years. While this age group was the basis of the NIAC recommendations published in October 2023, NIAC published updated recommendations for the vaccination of older adults against RSV in October 2025. In these updated recommendations, RSV vaccination is recommended for those aged 75 years and older; aged 60 to 74 years with any additional risk factors for severe RSV disease; and aged 60 years and older living in long-term care facilities for older adults.[135] This economic analysis in Chapter 6, and population estimates from Chapter 3, highlighted the large number of older adults that would be eligible for vaccination. Specifically, if considering the cohorts identified in the updated NIAC recommendations, this would include 384,637 individuals aged 75 years and older, 140,892 individuals aged 60 to 74 years with additional risk factors for severe disease, and 28,750 individuals aged 60 years and older living in long-term care facilities. Providing vaccination for all of these cohorts within the first year of a programme would likely prove challenging given the number of individuals involved, the substantial budget impact, and given commitments under existing immunisation programmes for these cohorts.

Internationally, countries have taken a varied approach to vaccine rollout, as described in Chapter 2, with some countries implementing a catch-up programme in the first year of rollout for those who would otherwise miss out on vaccination. If a particular age group is chosen to receive vaccination, for example those aged 75 years, then consideration could be given to a phased catch-up programme for those aged 76 years and older. However, a catch-up programme would ultimately lead to a larger budget impact and place an additional demand on GPs and pharmacies.

RSV vaccine may be given at any time of the year; however, given evidence of waning immunity, NIAC has recommended that vaccination will have most individual benefit if administered just before the RSV season. Consideration must therefore be given to other vaccines that may be administered at this time. Existing funded vaccinations for older adults include the annual seasonal influenza and COVID-19 vaccination programmes, and the once-off provision of pneumococcal vaccine (PPV23) for adults aged 65 years and older.[159, 359, 362] Funding changes relating to PPV23 vaccination announced in September 2025 as part of the Community Pharmacy Agreement 2025 mean that all three of these vaccines can now be provided free at the point of care to eligible older adults in both pharmacies and general practices.[363] It is assumed that RSV vaccination of older adults could similarly be provided through these primary care settings. It is noted that community pharmacies play an essential role in delivering vaccines. Over 70% of community pharmacies participate in administering vaccines reimbursed through the HSE programmes, and in the 2024/25 seasonal autumn winter programme, they provided over 30% of all vaccines delivered.[364]

Uptake of the vaccines funded for older adults in Ireland, along with RSV vaccine uptake internationally, is described in Chapter 3, section 3.8. It is noted that higher pneumococcal and influenza vaccine uptake rates are reported among older adults enrolled in the HSE Structured Chronic Disease Management Treatment Programme compared with those among the general population. This would suggest that uptake is higher among older adults with additional risk factors for severe disease, possibly due to the provision of targeted information through the structured reviews with their GP or practice nurses as part of the programme (two free reviews in every 12-month period), which includes review of recommended immunisations and the development of personal care plans for the individuals.[157]

In terms of co-administration of an RSV vaccine with one or more of these existing vaccines, the evidence is varied. There is no interaction study examining RSV vaccination and pneumococcal vaccination referenced in the summary of product characteristics (SmPC) of the three currently licensed RSV vaccines.[7-9] In relation to interaction with influenza and or COVID-19 vaccines, the information differs for the three RSV vaccines, as outlined in Chapter 2. Briefly, guidance indicates RSVPreF3 can be administered concomitantly with specific seasonal influenza vaccines (standard dose unadjuvanted, standard dose adjuvanted, and high dose unadjuvanted) albeit with numerically lower neutralising titres for RSV A and B and numerically lower haemagglutination inhibition titres for influenza A and B. RSVpreF can be administered concomitantly with specific seasonal influenza vaccines (standard dose adjuvanted or high dose unadjuvanted) and with COVID-19 mRNA vaccines (with or without concomitant high-dose unadjuvanted influenza vaccine). In its recommendations, NIAC has noted that the clinical significance of these

decreased immune responses is uncertain and thereby suggested that the benefits of giving the RSV and influenza vaccines at the same time, where there is an opportunity to do so, may outweigh such concerns.

Recommendations relating to the co-administration of RSV vaccines with influenza and or COVID-19 vaccines differ internationally. In the UK, the Department of Health and Social Care accepted advice from the Joint Committee on Vaccination and Immunisation (JCVI) and published updated advice in July 2025 noting that RSV vaccines could be administered concurrently with COVID-19 vaccines.(365) With respect to co-administration of RSV vaccines with COVID-19 mRNA vaccines, the JCVI noted that the RSV mRNA vaccine appeared to have lower immunogenicity for RSV-neutralising antibodies when co-administered, albeit meeting the non-inferiority threshold. However, the JCVI outlined that RSVpreF appeared at least as good when co-administered with an mRNA COVID-19 vaccine as with separate administration. For practical reasons, the JCVI decided against distinguishing between the different types of RSV vaccines when deciding to advise in favour of co-administration with COVID-19 vaccines. The minutes from the JCVI meeting in June 2025 detail that the JCVI had advised not to co-administer RSV vaccination with influenza vaccines because of a potential blunting against influenza strain A(H3N2) and lower immunogenicity against RSV.(366)

In France, the Haute Autorité de Santé (HAS) published an updated recommendation in March 2025 regarding the co-administration of RSV vaccines.(367) HAS advised that RSVpreF can be administered with seasonal influenza and COVID-19 vaccines, while RSVPreF3 can be given concomitantly with seasonal influenza vaccines only. In March 2025, the Health Council of the Netherlands published advice recommending RSV vaccination for older adults, stating that the committee had no objection to concomitant administration of RSV vaccines with existing programmes, while also noting that the evidence base is limited and advising that the effectiveness and safety of vaccination after simultaneous and separate administration should be monitored.(368) In January 2025, the Standing Committee on Vaccination (STIKO) in Germany advised that RSV vaccination can be administered at the same time as seasonal influenza vaccination, and that the RSV vaccine should ideally be administered in September or early October to provide optimal protection.(38)

Given the varied recommendations relating to the co-administration of RSV vaccines with seasonal influenza and or COVID-19 vaccines, a decision concerning the timing of a potential RSV vaccine for older adults would need to carefully consider any potential impact on the existing vaccination programmes since seasonal influenza and COVID-19 vaccines are typically offered at the same time. In addition, the HSE advise that individuals can get the pneumococcal vaccine at the same time as their influenza and COVID-19 vaccines, meaning certain adults may already be offered up

to three vaccines in a single visit.[159] In terms of timing of vaccination, the seasonal influenza vaccination programme typically runs from October until April, which overlaps with the typical RSV season. Seasonal influenza vaccines and COVID-19 boosters are given each year, whereas the current guidance for RSV vaccination for older adults recommends a single once-off vaccine. As noted above, NIAC has highlighted that RSV adult vaccine would have the most individual benefit if administered just before the RSV season and can be co-administered with other vaccines such as COVID-19, influenza, zoster and pneumococcal vaccines, albeit acknowledging that the immune responses to certain strains of influenza are reduced when co-administered.[135].

While the evidence base supports the safety of RSV vaccines, as described in Chapter 4, studies investigating the co-administration of RSV vaccines with another vaccine(s) have reported slightly higher local and or systemic reactions among the concomitant vaccine administration groups compared with when these vaccines are administered separately.[369, 370] Increasing the likelihood of a person experiencing an adverse reaction after vaccination, even if mild-to-moderate in severity, could negatively impact uptake of the existing programmes in subsequent years. Moreover, while offering three or four vaccines at the same time could be logistically convenient, individuals may be hesitant to receive three (or four) injections at the same time. As outlined in Chapter 2 of the Immunisation Guidelines for Ireland, multiple vaccines requiring intramuscular injections at the same site must be given at least 2.5cm apart at the same site (where administered in the same limb), and if necessary, in different limbs.[371] Additionally, the risk of administering an incorrect vaccine (for example, two doses of a single vaccine) could increase with multiple different vaccines being administered in the one visit. Apart from vaccine fatigue, providing multiple vaccinations in a single visit could be overwhelming for individuals from the perspective of how much information is provided to them regarding the different vaccines and associated diseases. Expectations and perceptions towards vaccinations are explored in Chapter 8, section 8.2.4.

7.2.3 Impact of implementing an RSV immunisation programme

As described in Chapter 3, RSV activity peaks during the winter months. Historically, this has represented a substantial burden for primary and secondary healthcare services, particularly during Q4 (October to December) for infants aged less than six months, as reflected in the RSV-related ED and hospital admissions data described in Chapter 3. Specifically, in the absence of an RSV immunisation programme for the general population, there were on average 133 (range: 67 to 91) and 1,633 (1,031 to 2,195) hospital discharges that did and did not include an ICU stay each year, respectively. Infants aged less than one year accounted for 86% of discharges without an ICU stay and 91% of discharges that included an ICU stay, with the

highest burden seen in those aged less than six months. This burden on primary and secondary care services occurs over a small number of weeks and during a period when other respiratory viruses such as influenza virus are circulating, placing considerable pressure on the overall delivery of care.[372] The resulting impacts can include hospital capacity limits being reached with bed shortages particularly in neonatal intensive care units, cancellation of elective or other procedures and appointments, challenges with cohorting patients resulting in increased risk of hospital-acquired infections due to close proximity of patients on busy wards, and pressure and stress on staff due to extreme workload, all of which may lead to a worse patient experience and an increased risk to patient safety. The emerging national and international evidence that RSV immunisation leads to a reduction in medically attended RSV healthcare visits, ED visits, and hospitalisations as described in Chapters 3 and 4, highlight the potential to mitigate this substantial and predictable seasonal burden.

For the secondary healthcare system, the greatest offsets will be in paediatric healthcare settings, given the disproportionate burden in those aged less than one year. While not identified in the evidence specific to RSV included in Chapters 3 and 4, there may also be potential to reduce the burden on primary and community services. As noted in Chapter 3, the prevalence of frailty among hospital inpatients aged 65 years and older has been estimated at 66% (range 26 to 100) in Ireland.[373] Frailty at time of hospital admission is associated with adverse outcomes, and therefore care pathways for older adults with frailty include access to inpatient and outpatient rehabilitation and other community care services to assist in areas of identified high complex needs.[374] Following an acute hospital admission, the HSE's Specialist Geriatric Services Model of Care notes that 35% of 70-year-olds show functional loss at time of discharge compared with their pre-admission status, with this figure increasing to 65% for 90-year-olds.[375] Following resolution of the issues that contributed to the admission, patients may therefore require specialist gerontology post-acute inpatient rehabilitation and or support from community-based services to facilitate timely discharge, aid recuperation and maximise functional outcomes.[376] Hospital avoidance in this cohort is therefore noted to be beneficial, with the Model of Care emphasising the importance of interventions that enhance healthy aging and prevent disease.[375]

7.3 Resources

A decision to fund RSV immunisation in Ireland would have resource implications for the health service as a whole. The economic evaluation and budget impact analysis (Chapter 6) aimed to capture these resource implications over a five-year time horizon and to examine the incremental costs to the health service associated with implementing different RSV immunisation strategies. As discussed in Chapter 6,

given the assumptions underpinning the economic evaluation, none of the infant-based or adult-based immunisation strategies would be deemed cost effective at a willingness-to-pay threshold of €45,000 per quality-adjusted life year (QALY). In terms of the five-year incremental budget impact, this was estimated to range between €15.6 million and €58.5 million for the infant-based strategies, and between €70.6 million and €73.7 million for the adult-based strategies.

7.3.1 Staff

For infants born during the RSV season, immunisation with an EHL-mAb was piloted for the 2024/25 and 2025/26 RSV seasons, with nirsevimab administered to the seasonal, and seasonal and catch-up cohorts, respectively. Learnings from the first pilot informed programme implementation in the 2025/26 season and the economic evaluation in this HTA, with the inclusion of costs for pharmacy technician staff to support delivery of the seasonal programme within hospitals. Moreover, learnings from the pilot programmes have informed updates to the HSE's standard operating procedure (SOP) for nirsevimab administration, including in relation to home and domiciliary births which account for approximately 0.6% of all births in Ireland, as highlighted in Section 7.2.1 above.[31]

During both the 2024/25 and 2025/26 RSV seasons, nirsevimab was also offered to the high-risk cohort previously eligible for palivizumab. Immunisation of eligible infants and children was delivered at CHI and by contracted nurse-led services for those in the community, with an aim for these infants and children to be immunised as close to the start of the season as possible.[31] The availability of SOPs that specify details of where, when, how and by whom immunisation should be administered are intended to support clearly communication with key stakeholders responsible for the implementation of the programme.

The impact of a decision to include a catch-up programme for infants born outside of the RSV season on staffing would depend on how such a programme is implemented. As described above, the RSV Immunisation Pathfinder Programme 2.0 currently underway for the 2025/26 RSV season allows for the immunisation of these infants in dedicated HSE immunisation clinics. However, for the purposes of this HTA, it was assumed that if implemented on a long-term basis, immunisation of this cohort would be delivered in general practice settings by GPs and practice nurses, as this would be consistent with the approach adopted for vaccines administered as part of the primary childhood immunisation schedule. As highlighted in Section 7.2.1, if delivered in general practice settings there may be an opportunity to schedule RSV immunisation for some of the catch-up cohort to coincide with an existing scheduled post-natal or primary childhood immunisation schedule visit, potentially reducing the requirement for an additional visit. In the economic model, it was assumed that the fee for administration of the EHL-mAb would be paid irrespective of whether there

was a dedicated appointment at which it was administered or if administration was scheduled to coincide with a planned visit.

As outlined in Section 7.2.2, the provision of RSV vaccination for older adults will likely require an additional GP visit or pharmacy visit, necessitating redeployment of resources from other practice and pharmacy activities and or additional staff. Administration of an additional vaccine at an existing appointment may also place an additional burden on the GP practice or pharmacy team, both in terms of vaccine delivery and the administrative burden associated with obtaining consent, dealing with queries and concerns, and recording the vaccine administration on the appropriate system. However, the fee provided by the HSE to GPs and pharmacies for administering the vaccine may facilitate the recruitment of locum staff to ease the burden during busy vaccination periods. In the economic model, as for the catch-up cohort above, it was assumed this fee would be paid irrespective of whether there was a dedicated appointment at which the RSV immunisation is administered or if administration is scheduled to coincide with a planned visit.

For specific groups of individuals in certain settings, HSE mobile vaccination teams are tasked with delivering immunisations. For example, for the Autumn/Winter Vaccination Programme 2025/26, HSE mobile vaccination teams are providing provide influenza and COVID-19 vaccination services to:[377]

- eligible residents in long-term care facilities for older adults
- those eligible who are housebound
- COVID-19 vaccination for those aged under 12 years
- COVID-19 vaccination for eligible persons in the custody of the Irish Prison Service
- COVID-19 vaccination for eligible in-patients in acute hospitals.

If a programme of RSV vaccination for older adults is adopted, it will be necessary to ensure these HSE mobile vaccination teams are resourced appropriately. Consideration will need to be given as to whether the vaccine would be delivered alongside the existing influenza and COVID-19 programmes, or at a separate time prior to the start of the RSV season. If administered at a separate time, this will entail a second visit by the vaccination team to these settings, which will presumably present additional logistical challenges in the context of the existing workload of these teams.

7.3.2 Immunisation storage and handling

The storage and handling requirements of the RSV immunisation products are described in Chapter 2. As per other immunisation products overseen by the National Immunisation Office (NIO), standard cold chain procedures must be

followed for RSV immunisation products. The NIO is responsible for managing vaccine procurement and distribution including coordinating the National Cold Chain Service (NCCS) which is provided by a contracted specialist distributor with the vaccines delivered directly to GP surgeries, pharmacies and local HSE offices.[378] An estimated cost for the NCCS was therefore included in the BIA for distribution of RSV EHL-mABs and vaccines. Given this existing service and well-established processes, organisational issues relating to storage and distribution associated with any expansion of the immunisation programme to include RSV were considered to be minimal. However, it is recognised that implementation of a number of the modelled strategies would reflect another seasonal intervention (that is, in addition to influenza), with an aim to achieve high uptake of these interventions in the weeks prior to the start of the respective seasons. While SARS-CoV-2 continues to lack seasonality, COVID-19 vaccination campaigns have targeted the autumn period, for ease of communication and given the potential for co-administration with the influenza vaccine. Given the potential for three seasonal interventions, providers may need to manage large amounts of stock over these months, and as such, an additional fridge may be required by certain GP practices and pharmacies.

Of note, four RSV immunisation products (both EHL-mAbs, RSVpreF and RSVPreF3) require refrigeration storage and transportation between 2°C and 8°C. The RSV mRNA vaccine may be stored and transported in a freezer (between -40°C and -15°C). Once thawed, as for the other products, it should be stored between 2°C and 8°C, but the stability data indicate that it is stable for only 30 days at this temperature; products cannot be refrozen. At the end of 30 days, the vaccine should be used immediately or discarded. This may present additional challenges with this vaccine for the NCCS given the potential requirement for additional freezer capacity. Alternatively, if transported between 2°C and 8°C as per the other products, there will be a requirement for tight stock management by GP practices and pharmacies to minimise waste and to ensure that patients do not receive product for which stability cannot be assured.

Once removed from the medication fridge, all of the products must be used within a defined time ranging from eight hours to five days depending on the product, with additional time constraints following reconstitution for products that are not provided as pre-filled syringes (that is, RSVpreF and RSVPreF3). While GP practices and pharmacies have long experience with the stringent requirements for the storage and handling of immunisation products, the sequential addition of items to the immunisation schedule has increased the range of products they must manage, presenting additional challenges when there are subtle differences in their storage and handling. As highlighted in Chapter 2, countries that have implemented RSV immunisation programmes have differed in their approach as to whether they fund a range of alternative products for the same population (for example, funding any of

the three authorised vaccines for the adult programme) or identifying a single preferred product. This may reflect an aim to achieve efficiencies through a competitive tender, and or to reduce complexity and potential risks associated with having multiple alternatives given the extensive storage and handling requirements.

7.3.3 Training

For the 2024/25 and 2025/26 RSV seasons, standard operating procedures and training materials were developed to facilitate registered nurses and midwives, including student nurses/midwives under supervision, and registered healthcare professionals included in S.I. 353 of 2025, employed by the HSE and Voluntary Hospitals, to safely and effectively administer RSV immunisations in maternity hospitals, neonatal units, and paediatric and community settings, including mobile vaccination teams.[31, 379] Healthcare professionals administering nirsevimab must have completed specified training within the previous two years, be competent in administration of intramuscular injections to infants (including epinephrine injection), and have an appropriate registration with their professional oversight organisation, such as:[31]

- a midwife or nurse on an active register maintained by Nursing and Midwifery Board of Ireland
- a doctor listed on the Irish Medical Council register
- a pharmacist listed on the Pharmaceutical Society of Ireland register
- a dentist listed on the Dental Council of Ireland register
- an advanced paramedic, paramedic or emergency medical technician registered with the Pre-Hospital Emergency Care Council
- a person registered with CORU such as physiotherapists, radiographers, and other appropriate health and social care professionals.

The Pharmaceutical Society of Ireland outlines the training that pharmacists must undertake to be permitted to supply and administer vaccines which includes a standard training programme for vaccination.[380] Appropriately trained pharmacists are authorised through Regulation 4B and 4F of The Medicines Products (Prescription and Control of Supply) regulations 2003 to 2024, to administer vaccines listed in Schedule 8 of the regulations.[381] In addition, pharmacists may administer other medicinal products on foot of prescriptions issued by registered prescribers. Currently, RSV vaccination is offered privately in Ireland by some pharmacies to individuals with a prescription from a registered doctor.[382] For pharmacists to provide RSV vaccination as part of a nationally-funded programme, the vaccines would need to be included within Schedule 8 of the legislation in a similar manner to the other vaccines currently administered by pharmacists. Should RSV vaccination be funded for specific groups, appropriate training should be provided for community pharmacists. However, as highlighted in section 7.2.2, over 70% of community

pharmacies already participate in administering vaccines reimbursed through the HSE programmes; therefore, a large proportion of community pharmacists have already completed the core training required for the administration of any vaccine.[383] GPs who intend to administer the vaccine will also need to complete additional training, which will mean time away from clinical practice. Ensuring that pharmacists, GP, nurses and midwifes receive sufficient training and information materials and or resources is also essential to build and maintain their confidence in acting as a trusted and informed information provider with patients. With respect to community pharmacists and immunisation programmes overall, the Community Pharmacy Agreement 2025 refers to steps taken to support enhanced immunisation programme development. This agreement includes a dedicated annual funding allowance of €2 million from 2026 which will be ringfenced for community pharmacy-delivered immunisation programmes.[363]

7.3.4 Immunisation availability

There is the potential for EHL-mAb or vaccine shortages, should international demand exceed available manufacturing capacity. Careful programme planning would be required to manage expectations and minimise any logistical issues. As alternative products become authorised and available for procurement, this could alleviate supply issues, should they arise. That said, as with other funded immunisation policies, consideration should be given to what would happen in the case of shortages, including which groups would be prioritised and whether there should be catch-up for those who missed out during periods of a shortage. In the context of RSV immunisation of infants, NIAC has recommended prioritisation of the youngest infants and high-risk infants in their first RSV season should there be supply shortages.[351]

7.3.5 Information and awareness

Public awareness campaign to support rollout

All information materials regarding vaccinations for the general public are developed and distributed by the National Immunisation Office (NIO), who also manage the national immunisation website www.immunisation.ie.

An information campaign for the public is an important component of any change to the national immunisation schedule, to educate parents and individuals regarding the changes that are being made, allay any concerns regarding the safety or effectiveness of the immunisations and enable informed consent. To support such a public awareness communication campaign, consideration would also need to be given to an educational programme for GPs, pharmacists and front-line nursing and midwifery staff given their important role both in immunisation administration and as

a trusted information source for other immunisations given as part of the national programme. Such information and awareness campaigns are also crucial to safeguarding the existing immunisation programmes for the respective age groups, so to minimise any negative impact arising from the introduction of one or more new immunisation interventions.

For the immunisation of newborns, either by EHL-mAb administration or maternal vaccination, the early timing of the communication of information to pregnant women is essential so that individuals have sufficient time to consider the relevant information and address any potential uncertainties or concerns, so that any decision with respect to immunisation can be considered and informed. Such early antenatal information provision and dedicated follow-up were found to be important enablers to maximise timely immunisation and uptake of nirsevimab during the 2024/25 RSV Immunisation Pathfinder Programme, given evidence that the most commonly reported group to refuse nirsevimab were those who did not receive information antenatally.(351)

Regarding the vaccination of older adults, if a decision is made to fund RSV vaccination for specific groups at increased risk of severe RSV disease, consideration could be given to tailored information campaigns targeting tertiary care services and chronic disease management programmes, in addition to primary care and community pharmacies. Such approaches may provide an opportunity to raise awareness and improve vaccine uptake among enrolled individuals.

It is important to consider what targeted information efforts may be required for specific groups that may be considered harder to reach, such as vulnerable or minority groups. A recent report by the Economic and Social Research Institute on barriers to social inclusion in Ireland noted worsening health outcomes in already disadvantaged areas when comparing data from 2022 to 2016.(384) The authors highlighted the importance of considering such factors in healthcare planning and resource allocation. The HSE NIO strategy for 2024 to 2027 includes as a priority action the identification of groups within the population with low vaccine uptake and the development of tailored immunisation programmes for them, with the aim of strengthening equity in immunisation programmes.(385) Within this context, they have prioritised strengthening national and regional partnerships with healthcare providers and community representative groups to inform their approach and identify barriers and enablers to immunisation within communities and at a local level. The RSV Immunisation Pathfinder Programme considered approaches to reach underserved groups, such as translating information materials into 10 languages and having them available online, while ethnicity information was collected on forms to facilitate equality monitoring. In addition, there was engagement with the National

Social Inclusion Office and Traveller, Roma and migrant representatives to identify how members of these various groups could be reached.

7.4 Current availability of RSV immunisation products in Ireland

7.4.1 EHL-mAbs

As highlighted in Section 7.2.1, in Ireland, the RSV Immunisation Pathfinder Programme commenced in September 2024 and offered nirsevimab to all babies born during the 2024/25 RSV season, up until the end of February 2025. This programme was renewed and updated for the 2025/26 RSV season, as described above. As the time of writing, clesrovimab is not marketed in Ireland.

7.4.2 Maternal RSV vaccination

The maternal RSV vaccine, RSVpreF, has been available for private purchase (prescription only) in Ireland since March 2024.[386] While communication from the manufacturer indicated a small volume of sales in the initial months, it is unclear as to whether these unit sales refer to use by pregnant women or older adults.

7.4.3 RSV vaccination of older adults

In Ireland, RSVPreF3 and RSVpreF are prescription-only items available for private purchase since October 2023 and March 2024, respectively.[386, 387] The RSV mRNA vaccine was authorised by the EMA in August 2024, but no information was identified regarding its marketing status in Ireland.

7.5 Programme monitoring and evaluation

RSV has been a notifiable disease in Ireland since 2012 under the Infectious Disease Regulations. The Health Protection Surveillance Centre (HPSC) monitors RSV activity year round through difference surveillance systems, as outlined in Chapter 3. Under a scenario whereby RSV immunisation is provided to infants and or older adults, existing surveillance systems would continue. The HPSC reports annually on vaccination uptake. Such existing mechanisms should provide a blueprint on which the annual reporting of RSV immunisation could take place. As outlined in HIQA's rapid HTA of immunisation against RSV in Ireland, details of immunisations administered must be recorded and retained locally at the site of immunisation administration, such as a GP practice, HSE Local Health Office, pharmacy, travel health clinical or occupational clinic. A patient may request records of immunisation directly from these sites.[388] One of the objectives of the HSE NIO Strategic Plan 2024 to 2027 was to develop an end-to end administered as part of the primary childhood immunisation programme for children born on or after the 1 October

2025, commenced in November 2025.[389] At the time of writing, the administration of COVID-19, influenza and pneumococcal vaccines by primary care providers are recorded through online portals such as GPVax and PharmaVax.[390-392] These systems link with the HSE's vaccination platform software system, CoVax, which is used to manage, monitor and support the process of administering these vaccines across Ireland.[390] The NIO Strategic Plan 2024-2027 notes that further milestones and implementation of all national immunisation programmes into the NISS are subject to future agreement.[385].[385] While updates to the NISS and CoVax systems would be required, it is assumed that it would be relatively straightforward to amend these systems to capture RSV immunisation of infants with an EHL-mAB and RSV vaccination of older adults, respectively. However, it is important to highlight that the NISS software as currently designed will only record interventions that the individuals themselves receive, with no linkage between mother and infant records for maternal vaccines. If a decision is taken to implement a maternal vaccination strategy for RSV, either alone or as part of a combination strategy, modification of the NIIS would be required to ensure that the mother's vaccination record is linked to that of the infant. The ability to link such records in the NIIS would be important to support healthcare workers in determining the immunisation status of the child and to support evaluation of immunisation uptake. National Immunisation Information System (NIIS) [385]. Phase 1 of this NIIS, which will prospectively capture vaccines

The RSV Immunisation Pathfinder Programmes for the 2024/25 and 2025/26 RSV seasons used a combination of approaches to record and monitor immunisation uptake. Immunisation of infants with nirsevimab was captured on the infant's electronic record in the six maternity units that use the Maternal-Newborn Clinical Management System (MN-CMS) electronic record system. For all other maternity hospitals/units and CHI, a multi-part paper data collection form was designed, with the original version stored in the infant's file and a copy stored securely by the hospital for central reporting. A data collection form was also agreed for nirsevimab administered in community settings, with records stored in line with the HSE National Records Retention Policy. An online survey was designed by the HPSC to capture nirsevimab uptake, with weekly reporting requirements for each site.[31] While this combination of approaches has been successfully used to report uptake for the 2024/25 and 2025/26 RSV Immunisation Pathfinder Programmes, the ability to capture RSV immunisation as part of the NIIS in any future programme would presumably reduce the administrative burden and the risk of incomplete records. As noted, more substantial modification of the NIIS would likely be required to facilitate linkage of mother and infant records should a decision be made to implement an RSV programme based on maternal vaccination. Beyond uptake, as for other immunisation interventions funded through the public healthcare system, integration

of immunisation records with other digital healthcare reports as part of the planned phased roll out of the National Shared Care Record (NSCR)[393] and National Electronic Health Record (EHR)[394] would facilitate appropriate sharing of patient information across healthcare settings as well as evaluation of the real-world effectiveness of immunisation programmes. In advance of these national records being fully implemented, systematic monitoring of immunisation status against relevant health outcomes (for example, hospital or ICU admission) would be of considerable benefit for evaluating the real-world effectiveness of immunisation against RSV.

7.6 Discussion

During the 2024/25 RSV season in Ireland, immunisation of newborns and infants against RSV was successfully implemented through the RSV Immunisation Pathfinder Programme. This programme was extended for the 2025/26 RSV season to additionally include catch-up of infants aged less than six months entering their first RSV season. The lessons learned from the evaluation of these programmes of immunisation should guide decision-making with respect to future RSV immunisation programme planning. These include but are not limited to: lessons specifically relating to the use of a EHL-mAb for newborns and infants; learnings that can be applied to maternal vaccination, such as communicating with pregnant women and delivering programmes of immunisation during pregnancy; and general findings that may be translatable to the immunisation of older adults such as resource requirements and mobilising immunisation teams.

With respect to the immunisation of newborns against RSV through maternal vaccination during pregnancy, notable organisational issues include the window of vaccination during pregnancy and timing of vaccination so as to not interfere with existing vaccines recommended during pregnancy. There are existing challenges in achieving high vaccine uptake during pregnancy in Ireland, with pertussis vaccine coverage estimated at 50% among pregnant women in 2019 and influenza vaccine uptake in pregnancy estimated at 62% in 2018 and 42% in 2020. Hence, it is imperative that any programme of RSV maternal vaccination does not negatively impact uptake of other currently recommended vaccines.

Considering a decision to offer RSV vaccination to older adults, there would be similar challenges in terms of avoiding any negative impact to the existing programmes of vaccination, which comprise COVID-19, influenza and pneumococcal vaccinations. Previous work by HIQA identified barriers and facilitators to influenza vaccination uptake and these are relevant to any changes for the adult immunisation programme. Specific decisions with respect to how an RSV vaccination programme would be implemented would determine the extent to which these barriers and

facilitators might impact vaccine uptake, such as any cost to the recipient and the age group eligible to receive the vaccine. While acknowledging the potentially large number of individuals that may be eligible for RSV immunisation (depending on the cohorts for which the vaccine is funded), it is recognised that healthcare services in Ireland have experience vaccinating large numbers of individuals each year. Specifically, within the HSE Seasonal Influenza Vaccine Programme, over one million individuals were vaccinated in 2023/24 season, with over 500,000 of these aged 65 years and older.[395] The majority of this uptake in older adults (>95%) is achieved between September and December.[396] This is likely feasible because of the large number of providers across GP practices, community pharmacies and HSE mobile vaccination teams involved. The challenge with adding RSV to the schedule, notwithstanding that it is indicated as a once-off vaccine, is that it would represent potentially a fourth vaccine (in addition to once-off pneumococcal vaccine and annual influenza and COVID-19 vaccination) for older adults, and may require a second healthcare visit in early autumn if aiming to limit the number of injections at a single visit and or avoid co-administration with the influenza vaccine.

While recognising that implementation of a long-term RSV immunisation programme for infants and or adults would be associated with organisational challenges and a large incremental budget impact (ranging from €15.6 million to €58.5 million for infant-based strategies and from €70.6 million to €73.7 million for adult-based strategies for the first five years depending on the strategy implemented), this must be considered in the context of the substantial and predictable seasonal impact RSV places on the healthcare system. This is most acutely evident in secondary paediatric healthcare services, due to the disproportionate burden of RSV in younger children, particularly those aged less than one year. For each of the potential target groups, it is essential that any programme of immunisation is appropriately planned and resourced. Importantly, consideration of typically underrepresented or hard to reach groups may require additional resources. Any information campaigns should clearly communicate sufficient information to all relevant healthcare workers and potential recipients of immunisation.

8 Ethical, patient and social considerations

8.1 Key Points

- This chapter examines the ethical, patient and social implications relevant to the immunisation strategies for infants and older adults that are included in the economic assessment (Chapter 7).

Patient and caregiver perspectives towards RSV and prevention strategies

- Parents of infants hospitalised with RSV report worry, guilt and anxiety; RSV prophylaxis programmes may provide peace of mind. Positive predictors of acceptance of infant or maternal RSV immunisation programmes include the perceived protection afforded by the products and the perceived severity of RSV. Concerns about the safety of the products were the primary reason for refusal or hesitation, along with a lack of knowledge of RSV.
- For older adults, RSV illness may negatively impact physical and emotional functioning, and symptoms may persist beyond the acute disease stage. While studies showed a limited knowledge and awareness of RSV among older adults, this population generally has positive attitudes towards prevention strategies.

Benefit-harm balance at an individual level

- As outlined in Chapter 4, there is consistent evidence that all currently authorised RSV immunisation products are safe and effective for the prevention of RSV and associated complications, over one season.
- The potential harms that are associated with immunisation must be considered in the context of the potential for clinical benefit within the population.
  - When weighing up the benefits and harms in infants, it should be noted that they are a vulnerable population, especially in the first few months of life. While the evidence in the infant population supports protection for a single RSV season only, this covers the period for when they are likely at most risk.
  - When weighing up the benefits and harms for older adults, it should be considered that those of advanced age, those residing in long-term care facilities and those with significant comorbidities may be particularly vulnerable. For older adults, there is evidence of waning immunity over time, with a maximum of three years' follow-up. As

such, there is a need to moderate expectations of long-term immunity post-vaccination in this population.

Benefit-harm balance at a population level:

- Wider societal benefits of preventing RSV-associated illness through an effective immunisation programme may include benefits to family members and or carers in terms of improving well-being and social productivity.
- A successful RSV immunisation programme should also ease the workflow for healthcare providers in primary and secondary care.
  - Prior to the introduction of the Pathfinder RSV immunisation programme, winter surges resulted in capacity constraints in paediatric ICUs with implications for patient safety and the provision of other necessary care including elective surgeries.
- It is possible that the introduction of a new immunisation programme may adversely affect established immunisation programmes. Careful consideration of how any funded RSV programme is rolled out is crucial in order to minimise any reduction in uptake of existing immunisation programmes.

Moral, religious or cultural differences

- Acceptance of immunisations may be tied to cultural backgrounds. Tailoring interventions that increase trust in immunisation and address concerns can help improve uptake.
- When considering the RSV immunisation of infants, a choice between the maternal RSV vaccine and the extended half-life monoclonal antibody (within strategies where both are funded) may be perceived as having moral implications for some parents. Some studies found a preference among parents for the maternal vaccine when efficacy is assumed to be equal.

Justice and equity

- While funding of an immunisation programme would improve equity of access, none of the included strategies were found to be cost effective at typical willingness-to-pay thresholds. Moreover, all strategies were associated with a substantial budget impact ranging from €15.6 million to €58.5 million for infant-based strategies and €70.6 million to €73.7 million for adult-based strategies (by five-year age band).
- Funding of interventions that have been found to be not cost effective could create issues of justice and equity with respect to a fair distribution of healthcare resources. However, it may also be viewed as unjust if infants

are not provided with the same level of protection in future seasons as those currently eligible for the Pathfinder programme.

Timing of assessment and availability of evidence

- The timing of assessment has important implications for the overall findings, given the recent (since October 2022) availability of the interventions under consideration and that new types of RSV immunisation, extensions to authorised indications and longer-term effectiveness and safety data are likely to become available in the near future. While there may be greater certainty regarding the most effective and cost effective immunisation strategy if an assessment is undertaken at a later date, this must be balanced with an aim to avoid undue delays in decision making that may prevent currently at-risk patient groups from receiving protection that would be highly beneficial to them.
- Any decision to implement or not implement a programme may need to be re-assessed in time to ensure that the decision represents an efficient and equitable use of healthcare resources.

8.2 Introduction

This chapter examines the ethical, patient and social implications relevant to the immunisation strategies for infants and older adults that are included in the economic assessment (Chapter 7). The analysis was undertaken broadly in line with the structure described in the European network of HTA (EUnetHTA) Core Model[397] and was informed by an ethics workshop held within the HIQA HTA directorate which allowed for a participatory exploration of the relevant domains. It is important that the ethical issues raised around a technology are assessed in relation to the prevalent social and moral norms relevant to the technology and consider the possible consequences of implementing and not implementing the health technologies under evaluation. This section also examines the ethical issues related to the HTA itself.

While governments have an obligation to protect the health and wellbeing of citizens, this must be achieved in a way that is equitable, non-discriminatory, transparent, and, as far as possible, non-coercive. Governments can prevent or reduce the spread of infectious disease through immunisation of the population. Although it is reasonable for a State to aim for high immunisation rates, the balance of benefits and harms to individuals and the wider population must be continuously reviewed. It must also be recognised that individuals have the right to opt-out of such immunisation programmes. As a result, there may be conflict between

individual and public interests, and a balance must be struck between competing values and principles.

As outlined in Chapter 2, updated recommendations with respect to the immunisation of infants were published by the National Immunisation Advisory Committee (NIAC) in March 2025. They recommend the passive immunisation with nirsevimab of all infants born during the RSV season; all infants aged six months or younger at the start of the RSV season; all high-risk infants aged 12 months or younger at the start of their first RSV season; and all ex-preterm infants aged less than 24 months with chronic lung disease in their second RSV season, as well as infants severely immunocompromised during the RSV season. For infants in the general population, a publicly-funded RSV Immunisation Pathfinder Programme first offered immunisation with nirsevimab as a temporary measure for those born during the 2024/25 RSV season,[11] with the programme extended for the 2025/26 season to include infants aged less than six months entering their first RSV season. Infants and children up to two years of age at high risk of severe disease previously eligible for palivizumab are now offered nirsevimab, with this also provided through the Pathfinder programme since 2024/25.[31]

With respect to older adults, guidance from NIAC was published in October 2023 recommending RSV vaccination for those aged 65 years and older with either RSVpreF or RSVPreF3.[398] In October 2025, NIAC published an update to these recommendations and now recommend vaccination for those aged 75 years or older and those aged 60 to 74 years with any additional risk factors for severe RSV disease or who are living in long-term care facilities.[135] The considerations that led to these updated recommendations are discussed in Chapter 2. As of October 2025, RSV vaccination of older adults is not publicly funded in Ireland.

In the context of this chapter, the technologies considered are RSV immunisation programmes aimed at the population of infants aged less than 12 months during their first RSV season and adults aged 65 years and older. Of note, while an adult is generally capable of providing informed consent, in order for a child to receive an immunisation, informed consent must be provided by a parent or guardian. For simplicity, parents are referred to in the subsequent text, but this also includes guardians.

8.3 Patient and caregiver perspectives

8.3.1 Experiences of parents of infants with RSV

A 2019 systematic review of parent self-reported experiences of and information needs related to bronchiolitis (which is a type of chest infection often caused by RSV) found that the available evidence primarily focused on cases requiring

hospitalisation.[399] The review found that most parents felt unprepared to deal with the hospitalisation of their child, and mothers in particular wanted to take an active role in their child's care but often felt isolated, uninformed, and misunderstood by healthcare providers. During their child's hospitalisation, parents reported guilt and anxiety. Conversely, RSV prophylaxis programmes were found to provide parents with peace of mind, although it is noted that the included studies pre-dated authorisation of interventions for the general population of infants, and as such, the cohorts eligible for prophylaxis would have been limited to infants at high risk of severe disease.[399]

A 2024 publication for the industry-funded ResQ Family study reported findings of an online survey of parents and caregivers (n=138) of children with an RSV-induced hospitalisation during the 2022/23 RSV season.[400] The study, conducted in Germany, France, Italy and Sweden, reported that the majority of parents (91%) felt quite worried or very worried about their child's overall health status during this period of hospitalisation. The occurrence of shortness of breath was found to be the symptom that worried parents the most in all participating countries. The study noted a significant reduction in parental health-related quality of life (HRQoL) and family functioning scores during the acute infection phase, although responses from a follow-up survey (n=59) completed six weeks following the acute phase indicated that these reductions had largely reversed by this time.

Some studies indicate that hospitalisation of a young infant may create barriers to breastfeeding when mothers and infants are physically separated or when an infant is very unwell. A 2021 systematic review of the challenges of breastfeeding infants who are medically complex (for example, due to acute or chronic illness, disability or congenital anomaly) noted that continued breastfeeding, breastfeeding duration and exclusivity are lower among those with more complex conditions, including those hospitalised due to acute illness.[401] This review included a 2017 survey of mothers (n=84) of infants aged six months or younger hospitalised with acute bronchiolitis in Paris. Half of the mothers reported that hospitalisation modified their breastfeeding with the study concluding that admission to hospital with bronchiolitis may adversely affect breastfeeding.[402] The causes of breastfeeding disturbance were noted to include the respiratory disease of the child and logistical difficulties within the hospital. A follow-up study concluded that more severe bronchiolitis poses the highest risk of weaning.[403] This is consistent with the finding of an Australian study of mothers of infants hospitalised for severe bronchiolitis who described feeling helpless as they were unable to breastfeed while an infant received oxygen therapy.[399] While there are limited data from Ireland, hospitalisation of infants due to a respiratory infection is likely to create barriers to breastfeeding. The HSE has set out priority areas to enhance breastfeeding supports [404] while CHI aims to support, promote and protect breastfeeding.[405]

8.3.2 Experiences of older adults with RSV

There is less literature on the experiences of older adults with RSV, however a 2022 systematic review included studies capturing self-reported symptoms associated with RSV infection in older adults.[117] Cough was the most frequently self-reported symptom followed by weakness/malaise, shortness of breath, sputum and fever among older adults.

A 2022 industry-funded qualitative patient experience study (n=30) characterised the impact of RSV on the quality of life of adults aged 50 years in the USA, based on a semi-structured interview completed between one and six months following an RSV episode. The majority of the respondents (73%) were entirely managed in primary care, while almost 14% required hospitalisation. The study suggested that the majority experienced impairment of physical (83%) and emotional (93%) functioning, due to RSV, with 62% reporting that symptoms lasted beyond the acute disease stage (range: a week to greater than one month).[406]

8.3.3 Expectations and perceptions of alternative forms of RSV immunisation for infants

As outlined in Chapter 2, options for the immunisation of infants against RSV include the intramuscular injection of the infant with a monoclonal antibody (mAb) or by vaccination of the pregnant mother between 24 and 36 weeks' gestation to provide passive protection of the infant from birth to six months of age through transplacental antibody transfer. Expectations and perceptions in relation to these alternative approaches to the immunisation of infants are outlined below.

Perceptions of monoclonal antibody immunisation

A 2025 systematic review of knowledge and attitudes regarding RSV prevention by Gavaruzzi et al. included 27 studies focused on the direct immunisation of infants using a mAb. While the majority of the included studies were limited to palivizumab and or predated national immunisation programmes for the general population of infants, the review found generally positive attitudes towards mAb-based prevention strategies. The main predictors for acceptance were the protection of the infant and perception of the illness as severe. The main predictors for refusal were concerns about safety and side effects.[407]

Perceptions of maternal RSV vaccination

The aforementioned 2025 Gavaruzzi et al. systematic review included 24 studies that focused on RSV maternal vaccination.[407] Again, these studies generally predated national immunisation programmes, with many undertaken to inform potential future RSV prevention strategies. Positive predictors of acceptance of RSV maternal

vaccination included perceived protection, the perceived severity of RSV (especially for infants), confidence in vaccines, and having received other maternal vaccinations. Concerns about the safety of the maternal vaccine, especially for the baby, were the primary reason for refusal or hesitation about vaccination, along with a lack of RSV knowledge.

A survey (n=528) of maternal awareness, acceptability and willingness towards RSV vaccination during pregnancy in Ireland conducted between December 2018 to April 2019, found that despite low levels of maternal awareness of RSV, pregnant women in Ireland are open to availing of antenatal vaccination.[408] The main factor making vaccination acceptable to women (76.4%) was that it protects their infant from illness.

A small qualitative study (n=8) in Ireland reported the results of eight semi-structured interviews with pregnant women between July and August 2022 around accepting or declining vaccinations in pregnancy.[409] They reported that maternal vaccination hesitancy stemmed from safety and efficacy concerns, a perceived lack of trustworthy information, exposure to misinformation, and fear of being judged for one's decisions. Factors associated with decisions to vaccinate included trust in the benefits of vaccination reinforced by other pregnant women's positive experiences, and a sense of duty to use available health resources.

Preferences for maternal RSV vaccination versus monoclonal-antibody based immunisation

The Gavaruzzi et al. review also included eight quantitative cross-sectional studies which examined preferences for the alternative approaches to RSV immunisation of infants.[407] Five of these studies reported the percentage of participants who would prefer maternal vaccination, infant immunisation with a monoclonal antibody (mAb), or a combination of the two as RSV prevention strategies. In four out of the five of these studies, a higher proportion preferred maternal vaccination, both when offered as a single option and when offered within the context of a combination strategy. An additional study included in the review with a discrete choice experiment (DCE) noted that all else being equal, pregnant women preferred the maternal vaccine over mAbs. However within this DCE, the type of immunisation (maternal vaccine or mAb) had limited influence on choice, with participants' preferences mainly influenced by the effectiveness and duration of protection of the immunisation product. A secondary analysis of the same DCE (published separately and included in the review as an additional study) classified participants based on their preferences. It reported that pregnant women whose preferences were driven by the effectiveness or duration of protection favoured maternal vaccination over mAb-based immunisation of the infant. Finally, an included US quantitative cross-sectional

study focusing on eligible pregnant women who refused maternal RSV vaccination found that a majority (63%) would avail of mAb-based immunisation of the infant. Overall, the review concluded that all things being equal, maternal vaccination tends to be more acceptable than immunisation of infants with mAbs.

Pregnant women (n= 34) who participated in a 2025 Australian study using online focus group discussions or interviews indicated a preference for maternal vaccination if it had similar efficacy and safety as an infant injection.(410)

A cross-sectional survey among pregnant women (n=1,001) and their partners conducted between February and April 2024 in the Netherlands showed that while there was a high acceptance rate for either strategy, when the choice was given, the majority of participants favoured maternal vaccination.(411)

Evidence specific to preferences of parents in Ireland is limited. A 2024 narrative review, which explored parental perspectives of maternal RSV vaccination versus mAb-based immunisation of the infant, reported that the factors that influence parental acceptance include healthcare provider recommendations, the perceived immunisation safety and efficacy, and disease severity.(412) This review predated the 2024/25 RSV Pathfinder programme which offered a mAB-based strategy and which achieved a high uptake (83%) in the target population.

8.3.4 Expectations and perceptions of older adult RSV immunisations

The aforementioned systematic review of knowledge and regarding RSV prevention by Gavaruzzi et al. included four quantitative cross-sectional studies focusing on older adults aged 60 years and older.(407) Overall, the studies indicated that this cohort had a limited knowledge and awareness of RSV, but had generally positive attitudes towards prevention strategies.

A 2025 industry-funded survey and literature review explored awareness of RSV and other respiratory disease vaccines among healthcare professionals and their patients. Included evidence suggested that among older adults, vaccine hesitancy is common, primarily due to lower levels of concern about respiratory infections, and due to considerable knowledge gaps with regard to the nature of the disease and its seasonality, symptoms and severity. The authors concluded that among both healthcare professionals and patients, awareness of and familiarity with RSV was lower than for other respiratory illnesses. The authors considered that this could contribute to sub-optimal vaccination adherence, particularly given the role of healthcare professions as trusted sources of information.(413)

In the US, two online surveys conducted in 2023 exploring intentions to receive RSV vaccination among adults aged 60 years and older reported that a considerable number of respondents were unlikely to seek out RSV vaccinations for the 2023/24

RSV season. One study reported results of a nationally representative survey of 1,200 US adults collected by YouGov between October and November 2023, of which 362 were aged 60 years and older.[414] Only 14% of respondents reported receiving an RSV vaccine, whereas 53% intended to never vaccinate against RSV. In this study, attitudes towards RSV vaccination were strongly influenced by prior vaccination behaviour towards COVID-19 or influenza vaccines, and the perceived safety and effectiveness of RSV vaccination. The second study reported results of a nationally representative survey collected using a survey panel in September 2023.[409] Of the 1,345 respondents aged 60 years and older, 9% had already been vaccinated against RSV while 42% had intentions to be vaccinated. Intention to vaccinate was lower among those who did not consider vaccines as safe, those with lower levels of perceived risk for RSV, and those with lower levels of trust in institutions. These surveys pre-dated the availability of national RSV immunisation programmes, with the earliest roll-out occurring during the 2023/24 RSV season, as described in Chapter 2. As noted above, the relevance of these studies is uncertain when considering increased roll-out of RSV immunisation programmes and increased availability of evidence supporting their effectiveness and safety, as outlined in Chapter 4.

8.4 Benefit-harm balance

As described in Chapter 2, RSV is a highly contagious respiratory virus.[15] In healthy individuals, infection with RSV is usually self-limiting.[28] However, RSV can cause more severe infections, such as pneumonia and bronchiolitis, which may lead to hospitalisation and death.[3] Those at increased risk of severe infection include infants aged under six months, premature infants, children aged under two years with congenital heart or lung disease, and older adults, particularly those with comorbidities or who are immunocompromised.[15]

The purpose of immunisation is to prevent or reduce the spread and severity of infectious disease. For many immunisation programmes, all or almost all of the target population are offered immunisation in the knowledge that perhaps only a small proportion will benefit. The benefit-harm balance must be appraised at both the individual level and at the population level. The decision to receive an immunisation is made by individuals, typically from the perspective of what the perceived benefit-harm balance is for them personally or for their child. Those responsible for making funding decisions on immunisation programmes, on the other hand, must also consider the benefit-harm balance at the population level. Both perspectives are analysed in this chapter.

8.4.1 Burden of RSV and epidemiology

Burden of RSV in infants

As reported in Chapter 3, data from the Health Protection Surveillance Centre (HPSC) and the Hospital In-Patient Enquiry (HIPE) system showed that of the populations included, the relative burden when measured via notified cases is greatest among children aged less than two years. Specifically, the data highlight the disproportionate burden associated with RSV in infants aged less than six months, with the highest rates of notified cases, emergency department visits, and hospitalisations including ICU admission consistently reported in this younger group and among those aged less than three months in particular, up until the 2024/25, RSV season when the HSE's Pathfinder Programme was introduced. This reported burden is substantially higher than among the adult population, including among adults aged 65 years and older. In addition to acute illness, RSV is also associated with long-term complications, such as recurring or persistent wheezing and the development of asthma, although the causal links are not yet established.[99]

Burden of RSV in older adults

When considering the burden of RSV among older adults, it is important to acknowledge that the notified case data are likely an underestimate of the total burden in older adults, particularly when considering the burden in primary care. As outlined in Chapter 3, while testing practices have changed, not all those with RSV undergo testing to be formally identified as a case. The lower absolute number of older adults with RSV-related ICU admissions (as compared with infants) should also be interpreted cautiously, as not all older adults with a clinical need for ICU care may necessarily be admitted. Such decisions are contingent on clinicians expecting a realistic benefit to admitting an older patient to a high-intensity setting, and the patient's own preference to undergo aggressive medical care.[415] It is also important to note when comparing the relative burden in the populations examined that older adults have a higher rate of RSV-related mortality relative to the infant populations.

RSV related mortality

As outlined in Chapter 3, overall RSV mortality rates are low in Ireland, but this is likely due to the availability of appropriate healthcare interventions and so the potential severity of RSV should not be minimised. RSV-related mortality in Ireland is also likely underestimated given that not all those with RSV are tested (particularly in primary care) and because it may not always be recorded as a cause of death. A 2015 systematic review reporting global disease burden estimates of RSV-related acute respiratory infection (ARI) in older adults documented higher rates of in-hospital RSV-ARI related deaths in older adults in low and middle-income countries as compared with high-income countries.[416] Similarly, when the burden of RSV internationally is examined, most paediatric RSV deaths are noted to occur in low and middle-income countries where supportive medical care is not always

available.[417] However, as outlined in Chapter 4, there is currently an absence of data to determine efficacy or effectiveness of RSV immunisation products against RSV-related mortality likely due to the very low number of such events in the included studies.

8.4.2 Benefits and harms at an individual level.

Benefits at an individual level

Reduced risk of RSV-related illness

According to the available evidence identified in Chapter 4 regarding the efficacy, effectiveness and safety of RSV immunisation, there is consistent evidence that all currently authorised RSV immunisation products are safe and effective for the prevention of RSV and associated complications, over one season. The certainty of evidence for the outcomes was assessed following the GRADE approach as outlined in Chapter 4, which considers both the quantity and quality of the evidence, with the evidence categorised as being of very low, low, moderate or high certainty. A determination that evidence is of low certainty should not be interpreted as meaning that an intervention is ineffective. Instead, it means that our confidence in the effect is limited, and the true effect may be substantially different (lower or higher) from the estimated effect.

It is important to consider the benefits of vaccination in the context of the age groups being considered for immunisation, that is infants and adults aged 65 years and older. For an individual who receives immunisation, the primary benefit, or perceived benefit, of implementing an RSV immunisation programme is to reduce the risk of RSV-related illness.

Benefits to an infant

With respect to the benefits to infants, as outlined in Chapter 4, there is evidence that maternal vaccination may reduce the risk of RSV-related hospitalisation and medically attended RSV-related lower respiratory tract disease (LRTD) up to six months of age. In addition, there is evidence that extended half-life-mAbs (EHL-mAbs) reduce the risk of medically attended RSV-associated lower respiratory tract infection (LRTI) and probably reduce hospitalisation with RSV associated LRTI over one season. There is also evidence that nirsevimab probably reduces RSV related ICU admission over one season. When weighing up the benefits to infants, it should be noted that they are a vulnerable population, especially those in the first few months of life when their immune systems are in the process of maturing.[418]

In the context of a prospective RSV immunisation programme, it is important to balance the likely benefits of immunisation with an individual's expectations. For the

cohort of infants, the efficacy and or effectiveness of EHL-mAbs and maternal vaccination against RSV-related health outcomes ranged from 69% to 83% and from 49% to 73%, respectively, over one season. The estimated duration of protection of EHL-mAbs is 150 days and begins immediately after administration. For maternal vaccination there is evidence that protection extends to 180 days following birth, assuming the mother was vaccinated at least 14 days before delivery. As such, the evidence for both interventions supports protection for a single RSV season only. As outlined in Chapter 3, there is a disproportional burden associated with RSV in infants aged less than six months, and among those aged less than three months in particular. Immunisation of infants born during the RSV season and those aged less than six months at the start of the RSV season would provide protection for when infants are likely at most risk. This should be clearly communicated to parents.

Benefits to an older adult

Regarding older adults, as outlined in Chapter 4, there is evidence to indicate that the currently authorised RSV prefusion vaccines reduce the risk of RSV-related LRTD and ARI. There is also evidence that RSV vaccination reduces RSV-related hospitalisations over one season. Overall, the efficacy and or effectiveness of RSV vaccines against RSV-related health outcomes ranged from 65% to 88% over one season. An additional benefit for older adults who are vaccinated against RSV highlighted by NIAC in their recommendations is that those vaccinated will be less likely to experience disruption to their work and or social lives. Given the higher burden associated with RSV in older adults with risk factors for severe disease including those with underlying vascular, pulmonary, renal and endocrine conditions as well as immunosuppressive treatments and conditions, NIAC considered that there may be a greater potential for these individuals to benefit from RSV vaccination.[135] Older adults in long-term care facilities may also particularly benefit in gaining protection from RSV immunisation as they may not have the ability to control their exposure to infection and outbreaks of RSV can spread quickly in such environments. For two vaccines (RSVpreF and RSVPreF3), there is evidence to support duration of protection over a second RSV season, and for RSVpreF specifically, over a third RSV season. However, there is evidence of waning immunity through the second and third season and as such, there is a need to moderate expectations of long-term immunity from RSV vaccination. As highlighted in Chapter 3, among older adults, the burden associated with RSV increases with increasing age, so waning immunity is a particular concern in this cohort. Life expectancy at age 65 years is estimated at 18.3 years and 21.0 years for men and women, respectively.[419] This raises uncertainty as to the optimal age for vaccination given that the need for a booster dose has not been established.

As summarised above and described in detail in Chapter 4, the currently authorised RSV immunisation products reduce the risk of medically attended RSV-related infections and associated complications. While the systematic reviews conducted in Chapter 4 did not identify evidence of the impact of RSV immunisation on quality of life, there is evidence that acute respiratory infections negatively impact quality of life, and as such it is plausible that prevention of such episodes would reduce this burden. Moreover, it is acknowledged that not all individuals with symptomatic infection seek medical assistance; despite this, they may still experience a loss of quality of life and or productivity which potentially could be averted through immunisation.

Awareness and increased knowledge of RSV

A potential benefit of implementing an RSV immunisation strategy is that, assuming communication and education is effective, an individual can gain an increased knowledge of RSV and how to lessen the chances of catching or spreading the virus. The administration of an immunisation product can create an opportunity for an individual to have a positive learning interaction with a healthcare provider. If an individual's questions and concerns regarding an immunisation are addressed with compassion and careful consideration, this may mitigate misperceptions, and increase their trust in healthcare providers and immunisation programmes in general.

Harms at an individual level

Potential adverse events

As outlined in Chapter 4, there is clear and consistent evidence that the authorised RSV immunisation products are safe and effective. However, the potential benefits of immunisation must be balanced against the potential for harm to the individual. As outlined in Chapter 4, serious adverse events are rare. Across the studies, the frequency of related serious adverse events was between 0.02% and 0.08% among older adults, 0.08% among pregnant women who received maternal vaccination (and 0% among newborns), and was between 0% to 0.04% among infants who received an EHL-mAB.

It is noted that implementation of an RSV immunisation programme would be in addition to existing programmes of immunisation for the respective cohorts. At least 1 in every 10 recipients of RSV vaccines will experience very common side effects such as headaches, muscle aches and injection site pain.[7-9] This is also true of other types of vaccines such as COVID-19[420] and influenza.[421] Moreover co-administration data indicate that some of these adverse events, such as fatigue, are more common when these vaccines are co-administered compared with when given

separately.[422] Although such side effects are usually mild and self-limiting, they may still be uncomfortable for an individual, and experiencing an adverse event can negatively affect an individual's perception of immunisations in general.[423, 424] Furthermore, it is important to acknowledge that co-occurrence of immunisation and a period of ill health may be perceived by an individual as being causally related, even though there may be no plausible mode of action to link the two events. Individuals, and in the context of EHL-mAb administration, parents of immunisation recipients, must provide consent for administration of the product and decide whether or not the level of risk is acceptable. A robust informed consent process ensures that this decision is made based on clear, relevant, and up-to-date information about the benefits and risks associated with RSV immunisation.

Regarding older adults, as highlighted in Chapter 4, recent post-marketing surveillance data have indicated an association between RSV vaccination and an increased number of cases of Guillain-Barré syndrome (GBS) in excess of those expected, although the absolute risk of GBS remains small. As noted, these data informed updated NIAC recommendations when considering the risk benefit balance associated with vaccination for various subgroups of older adults.

Perceptions and expectations of RSV immunisation

The complexity of the information about vaccine risks and benefits can be difficult to comprehend for many individuals.[425] Communication is particularly complex for RSV, where there are multiple authorised products, various immunisation strategies funded internationally, and uncertainty around the need for booster doses. If communication is not approached carefully, there is a risk that mis- and disinformation surrounding the topic could arise.[425] This could lead to an individual becoming distrusting of the advice of healthcare providers or immunisations in general. The implementation of any new immunisation programme, on top of existing ones, could also result in individual level immunisation fatigue[426] which could affect uptake of the newly introduced immunisation programme and or other established immunisation programmes.

Consideration of the potential benefits and harms of immunisations to an individual patient underscores the importance of immunisation decisions being evidence-based and is essential in order to maximise enablers to immunisation and minimise barriers.

8.4.3 Benefits and harms at a population level.

Benefits at a population level

Impact on existing national immunisation programmes

It is important to consider the impact of funding a new immunisation on established immunisation programmes. The addition of an RSV immunisation programme would broaden the protection provided by existing programmes, and as such may positively influence public perception. The addition of immunisation against an endemic virus such as RSV, which occurs seasonally each year, promotes the concept of preventive care in line with the current HSE Health Protection Strategy.[427] Potentially targeting infants and or older adults supports the delivery of lifelong health, especially given the association between RSV infection in early life with recurrent wheezing and asthma during childhood.[99]

Release of healthcare capacity

The estimated burden of RSV infection and associated complications on healthcare services in Ireland is described in Chapter 3, with evidence of substantial and predictable seasonal burden, especially for those aged less than one year. A successful RSV immunisation programme should ease the workflow for healthcare providers in primary and secondary care who previously treated RSV illness, with benefits to the healthcare workers and patients with other illnesses and their families, friends and carers. Prior to the introduction of the Pathfinder RSV immunisation programme, Irish paediatric hospitals experienced winter surges in RSV-associated ED attendances and hospitalisations, including ICU admissions, particularly in infants aged less than one year. These winter surges resulted in greater than 100% paediatric ICU bed occupancy and consequent cancellation or postponement of elective surgeries,[191] with late cancellations of planned surgery occurring 67 times in 2023.[428] Such cancellations of planned surgeries have patient safety implications especially for infants and children who are vulnerable. As outlined in Chapter 7, busy or overcrowded wards may also increase the risk of hospital-acquired infections, while insufficient bed capacity and high bed occupancy rates are linked to higher patient mortality, poor in-hospital outcomes, and risks to hospital staff welfare.[429] The potential for an RSV immunisation programme to mitigate the substantial burden on the healthcare system is particularly important when considering the limited paediatric critical care unit (PCCU) capacity in Ireland, given consistently high average bed occupancy rates in this setting, particularly in CHI, where average annual bed occupancy exceeded 100% in 2023.[428]

A reduction in RSV-related presentations in primary and secondary care should result in an overall alleviation of burden in healthcare even taking into account the increased workload associated with administering immunisations. This is because the time requirements of administration (15 minutes per patient) are usually predictable and resources can be allocated in a planned manner compared with the unscheduled nature of treating acute respiratory infections. A release of healthcare capacity in primary and or secondary care would also be supported by fully utilising community

mobile vaccination teams to reach population groups who may require more time-intensive and targeted approaches to encourage uptake.

Wider societal impact

There are potential indirect benefits to society of introducing a funded RSV immunisation programme due to fewer workdays missed by older adults within the workforce and parents of ill infants. In terms of infant immunisation, potential wider benefits include improved family well-being and avoidance of financial strain through parents not having to take time off work or other activities when the illness occurs after paid maternity or paternity leave has ended. In terms of the immunisation of older adults, preventing RSV-associated illness may benefit family members and or carers in terms of wellbeing and social productivity, as they may otherwise be required to take time off paid work while they help the individual recover.

Potential societal benefits to note include a possible reduction in antibiotic prescribing and resulting antibiotic resistance[430] although this was not observed in the studies included in Chapter 4.

It is noted that the implementation of an RSV immunisation programme could stimulate an increase in testing. While this could provide greater understanding of the true incidence of RSV disease and allow for a more accurate measure of the impact of vaccination, these potential benefits would need to be balanced with the increased opportunity cost and financial cost associated with increased testing activity.

There would also be considerable benefits for the commercial entity that develops a particular immunisation product if it is nationally funded. The decision to fund and implement an RSV immunisation programme should therefore be based on ensuring wider population benefits though a reduction in public resources being spent on treating RSV illness and its complications to enable increased spending on other public health priorities.

Potential harms at a population level

Impact on existing national immunisation programmes

Attending immunisation appointments requires a time commitment. In terms of infant immunisation with an EHL-mAb, newborn administration is unlikely to incur an additional appointment, but would add approximately 15 minutes on average to the workload of nurses and or midwives administering the immunisation to newborns. This additional time commitment mostly applies to the maternal vaccination and older adult vaccination scenarios. Pregnant women are currently recommended to receive Tdap vaccination during pregnancy, and current guidance advises a

minimum of two weeks between Tdap vaccination and administration of the maternal RSV vaccine, so an additional appointment may be required.

As highlighted in Chapter 2, there is some evidence that co-administration of RSV and certain influenza vaccines may not be optimal. The clinical relevance of these findings is unknown. Therefore the introduction of a new RSV immunisation programme could, if intended to be administered at the same time, have an uncertain impact on their effectiveness of influenza vaccines.

There are currently two autumn/winter vaccines funded in Ireland for older adults, COVID-19 and influenza, and these are suitable for co-administration with each other.[431] As per intramuscular injection technique training, vaccines that are given at the same time should be given in different limbs, where possible.[432] [433, 434] Therefore, vaccinators who prefer to administer vaccines in the arm rather than the thigh may decide to administer a maximum of two vaccine injections per appointment. If administration in separate limbs is not feasible or desired, such as in cases where a patient wishes to receive three vaccines at the one appointment, then two administrations in the same arm may be appropriate.[434] However, if a third autumn/winter vaccine was nationally funded for older adults, there may be a preference for an additional appointment which may represent a potential barrier to its uptake and or lead to a reduction in the uptake of one of the established older adult vaccine programmes. Such a reduction would represent a societal harm given the significant burden of influenza and COVID-19 in older adults.[435, 436] Vaccine fatigue can occur at a population level and may be associated with the perceived frequency of immunisation demands.[426] Careful consideration is therefore required when recommending new or additional immunisations so that uptake of other established immunisation programmes is not negatively affected.

The addition of a new immunisation programme will add to the primary and or secondary care workload in terms of training, education, and time spent administering the immunisation. Careful consideration of a fair use of resources should take into account the results of the economic evaluation (Chapter 6) which noted that none of the included strategies were cost effective at typical willingness-to-pay thresholds. Implementing RSV immunisation programmes that are not cost effective could require reallocation of resources, potentially impacting the existing healthcare system by diverting resources from other more cost-effective interventions or from the overall healthcare fund.

Perceptions and expectations of RSV immunisation

Developing the education that is needed to support new immunisation programmes will necessitate discussion of RSV immunisation specific adverse events. If sensationalised via traditional media or social media, this may affect the public

perception regarding the risk of immunisations in general. In relation to RSV immunisation in particular, a policy decision to choose one immunisation strategy over another, or the implementation of a strategy with multiple funded products will require clear communication to minimise the risk of misperceptions amongst the public and help support the resilience of existing programmes. Patient trust in healthcare providers and their recommendations has been noted as a key determinant for individuals in terms of the acceptability of RSV immunisation, along with perceived risk and severity of RSV-related disease, and the perceived safety of immunisation.[411, 437, 438] As with the other national immunisation programmes, there should be appropriate training and education provided to healthcare professionals who may have a role in communicating information to potential recipients of RSV immunisation, and to parents in the case of infant immunisation.

8.5 Autonomy

8.5.1 Autonomy of vaccine recipients

The rollout of RSV immunisation could have implications for the autonomy of recipients, particularly population cohorts that are vulnerable. Autonomy refers to an individual's ability to make informed, voluntary decisions about their own healthcare. Autonomy is upheld when individuals have access to clear, comprehensive information about an immunisation, including the implications of both receiving and not receiving it, as well as the risks associated with the condition that the immunisation seeks to prevent. This includes details about the immunisation's purpose, effectiveness, potential risks, and any alternatives. Adequate communication and education efforts are essential to ensure that adults or parents consenting on behalf of children have the information they need to make informed decisions. This is particularly important for individuals who may face challenges in accessing healthcare information independently. Healthcare professionals should engage in open and respectful discussions, acknowledging the autonomy of patients or their parents to either accept or decline the immunisation based on their values, preferences, and individual health circumstances.

8.5.2 Informed consent

In order to receive informed consent, a healthcare worker should ensure that an individual understands their right to say yes or no to immunisation and that they are able to make a decision without feeling pressured.[439] They must also be able to understand the information provided and have capacity to make an informed decision. For all patient groups included in this HTA there are established processes around informed consent for immunisation programmes already in place.[439-442]

Informed consent on behalf of infants

For four of the six possible immunisation strategies under assessment in this HTA, infants would be the recipients of the immunisation. Children under 16 years of age cannot legally consent to medical interventions and parents must sign consent forms on their behalf. While it is commonly accepted that children have a right to be protected from preventable harm,[443] immunisation is provided to asymptomatic individuals to prevent the onset of illness and, as a result, its benefits may not be visible to the parents of infants who receive it. As such, immunisation may be viewed as an intrusion on individual autonomy because in situations where immunisation is not mandated, individuals, particularly parents, may feel under pressure to comply with recommendations. While high rates of childhood immunisation coverage indicate that immunisation continues to be a widely accepted public health intervention, some individuals perceive it to be unnecessary.[444]

Informed consent for maternal RSV vaccination

The task of gaining informed consent may be more complex when pregnant women receiving a maternal vaccine need to consider not only the benefits and potential harms for their infant but also for themselves. Some parents may have concerns about administering an immunisation so soon after birth as the first childhood immunisations in Ireland are not normally administered until the baby is two months old. Parents routinely make a decision around consenting to newborn bloodspot screening and vitamin K injections shortly after birth,[445] but these may be perceived differently to immunisation. However, historically the BCG vaccine was given at birth[446] and the specific learnings from the RSV Pathfinder Programme can inform the best approach to allaying concerns about immunising this age group.

Informed consent for older adult RSV vaccination

Generally speaking, older adults are capable of making informed decisions regarding their own care. However, some sub-groups within this population may have capacity issues such as in cases of cognitive impairment and dementia. For individuals facing cognitive or decision-making challenges, healthcare professionals may need to assess their capacity to make informed decisions. Note that the assisted Decision-Making (Capacity) Act 2015 created new decision-making arrangements to support people who have issues with making decisions. Vulnerable adults may have specific concerns or questions related to the vaccine, such as safety concerns or potential interactions with other medications. Addressing these concerns empowers individuals to make autonomous decisions.

In the context of multiple immunisation options, care and consideration should be taken to clearly communicate what options are available to a person, and whether alternatives may exist even if they are not funded through the national immunisation programme. Examples of such situations may include a preference between an EHL-

mAB administered directly to the newborn or a vaccine administered to a woman during pregnancy. In the context where only a specific immunisation product is funded through a national immunisation programme, to support informed decision-making, individuals should be informed of what is offered through the programme, and that alternatives may be available if paid for privately.

8.5.3 Specific supportive actions to respect patient autonomy

There are commonalties across all immunisation programmes in relation to supportive actions that respect patient autonomy. Informed consent materials must provide sufficient information in a way that meets plain language criteria. Sufficient time must also be afforded to parents and patients to enable them to reflect on the choices available to them before making their decision. There will likely be a need for targeted programmes for population sub-groups such as those living in areas with social deprivation or immigrant populations. Changes to the strategy from one year to another need to be clearly communicated as people may have preconceived expectations of the options offered based on their previous experience. This is especially pertinent with regard to the immunisation of infants, as the Pathfinder programme has allowed parents to choose to protect their infants against RSV for two seasons (2024/25 and 2025/26). If a future policy decision did not provide funded immunisation for infants, this could be seen as curtailment of autonomy.

It is important that any concerns about efficacy or safety are addressed adequately to respect the autonomy of parents providing informed consent on behalf of an infant and essential for the successful implementation of any longer term RSV immunisation programme.

8.5.4 Autonomy of healthcare workers

In general healthcare professionals have a significant role to play as advocates for immunisation. Healthcare professionals are responsible for direct communication of health information to their patients, and their perception of immunisation programmes can therefore influence the attainment of the national immunisation programme objectives.

While the introduction of a funded RSV immunisations is unlikely to change the traditional role of most healthcare workers, as per the implementation of the Pathfinder programme for the 2024/25 and 2025/26 RSV seasons, it can result in some additional duties for midwives who traditionally did not administer immunisations but were best placed to do so as part of the pilot programme. This raised the possibility that such change in their traditional role could have been perceived as impacting their autonomy.

The rollout of a new immunisation programme could impact healthcare workers' workload and time management. Autonomy in this context involves the ability to efficiently integrate immunisation activities into daily workflows without compromising the quality of care provided. Early engagement with stakeholders such as primary and secondary healthcare workers would respect their autonomy and is likely a prerequisite for successful implementation of any new immunisation programme. If implemented, an RSV immunisation programme would potentially be available for various subgroups of people considered at increased risk of RSV and it would be essential to establish clarity for healthcare workers regarding eligibility criteria for immunisation for any such subgroups. The introduction of a new immunisation programme may impact resource allocation within healthcare settings if not carefully managed.

8.6 Respect for people

Reflection is required in relation to the potential impact of the implementation or use of the technology on human dignity; moral, religious or cultural integrity; and privacy.

8.6.1 Right to privacy

It is important to respect an individual's privacy during the immunisation process. While pharmacies and GP practices in Ireland have patient consultation areas with the purpose of discussing any health matters or concerns patients may have in private, maintaining privacy can be a challenging task in long-term care facilities (where older adult residents may experience reduced privacy during vaccination clinics organised to administer vaccines to them) or in busy hospital wards. While this concern extends beyond RSV immunisation, and there is a precedence with other vaccines administered as part of nationally-funded immunisation programmes, appropriate General Data Protection Regulation (GDPR) practices should also be adhered to in all vaccination settings.

8.6.2 Moral, religious or cultural differences

In order to elicit informed consent, information should be communicated clearly to the individual using plain language. Failure to provide clear easily understandable communication of the benefits and risks can negatively impact a person's dignity. It should be acknowledged that vaccine acceptance may be tied to cultural backgrounds and certain religious or cultural groups may have a moral objection to immunisation, including RSV immunisation.[447] It is essential for healthcare professionals to be aware of these perspectives and approach discussions with respect and cultural sensitivity. Improving health literacy and providing accurate information about the safety and efficacy of vaccinations are crucial steps in

addressing objections. Tailoring interventions that increase trust in immunisation and address concerns empowers individuals to make informed decisions about their health. As discussed in Chapter 7, the HSE NIO strategy for 2024 to 2027 supports the identification of groups with low immunisation uptake and the development of tailored immunisation programmes for such groups.

Specific to RSV immunisation, the decision between the maternal RSV vaccine and the EHL-mABs (within strategies where both are funded) may be perceived as having moral implications for some parents, as they may wish to spare a newborn from pain or side effects rather than basing this decision on other factors such as relative efficacy. However, as outlined in section 8.2.3, there is evidence that when a choice is given, survey respondents favour maternal vaccination.

8.7 Justice and equity

Currently in Ireland, two RSV vaccines (RSVpreF and RSVPreF3) are marketed and available to those who are willing to pay privately for vaccination. However, not all individuals can afford to pay for vaccination and many people may not be aware that vaccination is available. National funding of RSV immunisation programme would widen availability to all of those eligible. However, depending on how they are implemented, costs to patients such as administration fees could become a barrier to equal access.

As set out in Sláintecare, equality of access is based on individual patient need.[448] In order to ensure equality of access, the implementation of any immunisation programme needs to address potential barriers to access. Very rural areas may have a reduced number of locations where immunisation can be provided and there may be population groups without access to public or private transport underscoring the importance of allocating resources to mobile vaccination teams. Information regarding immunisation being available in a range of accessible formats and ensuring that patients have sufficient time to allow informed decision not only respects individual autonomy, but removes barriers to equal access.

It is important to note that uptake of nationally-funded immunisation programmes can sometimes be higher among well-resourced groups. Methods to increase uptake in groups with lower uptake could be considered where necessary, such as the involvement of community healthcare workers from a particular community to provide peer-to-peer education and encouragement on health-related matters.

Members of the Irish Traveller community in particular are less likely to avail of preventive health services such as immunisation.[449, 450] As outlined in the HSE National Traveller Health Action Plan, there are partnership projects between the HSE and Traveller organisations that provide ongoing support for Traveller families

on the ground and act as an interface between mainstream health services and Traveller community health workers who are employed on a part-time basis to undertake health advocacy in a range of health areas including immunisation.[451]

There is evidence that in the UK, uptake of vaccines among older adults is highest among the least deprived which shows the importance of targeted, evidence-based programmes. A 2021 linked data study in England found that greater area deprivation and less advantaged socioeconomic position (proxied by living in a rented home) and being disabled were associated with higher odds of not having received the COVID-19 vaccine.[452] A 2023 English cohort study found that less deprived areas had disproportionately larger increases in influenza vaccine uptake during the COVID-19 pandemic, which widened inequalities.[453] In the absence of immunisation mandates, people who choose immunisation are self-selecting and they may be more likely to be affluent. This may end up diverting resources towards people who can otherwise afford to pay and away from socially deprived groups or those with reduced health literacy.

Some RSV immunisation strategies modelled in Chapter 6 may exclude patient cohorts at similar or greater risk to those included. For infants, a decision to exclusively fund a seasonal maternal vaccine strategy may result in certain groups of infants not being protected (for example, infants born less than two weeks after maternal vaccination, infants born out of season or infants whose mothers have received the maternal vaccine in a previous pregnancy). The seasonal monoclonal antibody strategy does not include a catch-up for infants born prior to the RSV season. Both these strategies could be considered less equitable as compared with a strategy where all infants under a certain age during the season are protected. If an older adult single-dose vaccination strategy is limited to a defined age-based subgroup, then this could exclude some cohorts (such as those at a higher risk of complications) that may also benefit from vaccination. Moreover, a decision to fund an infant immunisation programme and not an older adult one, or vice versa, would exclude an important patient cohort who would otherwise benefit from vaccination. Therefore, the principles of justice and equity should be considered if choosing between strategies to ensure that access to healthcare interventions, especially preventive measures like immunisation, is distributed fairly among those who stand to benefit the most.

As outlined in Chapter 6, none of the included immunisation strategies were found to be cost effective at typical willingness-to-pay thresholds. Moreover, all strategies were associated with a substantial budget impact ranging from €15.6 million to €58.5 million for infant-based strategies and €70.6 million to €73.7 million for adult-based strategies. While funding an immunisation programme would improve equity of access, allocation of resources to an RSV immunisation programmes may prevent

spending on alternative healthcare services. If the burden on those administering a new immunisation programme (whether in primary or secondary care) is not carefully considered, this could also disadvantage patients who wish to access these same healthcare providers for other healthcare needs. Funding interventions that are not cost effective could create issues of justice and equity with respect to a fair distribution of benefits and burdens. However, acknowledging that the RSV Pathfinder programme has already provided immunisation to infants for two seasons is important. Due to this precedent, if infants are not provided with the same level of protection in future seasons it may also be viewed as unjust.

8.8 Legislation

There are no express provisions in Irish law in relation to consent on behalf of children by their parents. Legal precedence supports the common practice of obtaining one parent's consent for medical interventions for children under 16 years of age. In more complex situations where a parent refuses to consent to an intervention which the healthcare worker reasonably believes to be in the best interests of the child, or where there is a dispute between parents as to the appropriate course of action, then the HSE's National Consent policy may guide healthcare providers on the appropriate course of action.(454)

With regard to adults, the assisted Decision-Making (Capacity) Act 2015 which commenced on April 26th 2023 establishes a modern legal framework for adults who require, or may require, support in exercising their decision-making capacity, either now or in the future.(454)

8.9 Ethical consequences of HTA

8.9.1 Data sources and economic model assumptions

While there are numerous potential RSV strategies, the number modelled were limited to those that were evidence based and considered most feasible from a health service standpoint. Specific to this HTA, the protocol specifies the perspective of the publicly-funded health and social care system (HSE), however consideration is also given to the societal perspective. Due to the lack of study data, not all of the main efficacy or effectiveness outcomes outlined in the protocol (for example, RSV-related mortality) could be evaluated. For all of the immunisations examined, only the main outcomes of RSV-related medically attended lower respiratory tract disease/lower respiratory tract infection and RSV-related hospitalisations could be examined for all products (Chapter 4).

From an economic modelling perspective, the impact of RSV immunisation programme is summarised by translating disease states into changes in quality of

life. By summarising illness into a set of discrete health states, there is a risk that an economic model oversimplifies the experience of ill-health. The use of quality-adjusted life-years (QALYs) to capture health benefits does, however, enable calculation of an incremental cost-effectiveness ratio (ICER), which facilitates comparisons with those estimated in other evaluations (for example, interventions for different diseases and or populations) and against a reference willingness-to-pay threshold.

A number of the parameters in the economic model were subject to uncertainty. As not all cases of RSV illness are detected in Ireland, basing the evaluation on the numbers of notified cases could lead to an underestimate of the true benefits of RSV immunisation while the assessment would likely more accurately detecting the potential harms. To account for this potential underestimate of the burden of RSV on primary care, a multiplier (four-fold), informed by international evidence, was applied to notified cases. Any evaluation should acknowledge that there may be some uncertainty around the generalisability of data from RCTs but the available real-world effectiveness data for the RSV immunisations products examined was broadly consistent with the efficacy data from the included RCTs. There is, however, a lack of head-to-head comparison studies between RSV immunisation products and limited data to determine efficacy or effectiveness of these products against RSV-related ICU admissions or RSV-related mortality. As with any economic modelling exercise, the certainty of the results is limited by the underlying assumptions that underpin the model structure, the availability of data to populate the model and the chosen parameter values. Based on extensive scenario and sensitivity analyses, the findings of the economic evaluations presented are largely robust to data and structural assumptions with the exception of the uncertainty over the price of EHL-mAbs and vaccines.

8.9.2 Timing of assessment and availability of evidence

The evidence identified in Chapter 4 on the efficacy, effectiveness and safety of RSV immunisation was collected at a specific point in time and the conclusions could change as more evidence becomes available. The RSV immunisation products included in this HTA are all subject to additional monitoring requirements owing to the fact that they contain new active substances and are new biological medicines. This is a rapidly changing area of research, and new types of RSV immunisation, extensions to indications and longer-term efficacy, effectiveness and safety data especially in sub-groups (such as those aged 80 years and older and women with high-risk pregnancies) are likely to become available. Availability of additional data may alter perceptions regarding the risk benefit balance as already evidenced by updated NIAC recommendations for older adults, which changed the age-based recommendation from 65 years and older to those aged 75 years and older. As

outlined in Chapter 2, NIAC considered that RSV vaccination of those aged 60 to 74 years should be limited to those with additional risk of severe disease due to uncertainty regarding the burden of RSV in those without risk factors and the risk of serious, albeit rare, serious adverse events. For infants, evidence from the 2024/25 Pathfinder programme provided evidence of the substantial potential benefits of RSV immunisation of infants born during the RSV season, with the programme appearing to have a very significant positive impact on pediatric critical care capacity. Therefore, when informing national policy decisions on such matters, it is important to determine if there is sufficient evidence while also acknowledging that delaying such decisions could expose currently vulnerable patients to a risk that could have been prevented.

8.10 Discussion

This chapter examined the ethical issues that should be considered in relation to RSV immunisation programmes aimed at the population of infants aged less than 12 months during their first RSV season and adults aged 65 years and older in Ireland. The evidence of the effectiveness and safety of immunisations against RSV are described in detail in Chapter 4. In summary, there is consistent evidence that all currently authorised RSV immunisation products are effective for the prevention of RSV and associated complications, over a minimum of one season. With respect to the benefits to older adults there is evidence of protection for two vaccines (RSVpreF and RSVPreF3) over a second RSV season, and for RSVpreF specifically, over a third RSV season. As outlined in Chapter 6, none of the included strategies were found to be cost effective at typical willingness-to-pay thresholds and the associated budget impacts were substantial. Funding of interventions that are not cost effective raises ethical concerns due to the finite nature of the healthcare budget and the need for fairness in the allocation of resources.

A lot of the literature regarding parent and patient perspectives of RSV and RSV immunisations relate to industry-funded studies published in recent years immediately prior to or since the authorisation of new interventions for infants in the general population and for adults. Consistent with the evidence for other seasonal respiratory viruses, the studies highlight the negative impact RSV can have on an infected individual as well as their caregivers. Parents in particular reported worry about their child's health during periods of hospitalisation. Many of the studies suggest limited awareness of the virus as compared with other respiratory illnesses, although this may be changing given the implementation of population-level immunisation programmes in many countries, particularly for infants. Despite limited awareness, the studies highlighted that there is generally a positive attitude towards immunisation against RSV, which would appear to be substantiated by the high reported uptake rates, particularly of infant immunisation programmes documented

in Chapter 3. Attitudes and perceptions may have evolved in the time since the identified literature was published, influenced by increased awareness of RSV and of RSV immunisation options, as well as a change in the perceived benefits and harms of these interventions given increasing availability of national and international data to support their safety and effectiveness, as described in Chapter 4.

At an individual level, the potential benefits of RSV immunisation to infants are considerable as they are a particularly vulnerable population with immature immune systems, and given the disproportionate burden associated with RSV in this age group. RSV immunisation may also be of particular benefit to older adults with risk factors for severe disease or those in long-term care facilities who may not have the ability to control their exposure to infection. As outlined in Chapter 4, there is consistent evidence that all currently authorised RSV immunisation products are safe and serious adverse events are rare. However recent post-marketing surveillance data have indicated an association between RSV vaccination and an increased number of cases of GBS among older adults although the absolute risk of GBS remained small. This changing evidence base highlights the potential ethical consequences of the timing of the HTA. Given that the available interventions have all only been authorised since 2022, publication of additional studies could have a considerable impact on the perceived benefit-harm balance for subsets of the population.

Decision-makers must consider the benefit-harm balance at a population level. In particular, immunising infants against RSV should ease the workflow for healthcare providers and in Irish paediatric hospitals given evidence that previous winter surges in infant RSV admissions have severely impacted critical care capacity resulting in delays to scheduled care and with potential implications for patient safety.

Potential harms at a population level include potentially reduced uptake within established immunisation programmes either due to vaccine fatigue and or because individuals prioritise RSV immunisation above these established programmes. This may particularly be the case for the seasonal adult immunisation programmes, given that introduction of RSV immunisation would represent a third autumn/winter vaccine and likely necessitate an additional appointment. As such, careful consideration of how any newly-funded RSV immunisation programme is rolled out, could be crucial to minimise harm to other immunisation programmes.

Some of the RSV immunisation strategies modelled in Chapter 6 may exclude patient cohorts at similar risk to those included. While Chapter 6 advises on the cost effectiveness and budget impact of each strategy, the choice between strategies should also take into account the principles of justice and equity. Consideration of this principle by a decision-maker will help ensure access to healthcare interventions,

especially preventive measures like immunisation, are distributed fairly among those who stand to benefit the most.

This is a rapidly changing area of research and new types of RSV immunisation, extensions to authorised indications and longer-term effectiveness and safety data are likely to become available in the near future. The availability of multiple alternative interventions for a given population may also support price reductions as part of a competitive tender. Therefore, there may be greater certainty regarding the most effective and cost-effective immunisation strategy against RSV if an assessment is undertaken at a later date. However, given the substantial benefits demonstrated by trials and immunisation programmes, particularly in infants, undue delays in decision-making may prevent currently at-risk patient groups from receiving protection that would be highly beneficial to them. Moreover, any decision to implement or not implement a programme may need to be re-assessed in time to ensure that the decision represents an efficient and equitable use of healthcare resources.

9 Discussion

A health technology assessment (HTA) is intended to support evidence-based decision-making as to the most efficient use of resources in the healthcare system. The aim of this HTA is to inform a long-term policy decision regarding a respiratory syncytial virus (RSV) immunisation strategy for infants and older adults in Ireland. For context, a rapid HTA was completed in August 2024 to inform an interim policy decision for the 2025/26 RSV season. The HSE implemented a Pathfinder Programme for the 2024/25 RSV season which offered immunisation to babies born during the season (September to February). The Pathfinder Programme is being continued for the 2025/26 RSV season, with the addition of a catch-up programme for those aged less than six months at the beginning of September 2025. A systematic approach to this assessment was employed; a protocol for the HTA was published, and the assessment was conducted in accordance with national and international HTA guidelines. An Expert Advisory Group (EAG) comprising a broad range of key stakeholders was established to support the assessment.

9.1 Interpretation of the findings of the HTA

A HTA is founded on the synthesis of available evidence to address a specific policy question. The interpretation of that evidence is heavily influenced by the quality and quantity of information available, and the extent to which it is directly relevant and applicable to the policy question.

9.1.1 Description of technology

Since 2022, several new preventive interventions have been authorised that aim to reduce the burden of RSV. Whereas previously such interventions were limited to children at high risk of severe disease (via monthly palivizumab injection throughout the RSV season), interventions are now available to reduce the burden in the general infant population. These comprise extended half-life monoclonal antibody (EHL-mAb) agents such as nirsevimab (currently authorised in the EU) and clesrovimab (authorised in the US and awaiting an authorisation decision in the EU) and the maternal RSV vaccine. Vaccines are also now available to reduce the burden of RSV in older adults, with three such vaccines now authorised: RSVpreF, RSVPreF3, and the mRNA vaccine mRESVIA.

The international review conducted by the HIQA evaluation team shows that some European countries, including Ireland, have funded infant- and adult-based immunisation programmes to protect against complications of RSV. These funding decisions were found to vary substantially across Europe and may be temporary or permanent. In Ireland, as noted, an expanded Pathfinder RSV immunisation

programme is in place, offering immunisation to all babies born during the 2025/26 RSV season in addition to babies aged less than six months old on 1 September 2025. This aligns with the WHO recommendation outlined in Chapter 2 for all countries to introduce products to prevent severe RSV disease in young infants although it is noted that this recommendation is dependent on the feasibility of implementation within the country's healthcare system, cost effectiveness and anticipated coverage. As of 19 November 2025, 22 countries across the EU/EEA and UK were identified as having publicly-funded infant RSV immunisation programmes, while eight countries or regions were identified as having age- and or risk-based RSV immunisation programmes for older adults. Many of these countries had newly introduced or amended their programmes for the 2025/26 RSV season. It is likely that updates to national practices will continue for the 2025/26 RSV season and subsequent seasons as further evidence becomes available for the authorised interventions, new indications are approved, and new products are authorised.

9.1.2 Epidemiology and burden of disease

RSV incidence data (for children aged 0 to 2 years and adults aged 65 years and older) were sourced from the Health Protection Surveillance Centre (HPSC) in Ireland for RSV seasons 2018/19 to 2024/25 inclusive. Hospital utilisation data were also sourced from the Hospital In-Patient Enquiry (HIPE) system (for 2018 to 2024 inclusive and 2025 Q1) for both cohorts.

Both HPSC and HIPE data indicate that the burden of RSV is disproportionately higher among children aged less than two years, with this cohort accounting for 41% to 69% of the total number of notified cases since 2018/19. RSV-related emergency department (ED) visit rates (range: 286.6 to 990.6 per 100,000) and hospital admission rates (range: 643.8 to 1,063.9 per 100,000) were also highest in this cohort. Infants less than six months old accounted for more than half of the burden in those aged less than two years, contributing to 55% of the notified cases, with 53% of the RSV ED visits and 57% of RSV-related hospitalisations occurring in this age group. Additionally, the average annual number of RSV-related inpatient discharges was also substantially higher among those under two years of age compared with all other age groups. Between 2018 and 2014, there was an average of 1,633 (range 1,342 to 2,195) discharges without an ICU stay and 133 (range 67 to 191) discharges with an ICU stay in those aged less than two years. The burden of RSV was substantially lower among adults aged 65 years and older, when measured in terms of notified case rates (range: 47.1 to 283.5 per 100,000), RSV-related ED visit rates (9.4 to 77.4 per 100,000) and RSV-related hospital admission rates (18.3 to 93.4). Among older adults, the burden increased with increasing age and was generally highest in the subgroup aged 80 years and older, with this sub-

group accounting for 47% of all notified cases, 46% of RSV-related ED visits and 48% of RSV-related hospital admissions in older adults.

The HSE's Pathfinder Programme, which offered RSV immunisation to babies born during the 2024/25 RSV season, had a positive effect in reducing the burden of RSV among the infant cohort. Based on an analysis of notified RSV hospitalisations spanning this and four previous seasons using generalised additive models, we estimated that there was a 75% reduction in the incidence rate for nirsevimab-eligible infants born this season, conditional on the age-group and season effects adjusted for in the model (incidence rate ratio 0.25; 95% CI 0.19 to 0.33). This corresponded to an estimated 532 RSV hospitalisations averted (95%CI 369 to 695) for this group, in this season.[331] A similar trend was also observed for the number of Paediatric Intensive Care Unit admissions in Ireland (comprising data from Children's Health Ireland (CHI) at Crumlin and CHI at Temple Street) for severe RSV bronchiolitis (170 in 2023/24 vs 55 in 2024/25). Data available from other countries that have implemented infant RSV immunisation programmes also suggest a positive impact of such programmes. A study evaluating the effectiveness of the RSV immunisation programme in the Valencia region, Spain, where immunisation was offered to infants aged less than six months and those at high risk of disease aged less than 24 months old during the 2023/24 RSV season, reported a threefold reduction in RSV incidence and a twofold reduction in ARI-related hospitalisation among an immunised cohort compared with a non-immunised cohort.[455] A multicentre Italian study that compared hospitalisation due to RSV bronchiolitis before and after the implementation of an RSV immunisation programme in the 2024/25 season indicated a 51% to 85% reduction in hospitalisation, depending on whether implementation started in November or December across the centres. The study also noted no protective effect in a centre that delayed implementation until January 2025.[456]

With the exception of the infant cohort in the 2024/25 RSV season, in Ireland there appears to be a trend of increased incidence of notified RSV cases and RSV-related hospital admissions over time. However, it is uncertain whether the increased incidence is due to an actual increase in the RSV cases or due to improved ascertainment in the context of increased testing for ARI viruses. Since the COVID-19 pandemic, the availability of laboratory testing for acute respiratory viruses has increased across Ireland along with the increased use of reverse transcriptase-PCR (RT-PCR) testing. Additionally, in late 2024 the HSE issued guidance on ARI testing recommending the use of multiplex testing for a panel of viruses including RSV by a method that detects viral nucleic acid. Reverse transcriptase-PCR testing is considered the most sensitive RSV diagnostic test for both infants and older adults. Given the increased laboratory capacity in hospital settings and the use of multiplex

testing with high diagnostic performance, the most recent Irish data are likely a more accurate reflection of the true burden of RSV on the healthcare system, especially at secondary care level. However, the true burden at the primary care level is likely higher than reported as not all RSV cases are laboratory confirmed and some discharges may not be coded.

Changes in testing practices aside, it is recognised that the circulation of RSV subtypes may vary substantially from year to year. As outlined in Chapter2, RSV can be broadly categorised into two major antigenic groups or subtypes, A and B, each comprising multiple genotypes. These may vary in predominance by season. While it is suggested that RSV-A may be associated with increased severity of disease in children, both subtypes are frequently associated with medically attended and hospitalised RSV cases, with conflicting literature regarding differences in clinical impact by subtype.[457] However, it is suggested that changes in the predominant subtype may impact trends in RSV circulation in subsequent years, potentially due to subtype specific immunity.[458] Moreover, it is suggested that binding site mutations on RSV-B have the ability to alter susceptibility to nirsevimab,[459] highlighting the ongoing importance of surveillance data, including genomic data where appropriate, to inform the monitoring and evaluation of preventive measures.

The reported Irish data on morbidity and mortality associated with RSV are not linked to immunisation uptake data or other patient risk status data, including the presence of chronic conditions. Therefore, for children, it is not known what proportion of the observed morbidity and mortality occurred in those at increased risk of severe RSV-related disease, or the immunisation status of those experiencing severe outcomes. However, a study comparing the PICU admissions before and after the implementation of the Pathfinder immunisation programme reported that disease severity was low among the immunised cohort, suggesting that immunisation had a protective effect.

For older adults, the reported Irish data on RSV-associated morbidity and mortality occurred in a population for which there was no organised immunisation programme and where there was limited to no private access to RSV vaccines. Data for older adults relating to incidence of RSV and associated clinical outcomes also lacked information relating to patients' risk status, aside from age. It is recognised that the risk of severe RSV-related disease is higher among people with chronic cardiovascular conditions, respiratory conditions, immunocompromise, chronic kidney disease, diabetes, chronic neurological conditions, and among residents of long-term care facilities. As such, the greatest benefits of vaccination are likely to be among those with additional risk factors. Therefore, a decision could be made to implement a vaccination strategy targeting those with additional risk factors and those with greatest burden of disease instead of a universal age-based strategy. As

noted in Chapter 2, most publicly-funded immunisation programmes for older adults in the EU/EAA region are either risk based or use a combination of an age-based and risk-based approach. For example, there are programmes offering vaccination to all those aged 75 years (Sicily) or 75 years and older (France, Germany, Greece) and to those with additional risk factors aged 60 years and older (Germany, Greece, Sicily) or 65 years older (France).

One factor that influences the overall effectiveness of an immunisation programme is uptake. The 2024/25 Pathfinder programme observed a high uptake of RSV immunisation among infants born during the RSV season. Details of uptake in the 2025/26 season, including for the catch-up cohort, are not yet available. As reported in Chapter 3, available data on uptake of nirsevimab for infants within other EU/EEA countries showed that the uptake was typically higher for those born during the RSV season who were immunised prior to discharge from the maternity hospital (range: 80% to 95%) compared with the catch-up cohort (range 65% to 90%). For pregnant women and older adults, there are no national level Irish data. However, insights on potential acceptance and uptake may be informed using research studies, existing immunisation programmes and from jurisdictions that have implemented RSV immunisation programmes targeting these cohorts. As outlined in Chapter 8, these data suggest a positive attitude towards RSV immunisation despite low levels of awareness. Moreover, they suggest a preference among pregnant women for maternal vaccination over an EHL-mAb for the immunisation of newborns. It is noted, however, that many of these studies predated the authorisation of the new interventions and or the roll out of national immunisation programmes. As such both awareness of and attitudes towards immunisation may have changed given the availability of national and international data supporting the effectiveness and safety of these interventions.

Data from the UK, where year-round nationally-funded programmes for maternal vaccination and vaccination of older adults have been implemented since September 2024, suggest a steady increase in uptake over time. For example, in England, uptake of maternal vaccination gradually increased from 40.5% in September 2024 to 53.1% in January 2025,[460] while uptake among older adults steadily increased from 22.6% in September 2024 to 64.8% by the end of August 2025.[177] These data highlight a potential challenge associated with offering a time-limited opportunity to avail of vaccination, for example, if offered only to those turning a given age for that RSV season and not in subsequent seasons, particularly if not accompanied by a considerable campaign to raise awareness and to reduce barriers to access. It is noted that in Scotland, where uptake rates were initially higher (70.8% by June 2025),[461] there was a proactive campaign whereby eligible individuals were contacted and offered appointments in immunisation clinics. In Ireland, uptake data

for other respiratory virus vaccines indicate that among older adults, vaccination uptake increases with increasing age, for example reaching 89.6% in those aged 80 years and older in the 2024/25 influenza season.[396] Moreover, data from the HSE's Chronic Disease Management Treatment Programme indicate even higher uptake of the influenza vaccine (98%) among individuals with chronic disease, suggesting that uptake may be higher when the perceived risk is higher and or when individuals receive proactive education and support.[157]

9.1.3 Clinical effectiveness and safety

Systematic review evidence was used to evaluate the efficacy, effectiveness and safety of authorised interventions for the prevention of RSV and associated complications via:

- active immunisation of adults aged 65 years and older through vaccination
- passive immunisation of infants through maternal vaccination
- passive immunisation of infants and young children through the use of extended half-life monoclonal antibodies (EHL-mAbs).

The certainty of evidence for the outcomes was assessed following the GRADE approach as outlined in Chapter 4, which considers both the quantity and quality of the evidence, with the evidence categorised as being of very low, low, moderate or high certainty. A determination that evidence is of low certainty should not be interpreted as meaning that an intervention is ineffective. Instead, it means that our confidence in the effect is limited, and the true effect may be substantially different (lower or higher) from the estimated effect.

Vaccination of older adults

Overall, data were included from three RCTs (97,547 individuals), three observational studies (two test-negative case control studies (81,595 individuals) and one target trial emulation study (146,852 vaccinated individuals matched to 582,936 unvaccinated controls)). There is high certainty of evidence from RCTs that the currently authorised RSV prefusion vaccines reduce the risk of RSV-related LRTD (78%) and ARI (67%) in older adults over one RSV season. For two vaccines (RSVPreF3 and RSVpreF), there is evidence from a single RCT for each to support the duration of protection over a second RSV season (cumulative vaccine efficacy: LRTD, 67%; ARI, 52%), and in the case of one vaccine (RSVPreF3), a third season (cumulative vaccine efficacy: LRTD, 69%). However, in-season data provide evidence of waning immunity over time (season one, 83%; season two, 46%;

season three, 48%), meaning that there is uncertainty regarding the persistence of immunity against RSV over multiple seasons.

There was moderate certainty of evidence from two test-negative case control studies that RSV vaccination (RSVPreF3 or RSVpreF) probably reduces RSV-related hospitalisations in older adults over one season (77%). Two RCTs additionally reported on medically attended RSV-related LRTD, with one reporting on medically attended RSV-related LRTD with two or more symptoms over two seasons (RSVpreF, 60%) and the other RCT reporting on medically attended RSV-related LRTD visits over three seasons (RSVPreF3, 76%). Altogether, these findings indicate that RSV vaccination probably reduces severe cases of RSV and reduce the burden on the healthcare system. However, due to limited data availability no studies reported on vaccine efficacy or effectiveness against RSV-related ICU admissions or RSV-related mortality. Another limitation of the evidence from these RCTs is that adults aged 80 years and older and those with immunocompromising conditions were poorly represented. Representation improved among the observational studies, with a larger proportion of adults aged 75 years and older included compared with the RCTs. Moreover, while eligibility for the RCTs was restricted to those whose chronic conditions were medically stable, no such restrictions were applied to populations included in the observational studies. As such, these observational data, which were generally consistent with the RCT data, would appear generally applicable to the broader population of older adults.

In terms of reactogenicity and safety outcomes in older adults, RCT data indicated that adverse events were mostly mild-to-moderate, while severe or related SAEs were rare. Several post-marketing surveillance studies evaluating the safety of vaccination with RSVPreF3 or RSVpreF were planned or ongoing at the time of writing. Data from the USA and Great Britian have highlighted an excess risk of Guillain Barré syndrome (GBS) associated with RSVpreF vaccination, although incidence remains very rare. In the USA, observational electronic health record data indicated an excess of 18 GBS cases per 1 million doses of RSVpreF administered among adults aged 60 years and older. In Great Britain, data from England and Scotland estimated a combined excess of between 15 and 25 excess cases of GBS per million doses of RSVpreF among adults aged 75 to 79 years. In the context of these findings, the Commission on Human Medicines in the UK advised that the benefits of vaccination against RSV outweigh the very rare risk of GBS among older adults. These vaccines continue to be subject to additional monitoring by regulatory authorities to inform their benefit-risk profile and ensure their safe and effective use.[23] In 2025, NIAC published updated recommendations, amending their 2024 aged-based recommendation for RSV vaccination from 65 years and older to 75 years and older, and introducing instead a risk-based recommendation for those aged 60 to 74 years, with vaccination recommended for those with additional risk

factors for severe RSV disease due to identified comorbidities and for those aged 60 years and older residing in long-term care facilities. While recognising the effectiveness of the authorised interventions in those aged 60 years and older, this change to the NIAC recommendations reflected a belief that the balance of benefit and risk differed for younger adults within this cohort, particularly for those without additional risk factors for severe disease. Specifically, it recognised their lower burden of RSV-related disease in the context of uncertainty regarding duration of protection and need for revaccination, and the risk of serious albeit very rare adverse events.

Maternal vaccination

Data were included from a single RCT (7,420 individuals) and one observational study (505 individuals). Based on the single RCT, there is moderate certainty evidence that the currently authorised maternal vaccine probably reduces medically attended RSV-related LRTD (49%) and RSV-related hospitalisation (55%) in infants up to six months after birth. Observational data supports the effectiveness of the maternal vaccine against RSV-related hospitalisation (73%) up to six months after birth, although the certainty of evidence from the single study was low. This finding is further supported by a prospective multicentre cohort study published on 18 July 2025 of infants in Scotland and England hospitalised with acute LRTI including data up to 20 January 2025.[277] When adjusted for site and month, age under three months, sex and prematurity, vaccine effectiveness against RSV-related hospitalisation in this study was 58%, increasing to 72% when restricted to mothers vaccinated more than 14 days before delivery. In terms of duration of protection beyond six months after birth, the RCT reported on RSV-related hospitalisations up to 360 days after birth, but there was no significant difference noted between the vaccine and placebo groups at this timepoint.

The evidence from a single RCT indicates that this vaccine is safe for pregnant women and their infants, as severe reactions or related SAEs were rare. In both pregnant women and infants, most adverse events reported in the period up to one month after vaccination were mild-to-moderate in severity. Severe events represented approximately 10% of all adverse events among both groups. Of 18 adverse events considered related to the study intervention among pregnant participants, 14 occurred in the vaccine group and four in the placebo group. Four of these adverse events were categorised as pregnancy, puerperium and perinatal conditions; three occurred among the vaccine group and one in the placebo group. No maternal deaths or still births were judged as related to the study intervention. Evidence from a post-hoc analysis of this RCT found a statistically significant increased risk of preterm birth among the vaccine group compared with placebo when vaccination was given from 28 to less than 32 weeks' gestation ((6.8% versus

4.8%; RR, 1.43 (95% CI: 1.02 to 2.02)). There was also an increased risk of preterm birth among the vaccine group compared with placebo in non-high income countries (7% versus 4%; RR 1.73 (95% CI: 1.22 to 2.47)). Post-marketing surveillance data from the US reported a disproportionate number of reports of preterm birth following RSVpreF vaccination, which authors noted could be indicative of a potential safety signal. It is noted that regulatory agencies and countries have differed in their interpretation of these data. The EMA authorised administration of the vaccine between 24 and 36 weeks' gestation, although some European countries advise later administration to avoid the potential risk of preterm birth; the USA advise between 32 and 36 week's gestation;[262] and the UK state that administration at less than 28 weeks' gestation is not advised.[267]

EHL-mAbs

Clinical trial data were from four RCTs (16,121 individuals) and included the authorised EHL-mAbs nirsevimab and clesrovimab. There is high certainty evidence based on pooled data from three RCTs that EHL-mAbs reduce the risk of medically attended RSV-associated LRTI (69%) over one RSV season. There is moderate certainty evidence based on pooled data from four RCTs that EHL-mAbs probably reduce the risk of hospitalisation with RSV-associated LRTI (83%) over one RSV season. There is no evidence of multi-season protection or increased RSV-associated disease severity in a second season in the RCTs for these EHL-mAbs.

Effectiveness data comprised evidence from 15 observational studies (96,392 individuals) on nirsevimab, reported in a systematic review. Based on pooled data from two of these studies, there was moderate certainty evidence that nirsevimab possibly reduces RSV-related LRTI (87%) over one season. Low certainty evidence from nine studies indicate that nirsevimab may reduce RSV-related hospitalisation (87%), while moderate certainty evidence from four studies indicate that nirsevimab probably reduces RSV-related ICU admission (73%). Overall, evidence from observational studies, while restricted to nirsevimab only, supported the findings from the RCTs, particularly against severe disease.

While local and systemic adverse events were common, these were mostly mild-to-moderate in severity with no indication from these RCTs of safety concerns up to one year after randomisation or dosing. All four RCTs reported on SAEs related to the intervention, with only two participants (out of 8,380) judged to have had an SAE related to EHL-mAbs, while one participant (out of 6,190) had an SAE related to placebo. Overall, post-marketing surveillance data, available for nirsevimab, supported its continued use while maintaining the need for continued monitoring and vigilance.

9.1.4 Economic evaluation

To establish the most up-to-date evidence relating to the models employed and parameters used for the economic evaluation of RSV immunisation, a rapid review was conducted. The findings of the rapid review were used to inform the development of an economic model used to assess the cost effectiveness of RSV immunisation programmes for infants aged up to one year and adults in the general population aged 65 years and older in Ireland. A budget impact analysis (BIA) was conducted for both RSV immunisation programmes. The budget impact of RSV immunisation for a cohort of adults aged 60 years and older with additional risk factors for severe disease was also estimated.

Results from the economic analysis indicate that overall incidence of medically attended RSV is expected to fall after the introduction of RSV immunisation for infants and older adults aged 65 years and over. It was estimated that the infant-based immunisation strategies would result in reductions of 11.6% to 43.2%, relative to no immunisation, in the annual number of medically attended RSV cases. The estimated reduction in the annual number of hospitalised cases in those aged up to one year ranged from 52.1% for S2 to 12.2% for S3. The highest reductions in hospitalised cases were reported in the 0- to 2-month-old age group, at 62.5% and 23.3% for S2 and S3, respectively. For the adult-based strategies, the estimated reduction (compared with no immunisation) in the total number of medically attended RSV cases in the immunised age group over the five years of the model, ranged from 41.9% for S8 (coverage rate of 88.4%) to 28.2% for S6 (coverage rate of 60.1%).

In terms of cost effectiveness, from both the payer and societal perspectives, the infant and adult-based strategies were deemed not cost effective, relative to no immunisation or the previous least costly strategy, at a willingness-to-pay (WTP) threshold of €45,000 per quality-adjusted life year (QALY) gained. At assumed prices of €301 and €165 (ex VAT) for the EHL-mAb and maternal vaccine, respectively, the ICERs for the infant-based strategies were €210,000 per QALY for Strategy 5 (seasonal maternal vaccine and EHL-mAb plus catch-up EHL-mAb) compared with no immunisation, and €310,000 per QALY for Strategy 2 (seasonal EHL-mAb plus catch-up EHL-mAb) compared with Strategy 5. Three of the five infant-based strategies (seasonal EHL-mAb, seasonal maternal vaccine, seasonal maternal vaccine and EHL-mAb) were eliminated from the analysis as their ICERs were higher than subsequent strategies. For older adults, at an assumed vaccine price of €165 (ex VAT) per dose, Strategy 9 (adults aged 80 years and over in year one and those aged 80 years thereafter), dominated (less costly and generated more QALYs) all other strategies included in the analysis. However, with an ICER of €232,576 per QALY compared

with no immunisation, this strategy was deemed not cost-effective at a WTP threshold of €45,000 per QALY gained.

The base-case results of the economic evaluation were robust to sensitivity analyses but are highly sensitive to the costs of the EHL-mAbs and vaccines. A threshold analysis identified that Strategy 2 (seasonal EHL-mAb plus catch-up EHL-mAb), would be cost effective relative to no immunisation at a price of €166 or less (ex VAT) for the EHL-mAb, that is at a reduction of at least 45% from the base case price of €301. For older adults, sensitivity analysis demonstrated that Strategy 9 (adults aged 80 years and older and over in year one and those aged 80 years thereafter) would be cost effective compared with no immunisation at a vaccine price of €20 or less (ex VAT), which is an 88% reduction from the base case price of €165. Both of these analyses considered cost effectiveness relative to a WTP threshold of €45,000 per QALY gained.

The five-year incremental budget impact of an infant-based RSV immunisation programme ranged from €15.6 million for Strategy 3 (seasonal maternal vaccine) to €58.5 million for Strategy 2 (seasonal EHL-mAb plus catch-up EHL-mAb). These estimates assumed coverage rates of 62%, 76% and 82.6%, respectively, for seasonal EHL-mAbs, the maternal vaccine and for EHL-mAbs offered as part of a catch-up programme. For an adult-based RSV programme, the five-year incremental budget impact ranged from €70.6 million for Strategy 9 (immunising adults aged 80 years and over in year one and aged 80 years thereafter) to €73.7 million for Strategy 6 (immunising adults aged 65 to 69 years in year one and aged 65 years thereafter), assuming age-specific coverage rates of 60.1% and 88.4% for S9 and S6, respectively. The majority of the budget impact associated with both infant-based (approximately 70% to 88%) and adult-based (82%) immunisation programmes relates to the cost of product procurement. When the eligibility for immunisation was limited to include adults aged 60 years and older with additional risk factors for severe disease due to comorbidity or who are resident in a LTCF, the total budget impact over five years, based on a coverage rate of 97.8%, was estimated at €93.4 million.

Although it is estimated that immunisation will reduce the burden of RSV in Ireland, the benefits come with substantial financial cost. The healthcare budget is finite and decisions regarding the introduction of a new immunisation programme, could impact the provision of other health technologies within the healthcare system.

Based on the economic evaluations of infant- and adult-based RSV immunisation programmes presented, the evidence suggests that at current vaccine and EHL-mAb prices, RSV immunisation does not represent an efficient use of healthcare resources in Ireland. These findings are broadly consistent with those in the published

economic literature, whereby a finding that immunisation of infants or adults was cost effective was frequently in the context of a significant reduction in the assumed price of the interventions relative to their list price. Where multiple products for protection against RSV are available, the potential to negotiate substantial price reductions, as part of a competitive tender, may be possible.

9.1.5 Organisational issues

An overview of potential organisational issues associated with the modelled RSV immunisation strategies for infants and older adults in Ireland was explored in Chapter 7. While it is noted that each strategy would have slightly different organisational implications, each would require the provision of additional resources, in terms of staffing, training, processes for the storage and handling of immunisation products, capacity and procurement planning, and ensuring sufficient information and awareness is provided to healthcare staff and the public. It is noted that approximately 27,500 infants would be eligible for immunisation each year with a seasonal programme, increasing to over 55,000 infants if a catch-up programme is also provided, while vaccination of all cohorts identified in the 2025 NIAC recommendations for older adults (that is adults aged 75 years and older, those aged 60 to 74 years with additional risk factors for severe disease, and those aged 60 years and older residing in long-term care facilities) would include over 550,000 individuals in the first year of the programme alone.

The RSV Immunisation Pathfinder Programme, implemented during the 2024/25 RSV season and again for the 2025/26 RSV season, could provide important lessons and guidance to inform a future infant-based RSV immunisation strategy. The evaluation of the 2024/25 campaign found that the programme was successful and achieved high uptake in maternity settings (82%), in Children's Health Ireland (96%) and in the community through a contracted nurse-led service (99%). A catch-up cohort was included in the 2025/26 programme and serviced through HSE immunisation clinics. If a decision were taken to fund EHL-mAb-based RSV immunisation for infants born during the RSV season on a long-term basis, then a continued policy of its administration in the maternity unit/hospital would seem most feasible and would be consistent with the approach adopted internationally. For the catch-up cohort, there are challenges given the large number of infants involved and the aim that they should be immunised as close to the start of the RSV season as possible, both to ensure that they are immunised before widespread circulation of the virus and to ensure that they are protected for the duration of the season. While use of dedicated immunisation clinics is an option, provision of EHL-mAb-based RSV immunisation in GP practices would be consistent with the approach adopted for other items on the primary childhood immunisation schedule. In some instances,

there may be opportunities to coincide RSV immunisation with another scheduled visit to reduce the burden on parents and providers.

With respect to the immunisation of newborns against RSV through maternal vaccination during pregnancy, communicating eligibility criteria is a notable organisational issue given that vaccination would be limited to those due to deliver during the RSV season. Moreover, consideration will need to be given to the timing of vaccination, so as not to interfere with the uptake of existing vaccines recommended during pregnancy. This particularly applies to the pertussis vaccine given the requirement for a two-week interval between RSVpreF and the Tdap (pertussis) vaccine. Under the Mother and Infant Care Scheme, enrolled pregnant women receive dual care from a GP and obstetrician, with the scheme providing for at least six scheduled prenatal GP visits. Similarly, pregnant women are routinely offered a hospital-based foetal anomaly scan at 20 weeks. There may be potential to use one or more of these existing prenatal visits to raise awareness of RSV and or for vaccination to be scheduled at, or at an appointment adjacent to, one of these visits. Such an approach may support improved uptake and reduce the burden on patients and providers.

Considering a decision to offer RSV vaccination to older adults, there would be similar challenges in terms of avoiding any negative impact to existing vaccines recommended for this cohort. Potential barriers and facilitators should be considered, such as how and when information is provided, risk of vaccine fatigue, access and any cost to the recipient, as well as the age group eligible to receive the vaccine. Adoption of a third autumn/winter vaccine may necessitate an additional healthcare appointment, given a potential preference not to administer three (or four if including also once-off pneumococcal vaccination) at the same visit, which may present logistical challenges for providers and or present a potential barrier to uptake. While influenza and RSV typically exhibit distinct seasonality with annual epidemics during the winter months, to date, COVID-19 lacks seasonality. Co-administration of an annual COVID-19 booster with influenza vaccination allows for efficiency and likely leads to improved uptake, but given its lack of seasonality, the requirement for the COVID-19 booster to be administered during the early autumn may be less critical. In contrast, while the need for an RSV booster has not been established, as highlighted in section 9.1.3, there is evidence of waning immunity following vaccination, with maximum follow up limited to three years. NIAC has therefore recommended that vaccination will have the most individual benefit if administered just before the RSV season. Challenges remain, however, given evidence of decreased immune responses to certain strains of influenza when this vaccine is co-administered with RSV, the clinical significance of which is uncertain. As highlighted in Chapter 7, some National Immunization Technical Advisory Groups,

NIAC included, have taken a pragmatic approach, suggesting that the benefits of administering RSV and influenza vaccines at the same time, where there is an opportunity to do so, may outweigh these concerns.

Any programme of immunisation should be appropriately planned and resourced. Groups considered traditionally hard-to-reach or underrepresented may require additional resources and accommodations to drive vaccine uptake among such cohorts. While there is currently no national database that stores details of all immunisation records in Ireland, the development of a National Immunisation Information System has been outlined as one of the objectives of the HSE NIO Strategic Plan 2024-2027.

9.1.6 Ethical, patient and social considerations

Although infants cannot share their experience of being hospitalised due to RSV illness, the perspectives of their parents illustrate the worry and distress caused within families when infants experience severe RSV illness. These experiences are consistent with those of other families whose child is hospitalised or requires admission to ICU due to an acute illness and to that of others experiencing severe disease associated with other respiratory tract infections.[400] The perspectives of older adults who experience RSV show that RSV can cause potentially distressing symptoms such as shortness of breath, which can negatively affect their physical and emotional functioning.

The assessment of the potential benefits and harms associated with RSV immunisation must be considered at an individual and population level for two different population groups, infants and older adults. The benefit-harm balance can therefore be expected to differ depending on the specific population cohort and the perspective taken.

At an individual level, research evidence demonstrates the efficacy, effectiveness and safety of these products both for infants and older adults. At a population level, the potential benefits of RSV immunisation to infants are considerable as there is a disproportionate burden associated with RSV in this age group. The Pathfinder Programme has provided evidence of the benefits within Irish paediatric settings where previous RSV winter surges resulted in capacity constraints in paediatric ICUs with implications for patient safety. In older adults, the risk-benefit balance must additionally consider the risk of rare but serious adverse events, such as Guillain–Barré syndrome. For those without risk factors for severe disease, the burden of disease is less certain, with uncertainty also around the optimal time to vaccinate given evidence of waning immunity and that maximum follow up data are limited to three years. Among the older adult population, there is a higher burden associated

with RSV in those with risk factors for severe disease, and as such NIAC considered that there may be a greater potential for these individuals to benefit from RSV vaccination.

Acceptance of immunisations may be tied to cultural backgrounds or lack of knowledge or awareness of RSV. Tailored interventions to increase trust in vaccines and address concerns can help dispel misconceptions and improve uptake.

For all these patient groups included in this HTA, there are established processes around informed consent for immunisation programmes already in place. However, the task of gaining informed consent may be more complex within strategies where both the maternal RSV vaccine and the EHL-mAbs are funded concurrently. If there is an option of choosing between an EHL-mAb and a maternal vaccine, such a choice may be perceived as having moral implications for some parents, with some earlier studies noting a preference among parents for the maternal vaccine when efficacy is assumed to be equal. Moreover, the decision on which time of year a newly funded older adult RSV vaccine would be administered could be crucial in order to minimise harm to other vaccine programmes in particular the COVID-19 and influenza autumn/winter vaccines currently funded in Ireland for older adults.

The timing of assessment has important implications for the overall findings, given the recent availability of the interventions under consideration. New types of RSV immunisation, extensions to authorised indications and longer-term effectiveness and safety data are likely to become available in the near future, and so there may be greater certainty regarding the most effective and cost-effective strategy. While it could be considered unethical to unnecessarily delay access to the authorised RSV interventions given the strong evidence base to support their safety and effectiveness in the populations under consideration, access must be balanced with the fact that none of the included strategies were found to be cost effective at typical willingness-to-pay thresholds; funding of interventions that are not cost effective create issues of justice and equity with respect to a fair distribution of healthcare resources. However due to the precedent set by the Pathfinder programme, withdrawing the option to protect infants during future RSV seasons could also be perceived as unjust. Given uncertainty around the duration of effectiveness, prices and relative prices of interventions, any decision may need to be revised or updated as new data and products become available.

9.2 Conclusions

The findings of this HTA highlight the substantial and predictable seasonal impact that RSV has on the healthcare system in Ireland. This is most acutely evident in secondary paediatric healthcare services due to the disproportionate burden in

young children, particularly in those aged less than one year. This can affect the delivery of other scheduled and unscheduled care, increase pressure on staff, increase the risk of hospital-acquired infections, and challenge the ability to provide safe and effective care.

There is clear and consistent evidence that all currently authorised RSV immunisation products are safe and effective for the prevention of RSV and associated complications, over one season. While local and systemic events are common, these are mostly mild-to-moderate in severity; serious adverse events are rare. For older adults, there is evidence of longer-term effectiveness, with data limited to a maximum of three years' follow-up; however, immunity wanes over time.

Based on the analyses presented, RSV immunisation would be associated with significant reductions in medically attended cases and RSV hospitalisations with the greatest impact seen in the paediatric setting due to the higher burden of disease in this cohort. However, these benefits would come at a high financial cost. Considerable reductions in the estimated current vaccine and EHL-mAb prices would be required for either an infant- or adult-based RSV immunisation programme to represent an efficient use of healthcare resources in Ireland. As such, policy decision-making regarding the potential introduction of an RSV immunisation programme in Ireland should consider both the price and the relative prices of EHL-mAbs and RSV vaccines that can be achieved in the tendering process.

Appendix

Appendix A2

A2.1 Identified conditions that categorise an infant as being at increased risk of severe RSV-associated lower respiratory tract disease, for countries with publicly-funded RSV immunisation programmes

	Belgium[65]	Finland[36]	Greece[48]	Liechtenstein[72]	Luxembourg[40]	Portugal[74]	Spain[42]
Any underlying conditions that increase the risk of serious RSV infection					✓		✓
Bronchopulmonary dysplasia		✓	✓			✓*	✓
Chromosomal abnormalities						✓	
Chronic congenital or acquired diseases as determined by the treating specialist that are associated with a persistently high risk of severe RSV				✓			
Chronic lung disease of premature babies	✓	✓					
Chronic lung disease that required continuous treatment in the six months preceding the RSV season						✓	

Congenital airway anomalies	✓						
Cystic fibrosis or severe lung disease	✓		✓			✓	
Down syndrome	✓	✓	✓				
Gestational age less than 32 weeks at start of RSV season			✓				
Hemato-oncological diseases						✓	
Hemodynamically significant cyanotic or acyanotic heart disease/ Hemodynamically significant congenital heart disease	✓		✓			✓	✓
Hereditary metabolic diseases with immune impairment or significant respiratory problems						✓	
HIV infection with severe immune suppression or severe immunodeficiency due to immunosuppressive treatment						✓	
Immunocompromised states	✓						
Neuromuscular disease with respiratory compromise	✓					✓	
Premature birth (born before 29 weeks or between 29 and 36 weeks with pre-school siblings)		✓					
Pulmonary hypertension (moderate or severe)						✓	

Sequelae of severe congenital diaphragmatic hernia						✓	
Serious heart disease requiring surgical intervention		✓					
Severe combined immunodeficiency						✓	
Severe neurological disorder affecting respiratory function			✓				
Severe immunodeficiency		✓	✓				

Note: *Moderate or severe.

It is possible that other countries continue to fund palivizumab for children up to two years of age at high risk of severe RSV-related disease, and or may fund nirsevimab for this cohort, but outside of a specific immunisation programme.[10]

Appendix A4

A4.1 Search strategies – safety and efficacy of RSV vaccines

Databases	**9.2.1 Number of results**	Date searched
Medline Complete via Ovid	172	09/01/2025
Embase via Elsevier	512	09/01/2025
The Cochrane Library	96	09/01/2025
Total	780	
Total after duplicates removed in Endnote and Covidence	**609**	

Searches were rerun on 25 April 2025. Forward citation searched was conducted in citation chaser https://estech.shinyapps.io/citationchaser/

Databases	**9.2.2 Number of results**	Date searched
Medline Complete via Ovid	88	25/04/2025
Embase via Elsevier	255	25/04/2025
The Cochrane Library	14	25/04/2025
Total	357	

Citation Chasing	**9.2.3 Number of results**	Date searched
Citation Chaser	804	25/04/2025
Citation Chaser	17	02/05/2025

SEARCH STRATEGIES

Database Name	Medline via Ovid

Date search was run	09 Jan 2025

Database(s): **Ovid MEDLINE(R) ALL** 1946 to January 06, 2025
Search Strategy:

#	Searches	Results
1	((exp vaccines/ or exp immunizations/ or exp Immunization Programs/) and (Respiratory Syncytial Virus Infections/ or Respiratory Syncytial Virus, Human/ or Respiratory Syncytial Viruses/)) or ((respiratory-syncytial-virus* or RSV) adj5 (Vaccin* or immunis* or immuniz*)).ti,ab,kw,kf.	3482
2	Respiratory Syncytial Virus Vaccines/	1175
3	((chimpanzee-coryza-agent* or Human-orthopneumovirus* or respiratory-syncitial-virus* or respirosyncytial-virus* or respiratory-syncytial* or RS-virus* or RS-virus* or RSV* or syncytial-respiratory-virus* or Syncytial-virus* or LRTI-RSV) adj5 (Vaccin* or immunis* or immuniz*)).ti,ab,kw,kf.	2733
4	(F-protein-vaccin* or RSVpreF or "mRNA 1345" or "PF 06928316" or "RSV Pre F" or "MVA BN RSV" or "MEDI M2-2" or "RSVcps2" or "Ad26.RSV.preF" or "MEDI-599" or "MEDI-534" or "BBG2Na" or "RSV F-020" or "F Nanoparticle vaccine" or "MEDI7510" or "PFP-2-subunit" or "PFP-3-subunit" or "MVA-RSV" or "PanAD3-RSV" or "rBCG-N-hRSV" or "ChAd155-RSV" or "mRNA-1777" or "BBG2Na" or "LID ΔM2-2" or "LID/ΔM2-2/1030s" or "cpts-248/404" or "rA2cp248/404/1030" or AREXVY).ti,ab,kw,kf.	235
5	((respiratory-syncytial* or RSV) and (Pre-fusion or PFP-2 or Fusion-protein or PFP-3) and vaccin*).ti,ab.	318
6	1 or 2 or 3 or 4 or 5	3629
7	Animals/ not (Animals/ and Humans/) (462)	10115
8	6 not 7	3628
9	(letter or historical article or comment or editorial or news or case reports).pt.	5079221
10	8 not 9	3432
11	limit 10 to dt=20240408-20250131	370
12	Epidemiologic studies/ or exp case control studies/ or exp cohort studies/ or epidemiologic methods/ or Cross-Sectional Studies/ or Case control.tw. or ((follow-up* or followup* or concurrent* or	4962019

	incidence* or population*) adj3 (study* or studies* or analy* or observation* or design* or method*)).ti,ab. or (longitudinal* or prospective* or retrospective* or cohort* or cross-section* or crosssection*).ti,ab.	
13	(randomized controlled trial or clinical trial).pt. or randomi?ed.ti,ab. or placebo.ti,ab. or dt.fs. or randomly.ti,ab. or trial.ti,ab. or groups.ti,ab.	6384319
14	13 or 12	9724667
15	11 and 14	172

Database Name	Embase 1974 to 2024 via Elsevier
Date search was run	09 Jan 2025

No.	Query	Results
#15	#11 AND #14	512
#14	#13 OR #12	12324872
#13	'crossover procedure':de OR 'double-blind procedure':de OR 'randomized controlled trial':de OR 'single-blind procedure':de OR random*:de,ab,ti OR factorial*:de,ab,ti OR crossover*:de,ab,ti OR ((cross NEXT/1 over*):de,ab,ti) OR placebo*:de,ab,ti OR ((doubl* NEAR/1 blind*):de,ab,ti) OR ((singl* NEAR/1 blind*):de,ab,ti) OR assign*:de,ab,ti OR allocat*:de,ab,ti OR volunteer*:de,ab,ti	3462982
#12	'clinical study'/de OR 'case control study'/exp OR 'family study'/de OR 'longitudinal study'/de OR 'retrospective study'/de OR 'prospective study'/de OR 'cohort analysis'/exp OR 'epidemiologic methods'/exp OR 'cross-sectional studies'/exp OR 'follow up'/de OR (('follow up*' OR followup* OR concurrent* OR incidence* OR population*) NEAR/3 (study* OR studies* OR analy* OR observation* OR design* OR method*)) OR longitudinal*:ti,ab OR prospective*:ti,ab OR retrospective*:ti,ab OR cohort*:ti,ab OR 'cross section*':ti,ab OR crosssection*:ti,ab OR 'case control':ti,ab	10190295
#11	#8 NOT #9 AND [08-04-2024]/sd NOT [01-02-2025]/sd	774
#10	#8 NOT #9	5792
#9	[letter]/lim OR [conference abstract]/lim OR [conference paper]/lim OR [conference review]/lim OR [editorial]/lim OR [note]/lim	9365973
#8	#6 NOT #7	7630

#7	[animals]/lim NOT ([animals]/lim AND [humans]/lim)	6625556
#6	#1 OR #2 OR #3 OR #4 OR #5	8865
#5	('respiratory syncytial*':ti,ab OR rsv:ti,ab) AND ('pre fusion':ti,ab OR 'pfp 2':ti,ab OR 'fusion protein':ti,ab OR 'pfp 3':ti,ab) AND vaccin*:ti,ab	347
#4	'f protein vaccin*':ti,ab,de,tn,dn OR rsvpref:ti,ab,de,tn,dn OR 'mrna 1345':ti,ab,de,tn,dn OR 'pf 06928316':ti,ab,de,tn,dn OR 'rsv pre f':ti,ab,de,tn,dn OR 'mva bn rsv':ti,ab,de,tn,dn OR 'lid/Î´m2-2/1030s':ti,ab,de,tn,dn OR 'medi m2-2':ti,ab,de,tn,dn OR 'rsvcps2':ti,ab,de,tn,dn OR 'lid Î´m2-2':ti,ab,de,tn,dn OR ad26.rsv.pref:ti,ab,de,tn,dn OR 'cpts-248/404':ti,ab,de,tn,dn OR 'ra2cp248/404/1030':ti,ab,de,tn,dn OR 'medi 599':ti,ab,de,tn,dn OR 'medi 534':ti,ab,de,tn,dn OR 'rsv f-020':ti,ab,de,tn,dn OR 'f nanoparticle vaccine':ti,ab,de,tn,dn OR medi7510:ti,ab,de,tn,dn OR 'pfp 2 subunit':ti,ab,de,tn,dn OR 'pfp 3 subunit':ti,ab,de,tn,dn OR 'mva rsv':ti,ab,de,tn,dn OR 'panad3 rsv':ti,ab,de,tn,dn OR 'rbcg n hrsv':ti,ab,de,tn,dn OR 'chad155 rsv':ti,ab,de,tn,dn OR 'mrna 1777':ti,ab,de,tn,dn OR bbg2na:ti,ab,de,tn,dn OR arexvy:ti,ab,de,tn,dn	399
#3	(('chimpanzee coryza agent*' OR 'human orthopneumovirus*' OR 'respiratory syncitial virus*' OR 'respiratory syncytial pneumovirus*' OR 'respiratory syncytial virus*' OR 'respiratory syncytial virus*' OR 'respirosyncytial virus*' OR 'rs virus*' OR 'rs virus*' OR rsv* OR 'syncytial respiratory virus*' OR 'syncytial virus*' OR 'respiratory syncytial*' OR 'lrti rsv') NEAR/5 (vaccin* OR immunis* OR immuniz*)):ti,ab,kw,de,tn,dn	4088
#2	'respiratory syncytial virus vaccine'/exp	2787
#1	('vaccine'/exp OR 'vaccine' OR 'immunization'/exp OR 'immunization' OR 'immunization program'/exp OR 'immunization program') AND ('human respiratory syncytial virus'/exp OR 'human respiratory syncytial virus' OR 'respiratory syncytial virus infection'/exp OR 'respiratory syncytial virus infection') OR ((('respiratory syncytial virus*' OR rsv) NEAR/5 (vaccin* OR immunis* OR immuniz*)):ti,ab,kw,de)	8756

Database Name	The Cochrane Library
Date search was run	9 Jan 2025

ID	Search	Hits
#1	MeSH descriptor: [Vaccines] explode all trees	17786
#2	MeSH descriptor: [Immunization Programs] explode all trees	350

#3	MeSH descriptor: [Respiratory Syncytial Viruses] explode all trees	324
#4	MeSH descriptor: [Respiratory Syncytial Virus Infections] explode all trees	569
#5	MeSH descriptor: [Respiratory Syncytial Virus Vaccines] explode all trees	107
#6	#1 OR #2	17866
#7	#3 OR #4	657
#8	#6 AND #7	184
#9	#8 OR #5	187
#10	((chimpanzee-coryza-agent* OR Human-orthopneumovirus* OR respiratory-syncitial-virus* OR Respiratory-syncytial-pneumovirus* OR Respiratory-syncytial-virus* OR respiratory-syncytial-virus* OR respirosyncytial-virus* OR RS-virus* OR RS-virus* OR RSV* OR syncytial-respiratory-virus* OR Syncytial-virus* OR respiratory-syncytial* OR LRTI-RSV) NEAR/5 (Vaccin* OR immunis* OR immuniz*)):ti,ab,kw	464
#11	(F-protein-vaccin* OR RSVpreF OR "mRNA 1345" OR "PF 06928316" OR "RSV Pre F" OR "MVA BN RSV" OR "MEDI M2-2" OR "RSVcps2" OR "Ad26.RSV.preF" OR "MEDI-599" OR "MEDI-534" OR "BBG2Na" OR "RSV F-020" OR "F Nanoparticle vaccine" OR "MEDI7510" OR "PFP-2-subunit" OR "PFP-3-subunit" OR "MVA-RSV" OR "PanAD3-RSV" OR "rBCG-N-hRSV" OR "ChAd155-RSV" OR "mRNA-1777" OR "BBG2Na" OR "LID ΔM2-2" OR "LID/ΔM2-2/1030s" OR "cpts-248/404" OR "rA2cp248/404/1030" OR AREXVY):ti,ab,kw in Trials	196
#12	(respiratory-syncytial* OR RSV) AND (Pre-fusion OR PFP-2 OR Fusion-protein OR PFP-3) AND vaccin*:ti,ab	42
#13	#9 OR #10 OR #11 OR #12 with Cochrane Library publication date Between Apr 2024 and Jan 2025	96

A4.2 Search strategies – safety and efficacy of extended half-life monoclonal antibodies

Databases	**9.2.4 Number of results**	Date searched
Medline Complete via Ebscohost	90	23/04/2024
Embase via Ovid	242	23/04/2024
The Cochrane Library	122	23/04/2024
ClinicalTrials.gov	70	23/04/2024
ICTRP	28	23/04/2024
Total	552	
Total after duplicates removed in Endnote and Covidence	**399**	

Database Name	Embase via Ovid
Date search was run	23 April 2025

Database(s): **Embase** 1974 to 2025 April 21
Search Strategy:

#	Searches	Results
1	Human respiratory syncytial virus/ or respiratory syncytial virus infection/	30024
2	('respiratory syncytial virus*' or rsv).ab,ti.	31297
3	1 or 2	39557
4	exp monoclonal antibody/	871487
5	exp antivirus agent/	1643597
6	(antiviral* or 'monoclonal antibod*').ab,ti.	443363
7	(Nirsevimab or Beyfortus).ab,ti.	353
8	(RSVpreF or Abrysvo or RSVPreF3 or "mRNA vaccine" or mResvia).ab,ti.	5684
9	4 or 5 or 6 or 7 or 8	2478057
10	exp Systematic Review/ or exp Meta Analysis/ or ((systematic* adj2 (review* or overview*)) or (meta analys* or meta analyz*) or (literature adj3 (review* or overview*))).ti,ab.	1215775
11	exp Randomized Controlled Trial/ or randomized controlled trial.pt. or ((random* adj3 trial) or (placebo* or single blind* or double blind* or triple blind*)).ti,ab.	1252997
12	10 or 11	2376916

13	3 and 9 and 12	1182
14	limit 13 to dc=20231101-20251231	242

Database Name	Medline via Ebsco
Date search was run	23 April 2025

#	Query	Limiters/Expanders	Last Run Via	Results
S14	S3 AND S9 AND S12	Limiters - Publication Date: 20231101- Expanders - Apply equivalent subjects Search modes - Proximity	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - MEDLINE Complete	90
S13	S3 AND S9 AND S12	Expanders - Apply equivalent subjects Search modes - Proximity	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - MEDLINE Complete	399
S12	S10 OR S11	Expanders - Apply equivalent subjects Search modes - Proximity	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - MEDLINE Complete	1,856,005
S11	MH "Randomized Controlled Trial" OR PT "Randomized Controlled Trial" OR TI random* N2 trial OR AB random* N2 trial OR TI placebo* OR TI "single blind*" OR TI "double blind*" OR TI "triple blind*" OR AB placebo* OR AB "single blind*" OR AB "double blind*" OR AB "triple blind*"	Expanders - Apply equivalent subjects Search modes - Proximity	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - MEDLINE Complete	1,084,586

S10	MH "Systematic Review" OR MH "Meta Analysis" OR PT "Meta-Analysis" OR TI systematic* N1 (review* OR overview*) OR AB systematic* N1 (review* OR overview*) OR TI "meta analys*" OR TI "meta analyz*" OR AB "meta analys*" OR AB "meta analyz* OR TI literature N2 (review* OR overview*) OR AB literature N2 (review* OR overview*)	Expanders - Apply equivalent subjects Search modes - Proximity	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - MEDLINE Complete	927,066
S9	S4 OR S5 OR S6 OR S7 OR S8	Expanders - Apply equivalent subjects Search modes - Proximity	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - MEDLINE Complete	645,913
S8	XB (RSVpreF OR Abrysvo OR RSVPreF3 OR "mRNA vaccine" OR mResvia)	Expanders - Apply equivalent subjects Search modes - Proximity	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - MEDLINE Complete	4,212
S7	XB (Nirsevimab OR Beyfortus)	Expanders - Apply equivalent subjects Search modes - Proximity	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - MEDLINE Complete	271
S6	XB (antiviral* or "monoclonal antibod*")	Expanders - Apply equivalent subjects Search modes - Proximity	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - MEDLINE Complete	343,139
S5	(MH "Antiviral Agents+")	Expanders - Apply equivalent subjects Search modes - Proximity	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - MEDLINE Complete	184,893

S4	(MH "Antibodies, Monoclonal+")	Expanders - Apply equivalent subjects Search modes - Proximity	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - MEDLINE Complete	294,587
S3	S1 OR S2	Expanders - Apply equivalent subjects Search modes - Proximity	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - MEDLINE Complete	26,402
S2	XB (respiratory syncytial virus* or rsv)	Expanders - Apply equivalent subjects Search modes - Proximity	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - MEDLINE Complete	24,704
S1	(MH "Respiratory Syncytial Viruses+") OR (MH "Respiratory Syncytial Virus, Human") OR (MH "Respiratory Syncytial Virus Infections")	Expanders - Apply equivalent subjects Search modes - Proximity	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - MEDLINE Complete	15,156

Database Name	The Cochrane Library
Date search was run	23 April 2025

ID	Search	Hits
#1	MeSH descriptor: [Respiratory Syncytial Virus Infections] explode all trees	570
#2	MeSH descriptor: [Respiratory Syncytial Virus, Human] explode all trees	170
#3	(respiratory syncytial virus* or rsv):ti,ab,kw (Word variations have been searched)	1671
#4	#1 OR #2 OR #3	1671
#5	MeSH descriptor: [Antibodies, Monoclonal] explode all trees	22059
#6	(antiviral* or monoclonal antibod* or Nirsevimab or Beyfortus or RSVpreF or Abrysvo or RSVPreF3 or "mRNA vaccine" or mResvia):ti,ab,kw (Word variations have been searched)	36395
#7	#5 OR #6	44727
#8	#4 AND #7 with Cochrane Library publication date Between Nov 2023 and Dec 2025	122

Database Name	Clinical Trials.gov
Date search was run	23 April 2025
Search 1	"respiratory syncytial virus" OR RSV | Monoclonal antibody | First posted on or after 11/01/2023
Search 2	"respiratory syncytial virus" OR RSV | antiviral | First posted on or after 11/01/2023
Search 3	respiratory syncytial virus OR RSV | monoclonal antibody| Primary completion on or after 11/01/2023
Search 4	respiratory syncytial virus OR RSV | antiviral | Primary completion on or after 11/01/2023
Search 5	"respiratory syncytial virus" OR RSV | Nirsevimab or Beyfortus
Search 6	"respiratory syncytial virus" OR RSV | RSVpreF

Search 7	"respiratory syncytial virus" OR RSV | Abrysvo
Search 8	"respiratory syncytial virus" OR RSV | RSVPreF3
Search 9	"respiratory syncytial virus" OR RSV | mResvia
Search 10	"respiratory syncytial virus" OR RSV | mRNA vaccine

Database Name	ICTRP
Date search was run	23 April 2025
Search Strategies	Search 1: respiratory syncytial virus* AND antiviral Search 2: respiratory syncytial virus* AND monoclonal antibod* Search 3: respiratory syncytial virus* AND Nirsevimab Search 4: respiratory syncytial virus* AND Beyfortus Search 5: respiratory syncytial virus* AND RSVpreF Search 6: respiratory syncytial virus* AND Abrysvo Search 7: respiratory syncytial virus* AND RSVPreF3 Search 7: respiratory syncytial virus* AND mRNA vaccine Search 8: respiratory syncytial virus* AND mResvia

A4.3 GRADE Summary of findings table for older adults

Population:	Older adults (aged ≥ 60 years)
Setting:	Any
Intervention:	Authorised RSV vaccines (RSVPreF3, RSVpreF, RSVmRNA)
Comparison:	Placebo or no vaccination

No of participants/ person years (studies) RSV season	Number of participants		Effect		Certainty of evidence	What does this mean?
	RSV vaccination	Placebo/ no vaccination	Relative (95% CI)	Absolute (95% CI)		
	Events/person year					
RSV-related acute respiratory illness over one season						
47,426 person years (3 RCTs) 2021-2022 RSV season	90/23,738 (0.4%)	275/23,688 (1.2%)	IRR 0.33 (0.26 to 0.41)	8 fewer per 1,000 person years (from 9 fewer to 7 fewer)	⊕⊕⊕⊕ High[a]	Authorised RSV vaccines reduce RSV-related acute respiratory illness in older adults over one season
RSV-related lower respiratory tract disease over one season						
47,459 person years (3 RCTs) 2021-2022 RSV season	31/23,748 (0.1%)	138/23,711 (0.6%)	IRR 0.22 (0.15 to 0.33)	5 fewer per 1,000 person years (from 5 fewer to 4 fewer)	⊕⊕⊕⊕ High[a]	Authorised RSV vaccines reduce RSV-related lower respiratory tract disease in older adults over one season
RSV-related hospitalisation over one season						
37,398 (2 test-negative case-control studies) 2023-2024 RSV season	2,226 cases	35,172 controls	OR 0.23 (0.17 to 0.31)	-	⊕⊕⊕◯ Moderate[a,b]	Authorised RSV vaccines probably reduce RSV-related hospitalisations in older adults over one season.
RSV-related ICU admissions						

-	-	-	-	-	-	-
RSV-related mortality over one season						
-	-	-	-	-	-	-
Serious adverse events related to the study intervention over one season						
94,663 (3 RCTs) 2021-2022 RSV season	17/47,416 (0.04%)	10/47,247 (0.02%)	RR 1.67 (0.78 to 3.58)	0 fewer per 1,000 (from 0 fewer to 1 more)	⊕⊕◯◯ Low[c]	While rare, due to the low certainty of evidence, it is unclear if authorised vaccines are associated with serious adverse events related to the study intervention over one season.
Serious adverse events related to the study intervention in the second RSV season						
15,024 (1 RCT) 2022-2023 RSV season	2/4,991(0.0%)	4/10,033 (0.0%)	RR 1.01 (0.18 to 5.49)	0 fewer per 1,000 (from 0 fewer to 2 fewer)-	⊕⊕◯◯ Low[c]	While rare, due to the low certainty of evidence, it is unclear if authorised vaccines are associated with serious adverse events related to the study intervention in the second season.

[a] Strong association – large effect (RR<0.5) warranted upgrading of evidence by 1 level

[b] Risk of bias – GRADE assessment started at low certainty of evidence due to ROBINS-I assessment (serious-to-moderate risk of bias)

[c] Imprecision – very small number of events and wide confidence intervals crossing null effect warranted downgrading by 2 levels

Key: CI – confidence interval; IRR – incidence rate ratio; OR – odds ratio; RCT – randomised controlled trial; RSV – respiratory syncytial virus

A4.4 GRADE Summary of findings table for maternal vaccination

Population:	Maternal vaccination for the passive immunisation of newborns and infants (age <12 months)
Setting:	Any
Intervention:	Authorised RSV vaccines (RSVpreF)
Comparison:	Placebo or no vaccination

No of participants (studies)	Number of participants		Effect			
	RSV vaccination	Placebo	Relative (95% CI)	Absolute (95% CI)	Certainty of evidence	What does this mean?
RSV-related acute respiratory illness (180 days follow-up)						
-	-	-	-	-	-	-
Medically attended RSV-related lower respiratory tract disease (180 days follow-up)						
7,307 (1 RCT) 2020-2021, 2021-2022 and 2022-2023 RSV seasons	67/3,660 (1.8%)	132/3,647 (3.6%)	RR 0.51 (0.38 to 0.68)	18 fewer per 1,000 (from 22 fewer to 12 fewer)	⊕⊕⊕◯ Moderate[a]	Maternal vaccination during pregnancy probably reduces lower respiratory tract disease caused by RSV infection in infants up to 180 days after birth
RSV-related hospitalisation (180 days follow-up)						
7,307 (1 RCT) 2020-2021, 2021-2022 and 2022-2023 RSV seasons	21/3,660 (0.6%)	47/3,647 (1.3%)	RR 0.45 (0.27 to 0.74)	7 fewer per 1,000 (from 9 fewer to 3 fewer)	⊕⊕⊕◯ Moderate[a,b]	Maternal vaccination during pregnancy probably reduces hospitalisation caused by RSV infection in infants up to 180 days after birth
RSV-related hospitalisation (180 days follow-up)						
505 (1 NRSI)	RSV positive Vaccinated: 51/286	RSV negative	OR: 0.287 (0.177 to 0.467)	-	⊕⊕◯◯ Low[c]	Maternal vaccination during pregnancy may reduce hospitalisation caused by RSV infection in infants up to 180

2024 RSV season Argentina (March-August)		Vaccinated: 109/219				days after birth, but the certainty of evidence is low
RSV-related mortality						
7,420 (1 RCT) 2020-2021, 2021-2022 and 2022-2023 RSV seasons	0/3,711 0%	1/3,709 0%	RR 0.33(0.01 to 8.18)	0 fewer per 1,000 (from 0 fewer to 2 more)	⨁⨁◯◯ Low[a,d]	It is unclear whether maternal RSV vaccination has an effect on RSV-related mortality in infants due to low certainty of evidence
Serious adverse events related to the study intervention						
7,385 (1 RCT) 2020-2021, 2021-2022 and 2022-2023 RSV seasons	3/3,698 (0.1%)	1/3,687 (0%)	RR 2.99 (0.31 to 28.78)	1 more per 1,000 (from 0 fewer to 8 more)	⨁⨁◯◯ Low[a,d]	While rare, due to the low certainty of evidence, it is unclear if authorised vaccines are associated with serious adverse events related to the study intervention

[a] Single study – A conservative interpretation of the certainty of the evidence was taken since the results are based on that of a single study. Downgraded one level from high to moderate certainty.

[b] Strong association – not upgraded for large effect as results based on a single study

[c] Risk of bias – GRADE assessment started at low certainty of evidence due to ROBINS-I assessment (moderate risk of bias)

[d] Imprecision – very small number of events and wide confidence intervals warranted downgrading by two levels

Key: CI – confidence interval; RR – relative risk; RCT – randomised controlled trial; RSV – respiratory syncytial virus

A4.5 GRADE Summary of findings table – efficacy, effectiveness and safety of EHL-mAbs

Population: Newborns and infants (age ≤2 years)
Setting: Any
Intervention: EHL-mAbs (nirsevimab, clesrovimab)
Comparison: Placebo or no immunisation

No of participants (studies) RSV season	Effect				Certainty of evidence	What does this mean?
	EHL-mAbs	Placebo or standard care	Relative (95% CI)	Absolute (95% CI)		
Medically attended RSV-associated LRTI over one season						
8,064 (3 RCTs) 2016-2017 & 2019-2021 RSV seasons	109/5,376 (2.0%)	174/2,688 (6.5%)	**RR 0.31** (0.25-0.40)	**45 fewer per 1,000** (49 to 39 fewer)	⊕⊕⊕⊕ High	EHL-mAbs reduce medically attended RSV-associated LRTI over one season.
Medically attended RSV-associated LRTI over two seasons						
4,429 (2 RCTs) 2020-2022 RSV season	72/2,960 (2.4%)	36/1,469 (2.5%)	**RR 0.99** (0.67-1.46)	**0 fewer per 1,000** (8 fewer to 11 more)	⊕⊕⊕ Moderate [a]	EHL-mAbs probably do not reduce medically attended RSV-associated LRTI over two seasons.
RSV-related LRTI incidence over 1 season (infants <12 months)						
355 (2 NRSIs) (2023-2024 RSV season)	34/91 37.4%	217/264 82.2%	OR 0.13 (0.07 to 0.23)	-	⊕⊕⊕◯ Moderate [b,c]	Administration of nirsevimab to newborns and infants probably reduces the risk of RSV-related LRTI
RSV-associated LRTI with hospitalisation, over one season						
16,121 (4 RCTs)	34/9,414 (0.4%)	135/6,707 (2.0%)	**RR 0.17** (0.12-0.25)	**17 fewer per 1,000** (15 to 18 fewer	⊕⊕⊕ Moderate [d]	EHL-mAbs probably reduce RSV-associated LRTI with hospitalisation over one season.

2016-2017, 2019-2021 & 2022-2023 RSV seasons						
RSV-associated LRTI with hospitalisation, over two seasons						
2,891 (1 RCT) 2020-2022 RSV season	3/1,944 (0.2%)	3/947 (0.3%)	**RR 0.55** (0.10-2.46)	**1 fewer per 1,000** (3-5 fewer)	⊕⊕⊕ Moderate [a]	Nirsevimab probably does not reduce RSV-associated LRTI with hospitalisation over two seasons.
RSV-related hospitalisation over one season (infants <12 months)						
9,012 (9 NRSIs) (2023-2024 RSV season)	754/5,551 (13.6%)	2,166/3,461 (62.6%)	OR 0.13 (0.08 to 0.20)	-	⊕⊕◯◯ Low [b,c,e,f,g]	Administration of nirsevimab to newborns and infants may reduce the risk of RSV-related hospitalisation, but the certainty of the evidence is low.
RSV-related ICU admissions over one season (infants <12 months)						
1865 (4 NRSIs) (2023-2024 RSV season)	85/1,374 (6.2%)	268/491 (54.6%)	OR 0.27 (0.16 to 0.48)	-	⊕⊕⊕◯ Moderate [b,c,h]	Administration nirsevimab to newborns and infants probably reduces the risk of RSV-related ICU admissions.
Hospital length of stay over one season (infants <12 months)						
1537 (3 NRSIs) (2023-2024 RSV season)	454	1,083	SMD -0.04 (-0.16 to 0.07)	-	⊕⊕◯◯ Low [e]	It is unclear whether hospital length of stay differs between immunised and unimmunised infants, and the certainty of the evidence is low.
Medically attended all-cause LRTI over one season						
8,064 (3 RCTs)	889/5,376 (16.5%)	560/2,688 (20.8%)	**RR 0.79** (0.72 to 0.87)	**44 fewer per 1,000** (58 to 27 fewer)	⊕⊕⊕⊕ High	EHL-mAbs reduce medically attended all-cause LRTI over one season.

2016-2017 & 2019-2021 RSV seasons						
Serious adverse events related to the study intervention						
14,570 (4 RCTs) 2016-2017, 2019-2021 & 2022-2023 RSV seasons	2/8,380 (0.0%)	1/6,190 (0.0%)	-	-	⊕⊕◯◯ Low [a,d]	While rare, due to the low certainty of evidence, it is unclear if EHL-mAbs are associated with serious adverse events related to the study intervention.

[a] Imprecision – wide confidence interval and or very few events.
b The risk of bias in the individual studies was assessed by the review authors using the JBI critical appraisal tool. These studies were scored as at low risk of bias. Certainty of evidence was not downgraded.
c Potential for plausible confounding to bias towards the no effect, however, GRADE guidance states not to upgrade for this domain for observational studies if an outcome has been downgraded for any reason. A conservative approach was taken not to upgrade for this domain for the various outcomes, in part due to the additional potential for residual confounding noted by the review authors.
d Risk of bias – HARMONIE RCT had 'some concerns' on RoB-2 assessment.
e The review authors noted that publication bias was detected for RSV-related hospitalisation by Egger's test (p=0.0075). The authors noted that RSV-related hospitalisation effect estimates remained consistent after adjusting for publication bias with trim-and-fill analysis, suggesting robustness of the effect estimate despite publication bias. As such, the certainty of evidence was not downgraded.
f Very large effect (RR~<0.2). Certainty of evidence upgraded by one level due to concerns relating to inconsistency and potential concern relating to publication bias.
g Potential for plausible confounding to bias towards the no effect, however, GRADE guidance states not to upgrade for this domain for observational studies if an outcome has been downgraded for any reason. A conservative approach was taken not to upgrade for this domain for the various outcomes, in part due to the additional potential for residual confounding noted by the review authors.
h Large effect (RR~<0.5). Certainty of evidence upgraded by one level.
Key: CI – confidence interval; EHL-mAb – extended half-life monoclonal antibody; ICU – intensive care unit; LRTI – lower respiratory tract infection; OR – odds ratio; NRSI – non-randomised study of intervention; RCT – randomised controlled trials; RR – risk ratio; RSV – respiratory syncytial virus; SMD – standardised mean difference.

A4.6 Outcomes and case definitions for pooled efficacy outcomes, as described across RCTs relating to vaccination of adults aged ≥65 years

Outcome, as per HIQA update	Outcome, as per RCT Case definition		
	Ison et al.,[219] 2025 **Ison et al.,[224] 2024** **Papi et al.,[221] 2023**	**Walsh et al.,[218] 2025** **Walsh et al.,[222] 2023**	**Wilson et al.,[223] 2023**
RSV-related ARI	**RSV-ARI** ≥1 RSV-positive swab detected by qRT-PCR and presence of: ▪ ≥2 respiratory symptoms/signs for ≥24 hours OR ▪ ≥1 respiratory symptom/sign plus 1 systemic symptom/sign for ≥24 hours. Respiratory symptoms and signs were: nasal congestion/rhinorrhoea; sore throat; new or increased sputum; new or increased cough; new or increased shortness of breath; new or increased wheezing; new or increased crackles/rhonchi based on chest auscultation; respiratory rate ≥20 breaths per minute; low or decreased S_pO_2 (that is, S_pO_2 <95% or ≤90% if baseline is <95%), need for oxygen supplementation.	**RSV-ARI** ≥1 of the following respiratory illness symptoms, lasting >1 day, with qRT-PCR-confirmed RSV infection within 7 days of symptom onset: ▪ new or increased sore throat ▪ new or increased cough ▪ new or increased nasal discharge ▪ new or increased nasal congestion ▪ new or increased wheezing ▪ new or increased sputum production ▪ new or increased shortness of breath.	**RSV-ARD** qRT-PCR-confirmed RSV infection plus new or worsening of ≥1 of: ▪ cough ▪ stuffy nose ▪ runny nose ▪ sore throat ▪ fever (≥37.8°C) ▪ shortness of breath ▪ observed tachypnoea (≥20 breaths per minute, or increase of ≥2 breaths per minute from baseline in those who have baseline tachypnoea) ▪ hypoxaemia (new S_pO_2 ≤93%, or new or increasing use of supplemental oxygen) ▪ wheezing ▪ sputum production ▪ hoarseness ▪ sinus pain ▪ chills

Outcome, as per HIQA update	Outcome, as per RCT Case definition		
	Systemic symptoms and signs were: fever/feverishness; fatigue; body aches; headache; decreased appetite.		▪ pleuritic chest pain for ≥24 hours.*
RSV-related LRTD	**RSV-LRTD** ≥1 RSV-positive swab detected by qRT-PCR and presence of: ▪ ≥2 lower respiratory symptoms/signs for ≥24 hours including ≥1 lower respiratory sign OR ▪ ≥3 lower respiratory symptoms for ≥24 hours. Lower respiratory symptoms included: new or increased sputum; new or increased cough; new or increased shortness of breath. Lower respiratory signs were: new or increased wheezing; new or increased crackles/rhonchi based on chest auscultation; respiratory rate ≥20 breaths per minute; low or decreased S_pO_2; need for oxygen supplementation.	**RSV-LRTI** A qRT-PCR-confirmed RSV infection within 7 days of ARI symptom onset, with ≥2 or ≥3 of the following LRTD symptoms: ▪ new or increased cough ▪ new or increased wheezing ▪ new or increased sputum production ▪ new or increased shortness of breath ▪ tachypnoea (≥25 breaths per minute or ≥15% increase from resting baseline).	**RSV-LRTD** A qRT-PCR-confirmed RSV infection plus new or worsening of ≥2 or ≥3 of the following symptoms: ▪ shortness of breath ▪ cough and or fever ▪ wheezing and or rales and or rhonchi ▪ sputum production ▪ tachypnoea ▪ hypoxaemia ▪ pleuritic chest pain for ≥24 hours.*
Medically attended	**Medically attended RSV-LRTD**	**Medically attended RSV-LRTI**	Not reported.

Outcome, as per HIQA update	Outcome, as per RCT Case definition		
RSV-related LRTD	RSV-related LRTD that included visits with a general practitioner or specialist and emergency department visits.	RSV-related LRTI that prompted healthcare visits, including telephone/telehealth medical practitioner consultation, doctor visit, urgent care visit, emergency department visit, or hospitalisation.	

Key: ARD – acute respiratory disease; ARI – acute respiratory illness; LRTD – lower respiratory tract disease; LRTI – lower respiratory tract illness; qRT-PCR – quantitative reverse transcriptase polymerase chain reaction; RSV – respiratory syncytial virus; S_pO_2 – oxygen saturation.

Note: *In the event of inability to fully assess other clinical parameters, a case could be confirmed by radiologic evidence of pneumonia with qRT-PCR-confirmed RSV infection.

A4.7 Outcomes and case definitions for pooled efficacy outcomes, as described across RCTs: efficacy and safety of EHL-mAbs

Outcome, as per HIQA update	Outcome, as per RCT Case definition			
	Griffin, 2020[233]	**MELODY** **Hammitt, 2022**[234] **Dagan, 2024**[231] **Arbetter, 2024**[229]	**HARMONIE** **Drysdale, 2023**[230] **Munro, 2025**[235]	**CLEVER** **Zar, 2025**
EHL-mAb	Nirsevimab	Nirsevimab	Nirsevimab	Clesrovimab
RSV-related ARI	Not reported	Not reported	Not reported	Not reported
RSV-related LRTI*	RSV RT-PCR positive & documented physical examination findings localizing to LRT: ▪ rhonchi ▪ rales ▪ crackles ▪ wheeze AND documentation of clinical severity: ▪ increased respiratory rate ▪ ≥ 60 breaths/min for <2-month old; ≥ 50 breaths/min for 2–6-month old; ≥40 breaths/min for 6–24-month old).	RSV RT-PCR positive & documented physical examination findings localizing to LRT: ▪ rhonchi ▪ rales ▪ crackles ▪ wheeze AND documentation of ≥1 clinical severity: ▪ increased respiratory rate ≥ 60 breaths/min for <2-month old; ≥ 50 breaths/min for 2–6-month old;	RSV RT-PCR positive & presence of the following symptoms: ▪ rhonchi ▪ rales ▪ crackles ▪ wheeze ▪ increased respiratory rate at rest: ≥60 breaths/min for <2-month old ≥50 breaths/min for 2–6-month old ≥40 breaths/min for >6 month old	RSV RT-PCR positive & presence of at least one of following symptoms: ▪ cough ▪ difficulty breathing AND at least one of the following indicators of lower respiratory infection or disease severity: ▪ wheezing ▪ chest-wall retractions ▪ rales or crackles ▪ hypoxemia in room air (SpO_2 <95% at sea level, <92% at altitude ≥1800 m) ▪ tachypnea

Outcome, as per HIQA update	Outcome, as per RCT Case definition			
	▪ hypoxemia in room air (S_pO_2 <95% at altitude ≤1800 m S_pO_2 <92% at altitude >1800 m) ▪ clinical signs of respiratory distress: ○ new onset apnoea ○ intercostal, subcostal, or supraclavicular retractions ○ grunting ○ nasal flaring ○ acute hypoxic or ventilatory failure ○ dehydration due to respiratory distress requiring IV hydration	≥40 breaths/min for 6–24-month old). ▪ hypoxemia in room air (S_pO_2 <95% at ≤1800 m S_pO_2 <92% at >1800 m) ▪ clinical signs of respiratory distress: ○ new onset apnoea ○ intercostal, subcostal, or supraventricular retractions ○ grunting ○ nasal flaring ○ acute hypoxic or ventilatory failure ○ dehydration due to respiratory distress requiring IV hydration	▪ hypoxemia in room air: S_pO_2<95%.	▪ dehydration caused by respiratory symptoms
Medically attended RSV-related LRTI*	Telephone call; inpatient or outpatient visit to either study site or other treatment site.	In-person medical advice in any clinical setting.	Telephone call; visit to physician's office or emergency department.	Telephone call; inpatient or outpatient facility for respiratory infection symptoms.

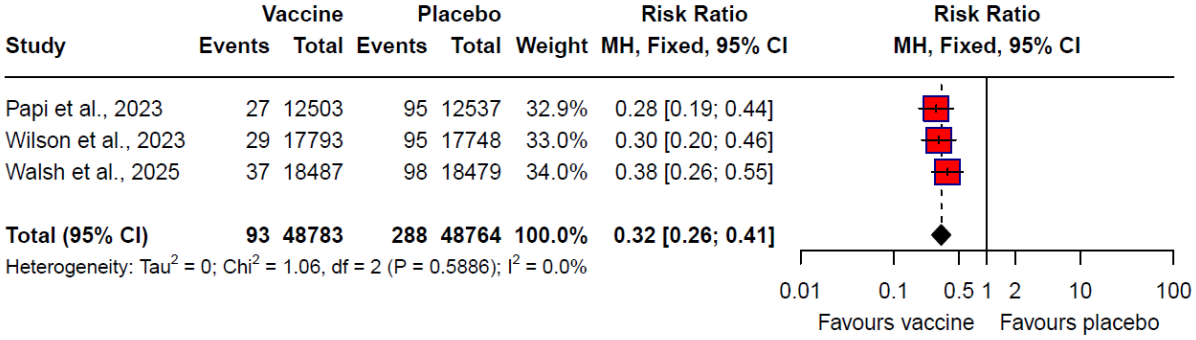
Key: ARI – acute respiratory illness; LRT – lower respiratory tract; LRTI – lower respiratory tract infections; MA – medically attended; RSV – respiratory syncytial virus; RT-PCR - reverse transcriptase-polymerase chain reaction; S_pO_2 – oxygen saturation

Note: * The CLEVER trial referred to low respiratory infection (LRI). For consistency with the reporting by other studies, this is referred to as LRTI in this chapter.

RSV vaccination efficacy results for older adults based on ITT analysis

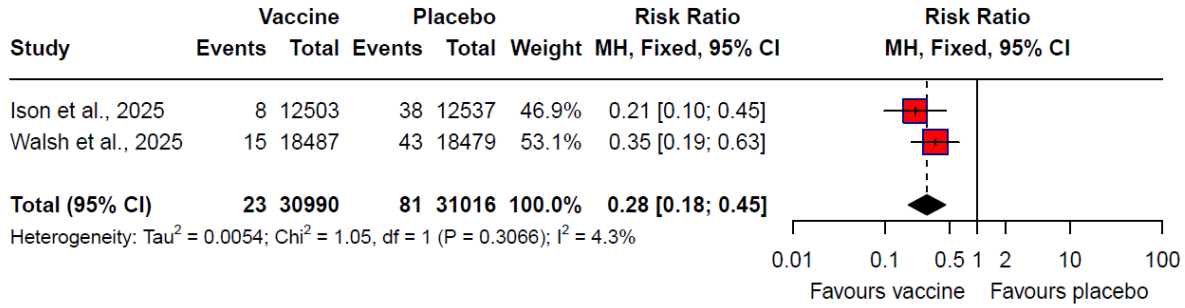
RSV-related ARI

A4.8 Efficacy of RSV F protein-based vaccines compared with placebo against RSV-related ARI over one RSV season in adults aged 60 years and older



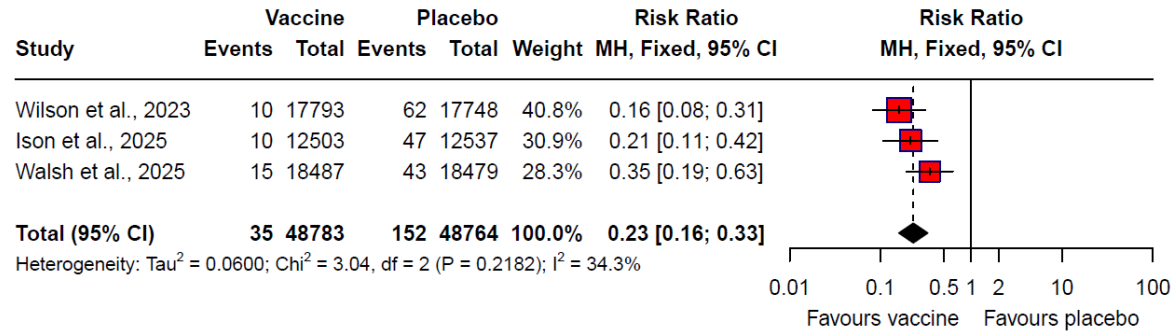
Medically attended RSV-related ARI

A4. 9 Efficacy of RSV F protein-based vaccines compared with placebo against medically attended RSV-related ARI over one RSV season in adults aged 60 years and older



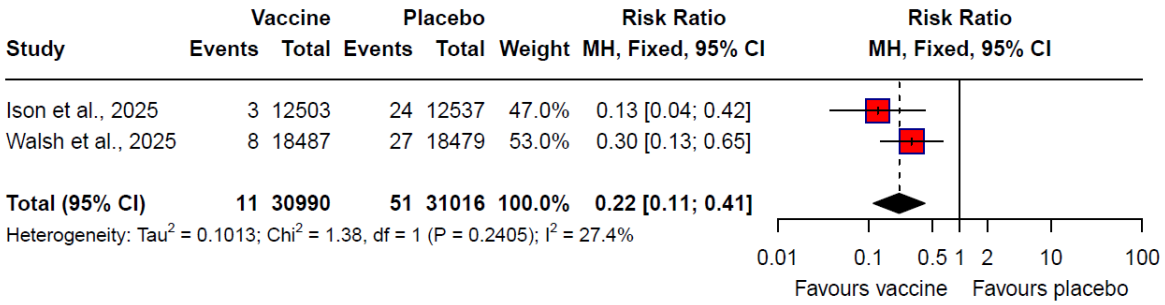
RSV-related LRTD

A4.10 Efficacy of RSV F protein-based vaccines compared with placebo against RSV-related LRTD over one RSV season in adults aged 60 years and older



Medically attended RSV related-LRTD

A4.11 Efficacy of RSV F protein-based vaccines compared with placebo against medically attended RSV-related LTRD over one RSV season in adults aged 60 years and older



Subgroup analyses for RSV vaccination results for older adults

A4.12 Reported vaccine efficacy against RSV-related LTRD by age and pre-existing condition

Author, year Efficacy follow-up	Sub-group	Vaccine Events/Total	Placebo Events/Total	Efficacy % (95%CI)	
Walsh et al; 2025 One season	Overall	15/18050	43/18074	65.1 (35.9 to 82.0)	
	Age 60-69 years	10/11619	25/11470	60.0 (13.8 to 82.9)	
	Age 70-79 years	4/5928	12/5822	66.7 (-10.0 to 92.2)	
	Age ≥80 years	1/1026	6/996	83.3 (-37.4 to 99.6)	
	With ≥1 high-risk condition^	8/9709	22/9562	63.6 (15.2 to 86.0)	
	Without ≥1 high-risk condition^	7/8865	21/8726	66.7 (18.6 to 88.0)	
Walsh et al; 2025 Cumulative across two seasons	Overall	54/18050	131/18074	58.8 (43.0 to 70.6)	
	Age 60-69 years	34/11619	80/11470	57.5 (35.8 to 72.4)	
	Age 70-79 years	15/5928	40/5822	62.5 (30.6 to 80.8)	
	Age ≥80 years	5/1026	11/996	54.5 (-41.9 to 87.6)	
	With ≥1 high-risk condition^	36/9709	71/9562	49.3 (23.2 to 67.0)	
	Without ≥1 high-risk condition^	18/8865	60/8726	70.0 (48.5 to 83.3)	
Ison et al; 2025 Cumulative across three seasons				Without season as covariate	With season as covariate
	Overall	48/12468	215/12498	69.1 (55.8 to 78.9)	62.9 (46.7 to 74.8)
	Age 60-69 years	28/6962	117/6981	66.9 (49.7 to 78.9)	60.3 (39.5 to 74.8)
	Age 70-79 years	15/4489	85/4489	75.6 (57.5 to 86.9)	70.6 (48.4 to 84.3)
	Age ≥80 years	5/1017	13/1028	45.6 (-62.6 to 84.8)	36.2 (-94.0 to 82.5)
	≥1 pre-existing condition of interest~	25/5014	116/4951	71.1 (55.2 to 82.0)	64.7 (45.1 to 78.1)
	No pre-existing condition of interest~	23/7454	99/7547	67.3 (48.2 to 80.2)	61.5 (38.6 to 76.7)

Note: ~Conditions of interest included cardiorespiratory conditions (any chronic respiratory or pulmonary disease [including chronic obstructive pulmonary disease and asthma] and chronic heart failure) and endocrine or metabolic conditions (type 1 or type 2 diabetes and advanced liver or renal disease).
^Pre-specified high-risk conditions included current tobacco use, diabetes, and lung, heart, liver, or renal disease

A4.13 Reported vaccine efficacy against RSV-related MA-LTRD by pre-existing condition

Author, year Efficacy follow-up	Sub-group	Vaccine Events/Total	Placebo Events/Total	Efficacy % (95%CI)
Ison et al; 2025 First season	Overall	3/12468	24/12498	87.5 (58.9 to 97.6)
	≥1 pre-existing condition of interest~	1/4937	11/4861	91.2 (39.3 to 99.8)
Ison et al; 2025 Cumulative across two seasons	Overall	12/12469	63/12498	With season as covariate: 73.1 (49.4 to 86.9)
	≥1 pre-existing condition of interest~	7/4983	37/4919	With season as covariate: 73.5 (39.3 to 90.1)
Ison et al; 2025 Cumulative across three seasons	Overall	18/12468	95/12498	With season as covariate: 70.2 (50.1 to 83.1)
	≥1 pre-existing condition of interest~	9/5014	61/4951	With season as covariate: 77.0 (53.1 to 90.0)

Note: ~Conditions of interest included cardiorespiratory conditions (any chronic respiratory or pulmonary disease [including chronic obstructive pulmonary disease and asthma] and chronic heart failure) and endocrine or metabolic conditions (type 1 or type 2 diabetes and advanced liver or renal disease).

A4.14 Reported vaccine efficacy against RSV-related ARI by age and high-risk condition

Author, year Efficacy follow-up	Sub-group	Vaccine Events/Total	Placebo Events/Total	Efficacy % (95%CI)
Walsh et al; 2025 First season	Overall	37/18050	98/18074	62.2 (44.4 to 74.9)
	Age 60-69 years	25/11,619	68/11,470	63.2 (41.1 to 77.7)
	Age 70-79 years	9/5928	22/5822	59.1 (7.6 to 83.4)
	Age ≥80 years	3/1026	8/996	62.5 (-56.2 to 93.6)
	With high-risk condition^	16/9709	47/9562	66.0 (38.9 to 82.0)
	Without high-risk condition^	21/8865	51/8726	58.8 (30.3 to 76.5)
Walsh et al; 2025 Cumulative across two seasons	Overall	186/18050	334/18074	44.3 (33.2 to 53.7)
	Age 60-69 years	126/11,619	229/11,470	45.0 (31.3 to 56.1)
	Age 70-79 years	50/5928	89/5822	43.8 (19.7 to 61.6)
	Age ≥80 years	10/1026	16/996	37.5 (-46.5 to 74.6)
	With ≥1 high-risk condition^	90/9709	169/9562	46.7 (30.8 to 59.2)
	Without high-risk condition^	96/8865	165/8726	41.8 (24.7 to 55.2)

Note: ^Pre-specified high-risk conditions included current tobacco use, diabetes, and lung, heart, liver, or renal disease.

A4.15 Reported vaccine efficacy against RSV-related MA-ARI by pre-existing condition

Author, year Efficacy follow-up	Sub-group	Vaccine Events/Total	Placebo Events/Total	Efficacy % (95%CI)
Ison et al; 2025 First season	Overall	8/12468	38/12498	79.0 (54.3 to 91.5)
	≥1 pre-existing condition of interest~	2/4937	18/4861	89.2 (54.9 to 98.8)
Ison et al; 2025 Cumulative across two seasons	Overall	32/12469	94/12498	With season as covariate: 52.0 (27.3 to 69.1)
	≥1 pre-existing condition of interest~	15/4983	53/4919	With season as covariate: 60.4 (28.2 to 79.4)
Ison et al; 2025 Cumulative across three seasons	Overall	38/12468	142/12498	With season as covariate: 58.6 (40.2 to 72.0)
	≥1 pre-existing condition of interest~	17/5014	83/4951	With season as covariate: 68.5 (46.2 to 82.6)

Note: ~Conditions of interest included cardiorespiratory conditions (any chronic respiratory or pulmonary disease [including chronic obstructive pulmonary disease and asthma] and chronic heart failure) and endocrine or metabolic conditions (type 1 or type 2 diabetes and advanced liver or renal disease).

A4.16 Reported vaccine effectiveness against RSV-related hospitalisation by immune status

Author, year Effectiveness follow-up	Sub-group	Vaccine Events/Total	No vaccine Events/Total	Effectiveness % (95%CI)
Payne et al; 2025 First season	**Immunocompetent**	35/2455	1567/25816	78 (69 to 84)
	Age 60–74 years	11/836	670/11048	79 (62 to 89)
	Age ≥ 75 years	24/1619	897/14768	77 (65 to 85)
	Critical illness~	5/2425	257/24506	81 (53 to 92)
	RSVPreF3	21/1812	1567/25816	82 (72 to 88)
	RSVpreF	13/642	1567/25816	68 (44 to 82)
	Immunocompromised*	10/820	314/7615	71 (46 to 85)

Note: ~Critical illness was defined as intensive care unit admission or in-hospital death (or both).
*Immunocompromising conditions, were defined based on the presence of ICD-10 discharge diagnosis codes for haematological malignancy, solid malignancy, transplant, rheumatologic/ inflammatory disorders, HIV and other intrinsic immune conditions or immunodeficiencies.

A4.17 Reported vaccine effectiveness against RSV infection by age group, immune status, CAN score, and vaccine product

Author, year Effectiveness follow-up	Sub-group	Vaccine Events/Follow-up PY	No vaccine Events/Follow-up PY	Effectiveness % (95%CI)
Bajema et al; 2025 First season	Overall	88/51281	372/50911	78.1 (72.6 to 83.5)
	Age 60-69 years	17/7494	74.9/7474	79.1 (68.0 to 88.3)
	Age 70-79 years	47/22251	204.8/22168	78.0 (70.3 to 84.0)
	Age ≥80 years	26/9601	93.5/9500	72.3 (57.9 to 84.6)
	Immunocompromised-Yes*	16/2753	54.2/2730	71.6 (55.4 to 85.2)
	Immunocompromised-No*	71/36554	325.5/36354	78.7 (73.2 to 83.4)
	CAN score~ 0-49	<11/	51.6/6119	88.2 (74.7 to 97.0)
	CAN score~ 50-89	53/25651	198.7/25570	75.7 (68.3 to 82.2)
	CAN score~ 90-99	30/7577	120.1/7461	72.7 (58.4 to 83.2)
	RSVpreF	66/25505	281.2/25376	77.4 (70.4 to 82.4)
	RSVPreF3	22/13411	94/13326	76.7 (66.0 to 86.7)

Note: *Defined as receipt of immunosuppressive or cancer medications excluding steroids, HIV with CD4 ≤200 cells per mm³, or documented haematological malignancy. ~Derived from the Veterans Health Administration predictive model for 1-year mortality among veterans receiving primary care; scores indicate percentiles, from 0 (lowest risk) to 99 (highest risk)

Clesrovimab efficacy outcomes at 150 and 180 days of follow up

A4.18 Clesrovimab efficacy outcomes at 150 and 180 days follow up

Clesrovimab study reported efficacy outcomes	Efficacy at 150 days follow up % (95% CI)	Efficacy at 180 days follow up % (95% CI)
RSV-associated medically attended LRI with ≥1 indicator of disease severity	60.4 (44.1 to 71.9)*	59.5 (43.3 to 71.1)+
RSV-associated medically attended LRI with ≥2 indicator of disease severity	88.0 (76.1 to 94.0)^	87.2 (75.1 to 93.4)^
RSV-associated severe medically attended LRI	91.7 (62.9 to 98.1)~	91.7 (62.9 to 98.1)~
RSV-associated hospitalisation for LRI	90.9 (76.2 to 96.5) ~	91.2 (77.2 to 96.6) ~

Clesrovimab study reported efficacy outcomes	Efficacy at 150 days follow up % (95% CI)	Efficacy at 180 days follow up % (95% CI)
RSV-associated hospitalisation	84.2 (66.6 to 92.6)+	81.3 (62.5 to 90.7)
RSV-associated acute respiratory infection	52.0 (39.5 to 61.9) ~	50.0 (37.4 to 60.1) ~
All-cause medically attended LRI	13.1 (-0.6 to 24.8) ~	Not reported
All-cause hospitalisation for LRI	49.0 (26.7 to 64.5) ~	Not reported

Key: CI – confidence interval; LRI – lower respiratory infection; RSV – respiratory syncytial virus.
Note: * denotes primary efficacy outcome.
+ denotes secondary efficacy outcomes.
^ denotes tertiary efficacy outcomes.
~ denotes post-hoc efficacy outcomes.

Quality appraisal summary for Sumsuzzman et al. review

A4.19 Quality assessment of included nirsevimab studies using the JBI critical appraisal tool as reported in the Sumsuzzman systematic review

Domain	1		2	3	4	5	6	7	8	9	10	11	Total	RoB
Checklist: cohort studies*														
Alejandre et al., 2024	Yes		Yes	Yes	Yes	Unclear	Yes	Yes	Yes	Yes	Unclear	Yes	9	Low
Ezpeleta et al., 2024	Yes		Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	11	Low
Jabagi et al., 2025	Yes		Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	11	Low
Reina et al., 2024	Yes		Unclear	Yes	No	No	Yes	Unclear	Yes	Yes	No	Unclear	5	Moderate
Checklist: case-control studies+														
Aguera et al., 2024	Yes		Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	NA	10	Low
Assad et al., 2024	Yes		Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	NA	10	Low
Carbajal et al., 2024	Yes		Yes	Yes	Yes	Yes	Unclear	No	Yes	Yes	Yes	NA	8	Low
Lefferts et al., 2024	Yes		Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	NA	10	Low
Lopez-Lacort et al., 2025	Yes		Unclear	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	NA	9	Low
Lenglart et al., 2025	Yes		Unclear	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	NA	9	Low
Moline et al., 2025	Yes		Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	NA	10	Low
Moline et al., 2024	Yes		Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	NA	10	Low
Nunez et al., 2025	Yes		Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	NA	10	Low
Paireau et al., 2024	Yes		Unclear	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	NA	9	Low

Domain	1		2	3	4	5	6	7	8	9	10	11	Total	RoB
Rodriguez-Fernandez et al., 2024	Yes		Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	NA	8	Low

Key: NA – not applicable; RoB – risk of bias

Note: *Checklist questions for cohort studies comprised: Q1 Were the two groups similar and recruited from the same population? Q2 Were the exposures measured similarly to assign people to both exposed and unexposed groups? Q3 Was the exposure measured in a valid and reliable way? Q4 Were confounding factors identified? Q5 Were strategies to deal with confounding factors stated? Q6 Were the groups or participants free of the outcome at the start of the study (or at the moment of exposure)? Q7 Were the outcomes measured in a valid and reliable way? Q8 Was the follow up time reported and sufficiently long for outcomes to occur? Q9 Was follow up complete, and if not, were there reasons to lose to follow up described and explored? Q10 Were strategies to address incomplete follow up utilised? Q11 Was appropriate statistical analysis used?

+ Checklist questions for case-control studies comprise: Q1 Were the groups comparable other than presence of disease in cases or absence of disease in controls? Q2 Were cases and controls matched appropriately? Q3 Were the same criteria used for identification of cases and controls? Q4 Was exposure measured in a standard, valid and reliable way? Q5 Was exposure measured in the same way for cases and controls? Q6 Were confounding factors identified? Q7 Were strategies to deal with confounding factors stated? Q8 Were outcomes assessed in a standard, valid and reliable way for cases and controls? Q9 Was the exposure period of interest long enough to be meaningful? Q10 Was appropriate statistical analysis used?

Appendix A5

A5.1 Search Strategies

Sources searched:

Databases	**9.2.5 Number of results**	Date searched
Medline Complete	648	10/09/2024
Embase	378	10/09/2024
The Cochrane Library	30	10/09/2024
CINAHL Complete	47	10/09/2024
INAHTA	4	10/09/2024
Total	1107	
Total after duplicates removed in Endnote and Covidence	**896**	

SEARCH STRATEGIES

Database Name	Medline Complete
Date search was run	10 September 2024

#	Query	Limiters/Expanders	Last Run Via	Results
S36	S9 AND S34	Limiters - Publication Date: 20201001 - Expanders - Apply equivalent subjects Search modes - Proximity	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - MEDLINE Complete	648
S35	S9 AND S34	Limiters - Publication Date: 20140101- Expanders - Apply equivalent	Interface - EBSCOhost Research Databases Search Screen - Advanced Search	1,018

		subjects Search modes - Proximity	Database - MEDLINE Complete	
Concept 3: CADTH filter Economic evaluations and models				
S34	S17 OR S18 OR S19 OR S20 OR S21 OR S22 OR S23 OR S24 OR S25 OR S26 OR S27 OR S28 OR S29 OR S30 OR S31 OR S32 OR S33	Expanders - Apply equivalent subjects Search modes - Proximity	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - MEDLINE Complete	5,925,979
S33	AB ((decision* N2 (tree* or analy* or model*))) OR TI ((decision* N2 (tree* or analy* or model*)))	Expanders - Apply equivalent subjects Search modes - Proximity	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - MEDLINE Complete	51,356
S32	(MH "Decision Theory+")	Expanders - Apply equivalent subjects Search modes - Proximity	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - MEDLINE Complete	13,810
S31	TI "monte carlo" OR AB "monte carlo"	Expanders - Apply equivalent subjects Search modes - Proximity	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - MEDLINE Complete	62,523
S30	(MH "Monte Carlo Method")	Expanders - Apply equivalent subjects Search modes - Proximity	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - MEDLINE Complete	33,208
S29	TI markov OR AB markov	Expanders - Apply equivalent	Interface - EBSCOhost Research	30,219

		subjects Search modes - Proximity	Databases Search Screen - Advanced Search Database - MEDLINE Complete	
S28	(MH "Markov Chains")	Expanders - Apply equivalent subjects Search modes - Proximity	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - MEDLINE Complete	16,397
S27	TI model* OR AB model*	Expanders - Apply equivalent subjects Search modes - Proximity	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - MEDLINE Complete	4,091,792
S26	(MH "Models, Economic+")	Expanders - Apply equivalent subjects Search modes - Proximity	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - MEDLINE Complete	16,480
S25	AB ((value N2 (money or monetary))) OR TI ((value N2 (money or monetary)))	Expanders - Apply equivalent subjects Search modes - Proximity	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - MEDLINE Complete	3,623
S24	AB ((cost* N2 (effective* or utilit* or benefit* or minimi* or analy* or outcome or outcomes))) OR TI ((cost* N2 (effective* or utilit* or benefit* or minimi* or analy*	Expanders - Apply equivalent subjects Search modes - Proximity	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - MEDLINE Complete	257,492

	or outcome or outcomes)))			
S23	AB (economic* or cost or costs or costly or costing or price or prices or pricing or pharmacoeconomic* or pharmaco-economic* or expenditure or expenditures or expense or expenses or financial or finance or finances or financed)) OR TI (economic* or cost or costs or costly or costing or price or prices or pricing or pharmacoeconomic* or pharmaco-economic* or expenditure or expenditures or expense or expenses or financial or finance or finances or financed))	Expanders - Apply equivalent subjects Search modes - Proximity	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - MEDLINE Complete	2,049,588
S22	TI budget* OR AB budget*	Expanders - Apply equivalent subjects Search modes - Proximity	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - MEDLINE Complete	37,908
S21	(MH "Budgets+")	Expanders - Apply equivalent subjects Search modes - Proximity	Interface - EBSCOhost Research Databases Search Screen - Advanced Search	14,248

			Database - MEDLINE Complete	
S20	(MH "Fees and Charges+")	Expanders - Apply equivalent subjects Search modes - Proximity	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - MEDLINE Complete	31,502
S19	(MH "Economics, Pharmaceutical") OR (MH "Economics, Medical") OR (MH "Economics, Nursing") OR (MH "Economics, Hospital+")	Expanders - Apply equivalent subjects Search modes - Proximity	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - MEDLINE Complete	41,965
S18	(MH "Costs and Cost Analysis+")	Expanders - Apply equivalent subjects Search modes - Proximity	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - MEDLINE Complete	272,721
S17	(MH "Economics")	Expanders - Apply equivalent subjects Search modes - Proximity	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - MEDLINE Complete	27,541
Concept 2: Vaccination				
S16	S9 OR S15	Expanders - Apply equivalent subjects Search modes - Proximity	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - MEDLINE Complete	4,958

S15	S10 OR S11 OR S12 OR S13 OR S14	Expanders - Apply equivalent subjects Search modes - Proximity	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - MEDLINE Complete	305
S14	TI mRESVIA OR AB mRESVIA	Expanders - Apply equivalent subjects Search modes - Proximity	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - MEDLINE Complete	1
S13	AB (arexvy OR "gsk 3844766a" OR gsk3844766a) OR TI (arexvy OR "gsk 3844766a" OR gsk3844766a)	Expanders - Apply equivalent subjects Search modes - Proximity	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - MEDLINE Complete	21
S12	AB (abrysvo OR "pf 06928316" OR "pf 6928316" OR pf6928316 OR pf06928316) OR TI (abrysvo OR "pf 06928316" OR "pf 6928316" OR pf6928316 OR pf06928316)	Expanders - Apply equivalent subjects Search modes - Proximity	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - MEDLINE Complete	23
S11	AB ("Respiratory syncytial virus prefusion F" or RSVPreF* or RSV-PreF* or RSV-PRE-F*) OR TI ("Respiratory syncytial virus prefusion F" or RSVPreF* or RSV-PreF* or RSV-PRE-F*)	Expanders - Apply equivalent subjects Search modes - Proximity	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - MEDLINE Complete	139

S10	AB (nirsevimab* OR nirsevumab* OR beyfortus* OR "sp 0232" OR "sp 232" OR sp0232 OR sp232 OR "medi 8897" OR medi8897) OR TI (nirsevimab* OR nirsevumab* OR beyfortus* OR "sp 0232" OR "sp 232" OR sp0232 OR sp232 OR "medi 8897" OR medi8897)	Expanders - Apply equivalent subjects Search modes - Proximity	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - MEDLINE Complete	165
S9	S4 AND S8	Expanders - Apply equivalent subjects Search modes - Proximity	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - MEDLINE Complete	4,863
S8	S5 OR S6 OR S7	Expanders - Apply equivalent subjects Search modes - Proximity	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - MEDLINE Complete	584,820
S7	AB (vaccine* or vaccinat* or immunis* or immuniz*) OR TI (vaccine* or vaccinat* or immunis* or immuniz*)	Expanders - Apply equivalent subjects Search modes - Proximity	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - MEDLINE Complete	517,097
S6	(MH "Immunization+")	Expanders - Apply equivalent subjects Search modes - Proximity	Interface - EBSCOhost Research Databases Search Screen - Advanced Search	218,402

			Database - MEDLINE Complete	
S5	(MH "Respiratory Syncytial Virus Vaccines")	Expanders - Apply equivalent subjects Search modes - Proximity	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - MEDLINE Complete	1,080
Concept 1: RSV				
S4	S1 OR S2 OR S3	Expanders - Apply equivalent subjects Search modes - Proximity	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - MEDLINE Complete	23,595
S3	TI RSV OR AB RSV	Expanders - Apply equivalent subjects Search modes - Proximity	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - MEDLINE Complete	16,439
S2	AB Respirat* Syncyt* Vir* OR TI Respirat* Syncyt* Vir*	Expanders - Apply equivalent subjects Search modes - Proximity	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - MEDLINE Complete	17,862
S1	(MH "Respiratory Syncytial Virus, Human")	Expanders - Apply equivalent subjects Search modes - Proximity	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - MEDLINE Complete	4,549

Database Name	Embase via Ovid

Date search was run	10 September 2024

Database(s): Embase 1974 to 2024 September 09
Search Strategy:

#	Searches	Results
1	exp Human respiratory syncytial virus/	10652
2	"Respirat* Syncyt* Vir*".ab,ti.	22013
3	RSV.ab,ti.	21880
4	1 or 2 or 3	32932
5	exp respiratory syncytial virus vaccine/	2540
6	exp mass immunization/	4990
7	(vaccine* or vaccinat* or immunis* or immuniz*).ab,ti.	600794
8	5 or 6 or 7	602203
9	4 and 8	6314
10	(nirsevimab* or nirsevumab* or beyfortus* or "sp 0232" or "sp 232" or sp0232 or sp232 or "medi 8897" or medi8897).ab,ti.	243
11	("Respiratory syncytial virus prefusion F" or RSVPreF* or RSV-PreF* or RSV-PRE-F*).ab,ti.	213
12	(abrysvo or "pf 06928316" or "pf 6928316" or pf6928316 or pf06928316).ab,ti.	28
13	(arexvy or "gsk 3844766a" or gsk3844766a).ab,ti.	26
14	mRESVIA.ab,ti.	1
15	10 or 11 or 12 or 13 or 14	457
16	9 or 15	6368
17	Economics/	246568
18	Cost/	64975
19	exp Health Economics/	1092597
20	Budget/	35129
21	budget*.ti,ab,kf.	51051
22	(economic* or cost or costs or costly or costing or price or prices or pricing or pharmacoeconomic* or pharmaco-economic* or expenditure or expenditures or expense or expenses or financial or finance or finances or financed).ti,kf.	370554
23	(economic* or cost or costs or costly or costing or price or prices or pricing or pharmacoeconomic* or pharmaco-economic* or expenditure or expenditures or expense or expenses or financial or finance or finances or financed).ab. /freq=2	581275
24	(cost* adj2 (effective* or utilit* or benefit* or minimi* or analy* or outcome or outcomes)).ab,kf.	318125
25	(value adj2 (money or monetary)).ti,ab,kf.	4396
26	Statistical Model/	179041

27	exp economic model/	4408
28	economic model*.ab,kf.	6800
29	Probability/	158449
30	markov.ti,ab,kf.	41337
31	monte carlo method/	54792
32	monte carlo.ti,ab,kf.	68052
33	Decision Theory/	1888
34	Decision Tree/	25784
35	(decision* adj2 (tree* or analy* or model*)).ti,ab,kf.	59810
36	or/17-35	2147660
37	16 and 36	711
38	limit 37 to dc=20201022-20241231	378

Database Name	CINAHL Complete via EBSCOhost
Date search was run	10 September 2024

#	Query	Limiters/Expanders	Last Run Via	Results
S16	S14 AND S15	Limiters - Publication Date: 20201001- Expanders - Apply equivalent subjects Search modes - Proximity	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Complete	47
S15	MH "Economics" OR MH "Costs and Cost Analysis+" OR MH "Economic Aspects of Illness" OR MH "Resource Allocation+" OR MH "Economic Value of Life" OR MH "Economics, Pharmaceutical" OR MH "Economics, Dental" OR MH "Fees and Charges+" OR MH "Budgets" OR MH "Decision Trees" OR TI budget* OR TI (economic* OR cost OR costs OR costly OR costing OR price OR prices OR pricing OR pharmacoeconomic* OR "pharmaco-economic*" OR expenditure OR expenditures OR expense OR expenses OR financial OR finance OR finances	Expanders - Apply equivalent subjects Search modes - Proximity	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Complete	465,662

	OR financed) OR TI (cost* N2 (effective* OR utilit* OR benefit* OR minimi* OR analy* OR outcome OR outcomes)) OR TI (value N2 (money OR monetary)) OR TI (markov OR monte carlo) OR TI (decision* N2 (tree* OR analy* OR model*)) OR AB budget* OR AB (economic* OR cost OR costs OR costly OR costing OR price OR prices OR pricing OR pharmacoeconomic* OR "pharmaco-economic*" OR expenditure OR expenditures OR expense OR expenses OR financial OR finance OR finances OR financed) OR AB (cost* N2 (effective* OR utilit* OR benefit* OR minimi* OR analy* OR outcome OR outcomes)) OR AB (value N2 (money OR monetary)) OR AB (markov OR monte carlo) OR AB (decision* N2 (tree* OR analy* OR model*))			
S14	S8 OR S13	Expanders - Apply equivalent subjects Search modes - Proximity	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Complete	768

S13	S9 OR S10 OR S11 OR S12	Expanders - Apply equivalent subjects Search modes - Proximity	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Complete	105
S12	AB (arexvy OR "gsk 3844766a" OR gsk3844766a) OR TI (arexvy OR "gsk 3844766a" OR gsk3844766a)	Expanders - Apply equivalent subjects Search modes - Proximity	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Complete	10
S11	AB (abrysvo OR "pf 06928316" OR "pf 6928316" OR pf6928316 OR pf06928316) OR TI (abrysvo OR "pf 06928316" OR "pf 6928316" OR pf6928316 OR pf06928316)	Expanders - Apply equivalent subjects Search modes - Proximity	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Complete	6
S10	AB ("Respiratory syncytial virus prefusion F" or RSVPreF* or RSV-PreF* or RSV-PRE-F*) OR TI ("Respiratory syncytial virus prefusion F" or RSVPreF* or RSV-PreF* or RSV-PRE-F*)	Expanders - Apply equivalent subjects Search modes - Proximity	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Complete	39
S9	AB (nirsevimab* OR nirsevumab* OR beyfortus* OR "sp 0232" OR "sp 232" OR sp0232 OR sp232 OR "medi 8897" OR medi8897) OR TI (nirsevimab* OR nirsevumab* OR beyfortus* OR "sp 0232" OR	Expanders - Apply equivalent subjects Search modes - Proximity	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Complete	61

	"sp 232" OR sp0232 OR sp232 OR "medi 8897" OR medi8897)			
S8	S4 AND S7	Expanders - Apply equivalent subjects Search modes - Proximity	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Complete	717
S7	S5 OR S6	Expanders - Apply equivalent subjects Search modes - Proximity	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Complete	91,281
S6	AB (vaccine* or vaccinat* or immunis* or immuniz*) OR TI (vaccine* or vaccinat* or immunis* or immuniz*)	Expanders - Apply equivalent subjects Search modes - Proximity	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Complete	81,266
S5	(MH "Immunization+")	Expanders - Apply equivalent subjects Search modes - Proximity	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Complete	35,094
S4	S1 OR S2 OR S3	Expanders - Apply equivalent subjects Search modes - Proximity	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Complete	4,256
S3	TI RSV OR AB RSV	Expanders - Apply equivalent subjects Search modes - Proximity	Interface - EBSCOhost Research Databases	2,404

			Search Screen - Advanced Search Database - CINAHL Complete	
S2	AB Respirat* Syncyt* Vir* OR TI Respirat* Syncyt* Vir*	Expanders - Apply equivalent subjects Search modes - Proximity	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Complete	2,934
S1	(MH "Respiratory Syncytial Virus Infections")	Expanders - Apply equivalent subjects Search modes - Proximity	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Complete	2,507

Database Name	Cochrane Library
Date search was run	10 September 2024

Search Name:
Date Run: 10/09/2024 16:45:38
Comment:

ID SearchHits
#1 (Respirat* Syncyt* Vir*):ti,ab,kw (Word variations have been searched) 1354
#2 (RSV):ti,ab,kw (Word variations have been searched) 1227
#3 #1 OR #2 1619
#4 (vaccine* or vaccinat* or immunis* or immuniz*):ti,ab,kw (Word variations have been searched) 35378
#5 #3 AND #4 540
#6 (nirsevimab* OR nirsevumab* OR beyfortus* OR "sp 0232" OR "sp 232" OR sp0232 OR sp232 OR "medi 8897" OR medi8897):ti,ab,kw (Word variations have been searched) 40
#7 ("Respiratory syncytial virus prefusion F" or RSVPreF* or RSV-PreF* or RSV-PRE-F*):ti,ab,kw (Word variations have been searched) 172
#8 (abrysvo OR "pf 06928316" OR "pf 6928316" OR pf6928316 OR pf06928316):ti,ab,kw (Word variations have been searched) 4
#9 (arexvy OR "gsk 3844766a" OR gsk3844766a):ti,ab,kw (Word variations have been searched) 7
#10 (mRESVIA):ti,ab,kw (Word variations have been searched) 0
#11 #6 OR #7 OR #8 OR #9 OR #10 212
#12 #5 OR #11 579
#13 (budget* OR economic* or cost or costs or costly or costing or price or prices or pricing or pharmacoeconomic* or pharmaco-economic* or expenditure or expenditures or expense or expenses or financial or finance or finances or financed):ti,ab,kw (Word variations have been searched) 129076
#14 (cost* NEAR/2 (effective* or utilit* or benefit* or minimi* or analy* or outcome or outcomes)):ti,ab,kw (Word variations have been searched) 46704
#15 (value NEAR/2 (money or monetary)):ti,ab,kw (Word variations have been searched) 450
#16 (model* OR markov):ti,ab,kw (Word variations have been searched) 188077
#17 ("monte carlo"):ti,ab,kw (Word variations have been searched) 1245
#18 (decision* NEAR/2 (tree* or analy* or model*)):ti,ab,kw (Word variations have been searched) 3667
#19 #13 OR #14 OR #15 OR #16 OR #17 OR #18 296826
#20 #12 AND #19 with Cochrane Library publication date Between Oct 2020 and Dec 2024 30

Database Name	INAHTA Database
Date search was run	12 September 2024

Respiratory syncytial virus
(Respiratory syncytial virus*)[abs]
(Respiratory syncytial virus) AND (vaccination)
(Respiratory syncytial virus) AND (vaccine)
(RSV)[abs] AND (vaccine* or vaccinat* or immunis* or immuniz*)[abs]
("Respiratory Syncytial Virus, Human"[mhe]) AND (vaccine* or vaccinat* or immunis* or immuniz*)
("Respiratory Syncytial Virus, Human"[mhe]) AND (vaccin* OR immuni*)
"Respiratory Syncytial Virus, Human"[mhe]

A5.2 Infant data extraction tables

General study characteristics	**Author name** **Year of publication** **DOI**	Alvarez Aldean J et al. 2024 https://doi.org/10.1007/s40121-024-00975-6
	Region or country	Spain
	Type of economic evaluation	Cost-utility analysis
	Population	Pregnant women
	Funding	Pfizer, S.L.U., Madrid, Spain.
Model characteristics	**Model type**	Static Markov Cohort Model ▪ Cycle: monthly ▪ Health states: uninfected or RSV infected (based on mother's vaccination status), hospitalisation, emergency department visits, primary care visits, death (for hospitalised cases only)
	Perspective	Health system (Spanish National Healthcare System) (Societal perspective considered in alternative scenario)
	Time horizon	One year (all costs and outcomes) QALY loss due to premature RSV death was calculated over a lifetime horizon
	Comparator	No vaccination
	Discount rates	3% (on both costs and outcomes)
	Sensitivity analysis	Deterministic and Probability sensitivity analyses
Intervention	**Strategies**	Year round vaccination of pregnant women with the RSVpreF vaccine
	Dosing schedule	Single dose
	Type of immunisation	Maternal vaccine (MV) - RSVpreF
	Age at immunisation	Between weeks 24 and 36 of gestation
	Coverage rate	70% (calculated as an intermediate value between the coverage observed in 2022 in pregnant women

<table>
<tr><td></td><td></td><td>against Tdap (86%) and the coverage in pregnant women for influenza (53%) in Spain)</td></tr>
<tr><td rowspan="2">Model input parameters</td><td>Efficacy/effectiveness</td><td>For term infants (≥37 wGA), vaccine efficacy by single month was derived from MATISSE trial data.

Monthly vaccine efficacy against RSV-hospitalisation by age:
0 to <1 month
▪ full term infant: 88.1%
▪ late preterm infant: 73.4%*
Monthly vaccine efficacy against RSV-emergency department/primary care by age:
0 to <1 month
▪ full term infant: 62.0%
▪ late preterm infant: 51.7%*
*For late preterm (32 to 36 wGA) infants, vaccine efficacy assumed as 83.3% of term infant values. For early (28 to 31 wGA) and extreme (≤27 wGA) preterm infants, and infants born <2 weeks after maternal vaccination, vaccine efficacy assumed as 0%.</td></tr>
<tr><td>Waning</td><td>Linear waning of vaccine effectiveness to 0% by age 9 to <10 months

<table>
<tr><td rowspan="2">Monthly vaccine efficacy by age and term status</td><td colspan="2">RSV-hospitalisation (%)</td><td colspan="2">RSV-ED/primary care (%)</td></tr>
<tr><td>Full term</td><td>Late preterm</td><td>Full term</td><td>Late preterm</td></tr>
<tr><td>1 to <2 months</td><td>80.0</td><td>66.7</td><td>57.7</td><td>48.0</td></tr>
<tr><td>2 to <3 months</td><td>72.0</td><td>60.0</td><td>53.3</td><td>44.4</td></tr>
<tr><td>3 to <4 months</td><td>64.0</td><td>53.3</td><td>49.0</td><td>40.8</td></tr>
<tr><td>4 to <5 months</td><td>55.9</td><td>46.6</td><td>44.7</td><td>37.2</td></tr>
<tr><td>5 to <6 months</td><td>47.9</td><td>33.9</td><td>40.3</td><td>33.6</td></tr>
<tr><td>6 to <7 months</td><td>35.9</td><td>29.9</td><td>30.2</td><td>25.2</td></tr>
<tr><td>7 to <8 months</td><td>23.9</td><td>19.9</td><td>20.2</td><td>16.8</td></tr>
<tr><td>8 to <9 months</td><td>12.0</td><td>10.0</td><td>10.1</td><td>8.4</td></tr>
</table>
</td></tr>
</table>

		9 to <10 months	0	0	0	0
	Costs included	**<u>Type of cost</u>** **Direct costs** Medical cost ▪ Hospitalisation ▪ ED visit ▪ Primary care visit Intervention cost ▪ Vaccine per dose: €166.5 ▪ Administration per dose: €6 **Indirect costs** N/A		**<u>Measurement and valuation</u>** **Direct costs** Medical cost ▪ Hospitalisation cost, ED visit and primary care events cost were per episode and by age and subgroups (extracted from observational Spanish studies) o <1 month, o 1 to <2 months, o 2 to <6 months, o 6 to <12 months old o wGA at birth grouping Intervention cost ▪ Cost of vaccine per dose o vaccine list price from the Spanish Official College of Pharmacists database o discounted by 7.5%. ▪ Cost of administration	
	Effects included	**<u>Type of Effects</u>** **Direct effects** ▪ RSV hospitalisation ▪ RSV ED encounter ▪ RSV primary care encounter ▪ RSV deaths **Indirect effects** N/A		**<u>Measurement and valuation</u>** **Direct effects** ▪ Number of RSV hospitalisations ▪ Number of RSV ED encounters ▪ Number of RSV primary care encounters ▪ Number of RSV-related deaths ▪ Discounted life years ▪ Discounted QALYs QALY loss (assuming 14 days illness): ▪ infants treated in hospital: 0.0157 ▪ infants treated in outpatient settings:	

			0.0061 Utility ▪ Infants without RSV (assumption): 1.00 ▪ Infants treated in hospital: 0.59 ▪ Infants treated in outpatient settings: 0.84 ▪ Aged ≥1yr: not provided but based on reference population norms of the Spanish population using the EQ-5D-5L ▪ Children aged 1-15yrs: estimated by linearly interpolating between values for children aged <1yr and >15yrs
Economic results	**Type of summary ratio**	**ICER** (incremental cost per QALY and incremental cost per LY)	
	Overall payer perspective result	Maternal vaccination was the dominant strategy (more effective and less costly) compared with no vaccination resulting in a net saving of €1.8million with 551 additional QALYs and 327 additional LYs	
	Overall societal perspective result	N/A	
Epidemiological results		Prevention of hospital admissions, emergency room visits, primary care visits, and deaths due to RSV reported.	
Authors conclusions	In Spain, maternal vaccination with bivalent RSVpreF could avoid a high number of hospitalisations, emergency room visits and primary care visits, while generating savings for the NHS, being a more efficient strategy (dominant) when compared with a non-prevention strategy.		

Key: ALRI – acute lower respiratory infection; CI – confidence interval; ED – emergency department; EQ-5D-5L - EuroQol 5-Dimensions 5-Levels; ICER- incremental cost-effectiveness ratio; LY - life year; N/A – not applicable; NHS – National Healthcare system; QALY- quality-adjusted life year; RSV - respiratory syncytial virus; RSVpreF – respiratory syncytial virus prefusion F vaccine; wGA – weeks gestational age.

General study characteristics	**Author name** **Year of publication** **DOI**	Gebretekle GB et al. 2024 https://doi.org/10.1016/j.vaccine.2024.126164
	Region or country	Canada

	Type of economic evaluation	Cost-effectiveness analysis
	Population	Infants, pregnant women
	Funding	Government – not explicitly stated for all authors but authors affiliated with Centre for Immunization Programs, Public Health Agency of Canada.
Model characteristics	**Model type**	Static cohort model ▪ followed monthly birth cohorts of newborns over a 1 year time period ▪ 3 mutually exclusive health states: healthy, RSV-infected, dead
	Perspective	Health system and societal
	Time horizon	1 year and lifetime for death due to RSV
	Comparator	Current standard of care, that is, monthly doses of the monoclonal antibody (mAb) palivizumab throughout RSV season for infants at high-risk and alternative intervention strategies Assumed palivizumab coverage: 80%
	Discount rates	1.5%(costs and outcomes)
	Sensitivity analysis	One way and two-way sensitivity analyses
Intervention	**Strategies**	i. Year-round nirsevimab program administered at birth for all infants ii. Seasonal nirsevimab program without catch-up, administered at birth for all infants born during the RSV season (i.e., from November to May) iii. Seasonal nirsevimab program with catch-up, in which all infants born during the RSV season receive their dose at birth and a catch-up dose is administered at the start of the RSV season (i.e., November) for all infants born outside of the RSV season (i.e., from June to October) iv. Year-round nirsevimab program, administered at birth for infants at moderate- and high-risk v. Seasonal nirsevimab program without catch-up, administered at birth for infants at moderate- and high-risk born during the RSV season (i.e., from November to May) vi. Seasonal nirsevimab program with catch-up, in which infants at moderate- and high-risk born during the RSV season receive their dose at birth and a catch-up dose is administered at the start of the RSV season (i.e., November) for infants at moderate- and high-risk born

<table>
<tr><td></td><td></td><td>outside of the RSV season (i.e., from June to October)
vii. Year-round RSVpreF for all pregnant women and pregnant people
viii. A combined program of a year-round RSVpreF offered to all pregnant women and pregnant people plus year-round nirsevimab offered to infants at high-risk (assuming no protection from RSVpreF)</td></tr>
<tr><td></td><td>Dosing schedule</td><td>Single dose for nirsevimab and RSVpreF</td></tr>
<tr><td></td><td>Type of immunisation</td><td>Extended half-life monoclonal antibody (EHL-mAb) - Nirsevimab,
Maternal vaccine (MV) - RSVpreF</td></tr>
<tr><td></td><td>Age at immunisation</td><td>At birth/at the start of the RSV season for nirsevimab
Between 24 and 36 wGA for RSVpreF</td></tr>
<tr><td></td><td>Coverage rate</td><td>Nirsevimab (among infants at moderate- and low-risk) -71%

Nirsevimab (among infants at high-risk) - 80%

RSVpreF - 64.8%</td></tr>
<tr><td>Model input parameters</td><td>Efficacy/effectiveness</td><td>Effectiveness during 0-1 month after administration (palivizumab), 0-5 months after administration (nirsevimab) and 0-5 after birth (RSVpreF)
<table>
<tr><th></th><th>Palivizumab % (range)</th><th>Nirsevimab % (range)</th><th>RSVpreF % (range)</th></tr>
<tr><td>RSV-LRTI</td><td>70.0 (19.0-90.0)</td><td>80.0 (70.0-87.0)</td><td>52.5 (28.7-68.9)</td></tr>
<tr><td>RSV-hospitalisation</td><td>82.0 (29.0-96.0)</td><td>81.0 (64.0-90.0)</td><td>56.4 (5.2-81.5)</td></tr>
<tr><td>RSV-ICU</td><td>Not reported</td><td>90.0 (54.0-98.0)</td><td>56.4 (5.2-81.5)</td></tr>
</table></td></tr>
<tr><td></td><td>Waning</td><td>Effectiveness of palivizumab (%)
Effectiveness >1 months: 0
Effectiveness of nirsevimab (%)
Effectiveness ≥6 months: 0</td></tr>
</table>

		Effectiveness of RSVpreF (%) Effectiveness ≥6 months: 0	
	Costs included	**<u>Type of cost</u>** **Direct costs** Medical cost ▪ Outpatient healthcare visits ▪ ED visits ▪ Hospitalisations in paediatric general ward and ICU Intervention cost ▪ Administration per dose: CAD $14.7 ▪ Product per dose: o RSVpreF CAD $230 o nirsevimab CAD $952 o palivizumab CAD $1,227 ▪ Wastage Patient-borne costs ▪ Out-of-pocket costs (only included in the societal perspective) o transportation o childcare and home help o other out of-pocket costs **Indirect costs** ▪ Productivity loss due to death from RSV disease ▪ Caregiver productivity loss	**<u>Measurement and valuation</u>** **Direct costs** Medical costs ▪ Cost per patient with RSV requiring outpatient healthcare provider/ED visit (by age group) obtained from a population-based matched retrospective case–control study using administrative data from Alberta. ▪ Paediatric general ward hospitalisation and ICU costs calculated using attributable per day costs and corresponding length of hospital stay derived from literature. Intervention costs ▪ Cost per product dose (Canadian list prices were used in the base case for nirsevimab and RSVpreF) ▪ Cost of administration per dose of nirsevimab (based on a Canadian study) ▪ Cost of administration per dose of RSVpreF (based on pertussis) ▪ Wastage costs were calculated as per the World Health Organization (WHO) recommendations. Patient-borne costs ▪ Out-of-pocket costs o cost of transportation (to vaccination or outpatient or inpatient care) o cost of childcare and home health after inpatient discharge o over-the-counter medications and other non-transportation or home

			expenses **Indirect costs** ▪ Productivity loss estimated using the human capital method ▪ Age specific labour force participation rates and average employment income were obtained from Statistics Canada ▪ Caregiver days lost due to hospitalisation (assumption based on a Canadian study) ▪ Caregiver days lost due to outpatient healthcare provider/ ED visits (assumption based on an English study) ▪ Caregiver days lost to visit healthcare provider for vaccination (assumption) ▪ Caregiver wages were calculated based on the average employment income and labour force participation of the population aged 25 to 54 years old (based on Canadian statistics)
	Effects included	**<u>Type of Effects</u>** **Direct effects** ▪ Outpatient healthcare provider visit ▪ ED visit ▪ Hospitalisation and ICU admission **Indirect effects** N/A	**<u>Measurement and valuation</u>** **Direct effects** ▪ Monthly incidence of RSV infection per 1,000 infants ▪ RSV-attributable hospitalisation (%) by gestational age ▪ RSV related ICU admissions (%) by gestational age ▪ Length of stay in hospital/ICU in days by gestation age ▪ RSV related mortality per hospitalised patient over 30 days (%) ▪ All-cause mortality per 1,000 population per year

			QALY loss ▪ RSV-associated QALY loss provided for both infants and their caregivers (Caregiver QALY losses were approximately 50% of children's losses) ○ outpatient healthcare provider visit: infants-0.00845(0.005-0.0454), caregivers-0.00423(0.0-0.025) ○ ED visit: infants 0.0135(0.008-0.0454), caregivers-0.00675(0.0-0.025) ○ Hospitalisation:infants-0.0169(0.01-0.0726), caregivers-0.0067 (0.0-0.0373) ○ ICU admission: infants-0.0245(0.0145-0.1053), caregivers-0.0097(0.0-0.0541)
Economic results	**Type of summary ratio**	Incremental cost per QALY	
	Overall payer perspective result	Seasonal nirsevimab for infants at moderate- and high-risk with catch-up was the most cost-effective strategy with ICER CAD $27,891 per QALY compared with the palivizumab programme. All strategies were dominated, except two: ▪ Year-round RSVpreF for all pregnant women plus nirsevimab for infants at high-risk with ICER CAD $204,621 per QALY compared with seasonal nirsevimab for infants at moderate- and high-risk with catch-up. ▪ Seasonal nirsevimab programs with catch-up (either for all infants or restricted to infants at moderate- or high risk) with ICER CAD $512,265 per QALY compared with year-round RSVpreF for all pregnant women plus nirsevimab for infants at high-risk.	
	Overall societal perspective result		

		Seasonal nirsevimab for infants at moderate or high risk, with catch-up was the most cost effective strategy with ICER CAD $14,948 per QALY compared with the palivizumab programme. All strategies were dominated, except two: ▪ Year-round RSVpreF with nirsevimab for infants at high risk with ICER CAD $343,421 per QALY compared with seasonal nirsevimab for infants at moderate or high risk, with catch up. ▪ Seasonal nirsevimab for all infants, with catch-up with ICER CAD $476,746 per QALY compared with year-round RSVpreF with nirsevimab for infants at high risk.
Epidemiological results		Reduction in outpatient healthcare provider visit, ED visit, hospitalisation and ICU admission
Authors conclusions	All modelled RSVpreF and nirsevimab programmes prevented additional cases of RSV disease compared to the current palivizumab programme. A year-round RSVpreF programme had lower intervention costs than all-infants nirsevimab programmes due to the lower per dose price of RSVpreF and lower assumed vaccine coverage, but its lower effectiveness and coverage led to higher RSV-related costs. Use of RSVpreF vaccine or nirsevimab in an infant's first season of RSV could significantly reduce the burden of RSV disease in this population. Nirsevimab programs were cost-effective when limited to infants born before 37 wGA or those residing in areas with higher RSV burden and healthcare costs such as remote communities. The authors commented that for all-infant programmes to be cost-effective, a substantial reduction in product prices is required. According to the authors' price threshold analysis, an all-infants seasonal nirsevimab programme with catch-up would be cost-effective if the price of nirsevimab was reduced by 80 to 88%.	

Key: CAD – Canadian dollar; ED – emergency department; EHL-mAb – extended half-life monoclonal antibody; ICER- incremental cost-effectiveness ratio; ICU – intensive care unit; LRTI – lower respiratory tract infections; MA – medically attended; mAb – monoclonal antibody; MV – maternal vaccine; QALY- quality-adjusted life year; RSV - respiratory syncytial virus; RSVpreF – respiratory syncytial virus prefusion F vaccine; wGA – weeks gestational age.

General study characteristics	**Author name** **Year of publication** **DOI**	Getaneh AM et al. 2023 https://doi.org/10.1016/j.vaccine.2023.01.058
	Region or country	Europe
	Type of economic evaluation	Cost utility analysis
	Population	Infants and pregnant women
	Funding	RSV Consortium in Europe funded through European Union's Horizon 2020 research and innovation programme and European Federation of Pharmaceutical Industries and Associations (EFPIA)

Model characteristics	**Model type**	Previously used static cohort model - MCMARCEL (Multi-Country Model Application for RSV Cost-Effectiveness policy) model States-Various health outcomes after RSV infection (RSV cases in primary care and hospitalisation setting) ▪ does not include RSV cases not seeking professional medical care, nor cases requiring only an outpatient or emergency department visit (due to limited data)
	Perspective	▪ Healthcare payer perspective (including only direct costs for RSV treatment and RSV intervention) ▪ Partial societal perspective (all direct costs + productivity loss due to workdays off from paid employment for caring for a child with RSV and for receiving an RSV intervention) ▪ Full societal perspective (all direct costs + economic cost of total time (including leisure time) lost due to caring for a child with RSV and for receiving an RSV intervention)
	Time horizon	5 years
	Comparator	No vaccination and each alternative strategy
	Discount rates	3.5/3.5% for Denmark, England and Scotland, 3/3% for Finland and Italy and 4/1.5% for the Netherlands
	Sensitivity analysis	Probabilistic sensitivity analysis (PSA)
Intervention	**Strategies**	▪ Year round MV program in the third trimester of pregnancy ▪ EHL-mAb administered at birth throughout the year ▪ EHL-mAb administered at birth during the RSV season from October to April ▪ seasonal EHL-mAb plus a catch-up program in October to protect children born in May to (including) September
	Dosing schedule	Single dose
	Type of immunisation	▪ MV- hypothetical vaccine (excluded from rest of extraction) ▪ EHL-mAb –nirsevimab (only EHL-mAb extracted from here)
	Age at immunisation	At birth for those born during RSV season, less than 1 month to 4 months for those born outside the RSV season
	Coverage rate	EHL-mAb- 90%
Model input parameters	**Efficacy/effectiveness**	EHL-mAb efficacy based on RCT data. Efficacy against hospital admission: 62.3% (12.1-98.0)

		Efficacy against primary care visit: 74.5% (53.2-90.3)	
	Waning	EHL-mAb protection wanes after 5 months (assumed no protection after 5 months)	
	Costs included	**<u>Type of cost</u>** **Direct costs** Medical cost ▪ Hospitalisation ▪ Outpatient (primary care visit) ▪ ICU Intervention cost ▪ Intervention per dose: €50 ▪ Administration ▪ Annual programme implementation cost (only for scenario analysis) **Indirect costs** ▪ Caregiver productivity loss	**<u>Measurement and valuation</u>** **Direct costs** Medical costs ▪ Varied by country ▪ Cost per hospitalisation/ICU admission (based on length of stay/admission, and age group but varied by country) ▪ Cost per primary care visit (based on the GP or family paediatrician's consultation price) ▪ Used age-specific number of RSV-related primary care o episodes, by assuming on average five RSV primary care episodes o for each RSV hospitalization for age 0–5 months, and 12.5 primary o care episodes for each RSV hospitalization for age 6–59 months (multiplication factors based on a study for England) ▪ Cost per ICU admission (England), per ICU hospital day (Netherlands) Intervention costs ▪ Intervention cost per dose of EHL-mAb (assumption based on the list price of rotavirus vaccine) ▪ A two-way price sensitivity analysis considering 25 combinations of o prices between €10 and €100 per dose (indicatively based on the o list prices of measles-mumps-rubella and meningococcal B vaccines). ▪ Administration cost per dose of EHL-mAb

			(varied by country) ▪ Cost vary depending upon whether the provided injection was the only dose given or together with another vaccine as a second injection ▪ Annual implementation costs per programme (scenario analysis only based on a study for Norway) **Indirect costs** ▪ Average productive hours per day assumed ▪ Productivity loss due to hospitalised RSV cases and primary RSV cases (due to workdays off from paid employment for caring for a child with RSV and for receiving an RSV intervention) ▪ No productivity loss if no separate appointment needed for vaccination ▪ Productivity hour loss due to RSV illness in infants younger than 1 year can be assumed to be zero in case of paid maternity/parental leave ▪ Productivity hours lost by caregivers due to RSV illness in children older than 1 year were not considered in our analysis because RSV burden is not preventable for this age group due to the relatively short protection period ▪ If the intervention are given together with another maternal/childhood vaccination program or during a regular check-up, no separate appointment would be needed, and the associated productivity hour lost can be assumed to be zero. ▪ For the partial societal perspective, productivity loss was obtained by multiplying the number of

			workdays off due to RSV illness and the time of receiving the intervention, by the average country-specific gross earnings per day ▪ The number of workdays off was assumed to be equal to the length of hospitalization for hospitalized children, and to be between 0 and 4.3 days for primary care cases ▪ For the full societal perspective, we calculated the costs of total time lost by the caregiver due to RSV illness in infants younger than 1 year (whether for work, leisure, or other activities) as the duration of illness in days multiplied by the average country-specific gross earnings per day
	Effects included	**<u>Type of Effects</u>** **Direct effects** • RSV hospitalisation • RSV-related primary care visit • Recurrent wheeze and asthma) • Total length of RSV illness for hospitalisations/primary care visits **Indirect effects** N/A	**<u>Measurement and valuation</u>** **Direct** ▪ RSV-ICD-coded hospitalization data by monthly age group (scenario analysis)-check ▪ RSV-attributable hospitalisation estimates (base case) by age group age groups: 0-2 months, 3-5 months, 6-11 months, 1-2, 3 years, and 3-4 years ▪ Number of RSV-related primary care visits per hospitalisation by age group ▪ Probability of recurrent wheezing/asthma in infant sunder 1-year-old by age group ▪ total length of RSV illness in days for hospitalisations/primary care visits (full societal perspective only) ▪ Age specific length of stay for hospitalisations for children < 5 years old (Denmark) ▪ Proportion of hospitalisations requiring ICU

			(%) (Finland, England, Scotland, Netherlands) ▪ Assumption- no RSV death case could be prevented (base case) QALY ▪ QALY loss per hospital admission ○ -0.01023 [0.0089 – 0.0117] ▪ QALY loss per primary care visit ○ -0.00625[0.0055-0.00704] ▪ QALY loss of recurrent wheezing/asthma per year-0.0392 [0.0116-0.0632]
Economic results	**Type of summary ratio**	ICER (incremental cost per QALY)	
	Overall payer perspective result	The cost-effective programmes for Denmark, England, Veneto region of Italy, and the Netherlands were either no programme, seasonal EHL-mAb, or seasonal EHL-mAb with catch-up, depending on the WTP value. Seasonal EHL-mAb was preferred for WTP values (per QALY gained) from: ▪ €4,444 (England) ▪ €9,129 (Denmark) ▪ €23,814 (Veneto region Italy) ▪ €21,187 (the Netherlands) Seasonal EHL-mAb with catch-up was preferred for WTP values (per QALY gained) from: ▪ €8,864 (England) ▪ €24,664 (Denmark) ▪ €42,245 (Veneto region Italy) ▪ €130,308 (the Netherlands) At lower WTP values (per QALY gained), no intervention was the preferred option. For Finland, seasonal EHL-mAb with catch-up was cost-effective from €13,373 per QALY gained, and for lower WTP values seasonal EHL-mAb without catch-up was preferred.	

		For Scotland, seasonal EHL-mAb with catch-up was preferred over all other programmes for the range of WTP values considered
	Overall societal perspective result	In all countries, the year-round EHL-mAb programmes are dominated by either no programme or seasonal EHL-mAb (with or without catch-up) programme from a full societal perspective. For all countries except the Netherlands, from a full societal perspective the seasonal EHL-mAb plus catch-up programme was the preferred strategy, regardless of WTP thresholds used. For the Netherlands, seasonal EHL-mAb without catch-up dominated all other programmes (the Netherlands was the only country for which paid workdays lost due to child care was considered from the partial societal perspective, due to shorter maternity leave)
Epidemiological results		Measured the reduction on the incidence of symptomatic cases, GP consultations, A& and E visits, hospital admissions, ICU admissions and deaths by intervention programme and age group. Also reported cases averted (RSV cases, hospital cases), and QALY gain by programme.
Authors conclusions	Seasonal EHL-mAb with or without catch-up is preferred over year-round EHL-mAb programmes. The choice between no programme, seasonal EHL-mAb, or seasonal EHL-mAb plus catch-up programmes depends on the country, the WTP value, the perspective taken and several key input parameters.	

Key: EHL-mAb – extended half-life monoclonal antibody; GP – general practitioner; ICER- incremental cost-effectiveness ratio; ICU – intensive care unit; MV – maternal vaccine; N/A – not applicable; QALY- quality-adjusted life year; RSV - respiratory syncytial virus; wGA – weeks gestational age; WTP – willingness to pay.

General study characteristics	**Author name** **Year of publication** **DOI**	Hodgson D et al. 2022 https://doi.org/10.1016/j.vaccine.2022.10.041
	Region or country	England and Wales
	Type of economic evaluation	Cost utility analysis
	Population	Infants
	Funding	Authors funded by various non-industrial funding source (National Institutes of Health and others)
Model characteristics	**Model type**	An existing dynamic transmission model was used States- Susceptible - Exposed - Infectious – Recovered

		Age structure - 25 age groups (monthly up to 11 months of age, and then 1, 2, 3, 4, 5–9, 10– 14, 15–24, 25–34, 35–44, 45–54, 55–64, 65–74, 75+ years Model states: symptomatic infection, GP consultations, hospital admissions, hospital bed days, and deaths
	Perspective	NHS (publicly-funded health and social care system) perspective
	Time horizon	10-year
	Comparator	Palivizumab
	Discount rates	3.5% for both costs and outcomes
	Sensitivity analysis	Univariate sensitivity analyses
Intervention	**Type of immunisation**	Extended half-life monoclonal antibody (Nirsevimab)
	Age at immunisation	One dose at birth or at 2-4 months or at 4 months or 1 to 6 months (seasonal catch up)
	Strategies	A single dose of extended half-lif monoclonal antibodies (EHL-mAb) ▪ to those infants who are currently eligible for Palivizumab at birth (Very high-risk), ▪ to all infants born from October to February at birth (Seasonal), ▪ to all children at birth year-round (Year-round) ▪ to all infants born October to February at birth in addition to all infants less than 7 months of age in October (Seasonal with catch-up) ▪ to all infants born September to February at birth in addition to infants at either 8, 12, or 16 weeks of age (to coincide with the existing National Immunisation Programme (NIP) in England) at the closest time to the start of the RSV season (Seasonal with NIP-integrated catch-up)
	Coverage rate	90% (70% used in scenario analysis)
Model input parameters	**Efficacy/effectiveness**	Efficacy against symptomatic RSV infection for 150 days from administration (% (95% CI))- 74.5% (49.6– 87.1)
	Waning	Base case: Duration of protection 150 days (exponential loss of protection at a rate of lambda = 1/150 days)

	Costs included	**<u>Type of cost</u>** **Direct costs** **Medical cost** ▪ RSV burden (primary care consultations and hospital bed days) ▪ Hospital admission **Intervention cost** ▪ Cost per dose (purchasing price per dose range) ▪ Annual vaccine administration **Indirect costs** N/A	**<u>Measurement and valuation</u>** **Direct costs** **Medical costs** ▪ primary care consultations and hospital bed days used to estimate the cost of RSV burden ▪ Hospital admission cost derived from a retrospective population based cohort study based in Ontario, Canada ▪ Outpatient cost based on estimates for patients with influenza **Intervention cost** ▪ PPPD values varied from £1–£4,600 in £1 intervals ▪ Annual administration cost **Indirect costs** N/A
	Effects included	**<u>Type of Effects</u>** **Direct effects** ▪ Symptomatic cases ▪ Hospital cases ▪ GP consultations ▪ Deaths ▪ Bed days **Indirect effects** ▪ Indirect protection	**<u>Measurement and valuation</u>** **Direct effects** ▪ Proportional reduction measured ▪ RSV hospitalised cases and symptomatic RSV cases averted per 1,000 children immunised **Indirect effects** ▪ Proportion of each healthcare outcome averted attributable to the indirect protection
Economic results	**Type of summary ratio**	ICER (incremental cost per QALY) at a WTP of £20,000/QALY	
	Overall payer perspective result	▪ The seasonal with NIP-integrated catch-up and the year-round programmes are always dominated, within the considered range of PPPDs ▪ PPPDs at which programmes are cost-effective at WTP threshold of £20,000/QALY o Seasonal programme to all infants: £63 or less	

		○ Seasonal plus catch up to all infants: £32 or less ○ Seasonal programme restricted to high risk infants: £64 or above
	Overall societal perspective result	N/A
Epidemiological results		Proportion of healthcare outcomes averted (symptomatic infection, hospital admission, death, GP consultations, and bed days)
Authors conclusions	This study concluded that nirsevimab could be cost-effective in England and Wales not only for use in high-risk infant but all infants at birth with a large-scale seasonal, or seasonal catch-up programme if the PPPD is £63 or less and may be preferable to the existing palivizumab programme.	

Key: EHL-mAb – extended half-life monoclonal antibody; ICER- incremental cost-effectiveness ratio; N/A – not applicable; NHS – National Health Service; PPPD – purchasing price per dose; QALY- quality-adjusted life year; RSV - respiratory syncytial virus; WTP – willingness to pay.

General study characteristics	**Author name** **Year of publication** **DOI**	Hodgson, D et al. 2024 https://doi.org/10.1016/j.lanepe.2024.100867
	Region or country	England and Wales
	Type of economic evaluation	Cost-effectiveness analysis (Cost-utility analysis)
	Population	Infants, Pregnant women
	Funding	National Institute of Health Research, UK
Model characteristics	**Model type**	Dynamic transmission model ▪ An existing model of RSV transmission in Wales and England was used ▪ 25 age groups: Monthly up to 1yr, yearly from 1 to 4yrs, then 5–9, 10–14, 15–24, 35–34, 35–44, 45–54, 55–64, 65–74, 75+ years. ▪ States - M: protected due to maternal antibodies, S: susceptible, E: exposed but not infectious, I: infectious and symptomatic, A: infectious and asymptomatic, R: recovered and protected, V_m: protected through maternal vaccination; $V_{B:}$ protected through monoclonal antibodies.
	Perspective	NHS (publicly-funded health and social care system)

	Time horizon	10 years
	Comparator	Palivizumab programme and the alternative intervention strategies
	Discount rates	3.5% per year for costs and outcomes
	Sensitivity analysis	▪ Univariate sensitivity analysis ○ Optimal programme calculated assuming WTP ICER of £30,000/QALY (base-case £20,000/QALY) ○ Considered impact of changing coverage rate of programmes (EHL-mAb 70%-90%; MV 50%-90%) ▪ Structural uncertainty analysis – how cost effectiveness changes if the EHL-mAb catch-up programme omitted.
Intervention	**Strategies**	EHL-mAb (3 strategies) ▪ Seasonal programme given at birth between September and February ▪ Seasonal programme given at birth between September and February and a yearly catch-up of all infants aged 1 to 6 months during September ▪ A year-round programme given at birth (MV) (2 strategies) ▪ A seasonal programme available to pregnant women 24 to 36 wGA between July and December ▪ A year-round programme available to pregnant women 24 to 36 wGA
	Dosing schedule	EHL-mAb – one dose at birth MV – one dose between 24 and 36 wGA
	Type of immunisation	Extended half-life monoclonal antibody (EHL-mAb) - nirsevimab Maternal vaccination (MV) – RSVpreF (infant outcomes); RSVPreF3 (pregnant women outcomes)
	Age at immunisation	EHL-mAb –at birth or 1 to 6 months (seasonal catch up) MV –between 24 and 36 wGA
	Coverage rate	EHL-mAb strategies: 90% uptake (based on vitamin K supplementation coverage at birth) MV strategies: 60% uptake (based on antenatal pertussis vaccine in England between 2019 and 2022)
Model input parameters	**Efficacy/effectiveness**	Fitted model realised efficacy against RSV infection based on clinical trial data: ▪ EHL-mAb: mean efficacy over the first 150 days after administration - 77.3% (95% CI: 65.4 to 86.5) ▪ MV infants: mean efficacy over, ○ the first 90 days after birth was 58.3%(95% CI: 41.5 to 72.8) ○ the first 120 days after birth was 55.7% (95% CI: 39.5 to 68.7) ○ the first 150 days after birth was 52.8% (95% CI: 37.2 to 65.2)

		○ the first 180 days after birth was 49.8% (95% CI: 34.2 to 62.1) ▪ MV pregnant woman: mean efficacy against RSV over the first 180 days after administration – 65.9% (95% CI: 51.2 to 77.2) Assumed higher efficacy for more severe outcomes (ED attendance, hospital admission, ICU admission, death). Risk of severe outcomes adjusted in the economic model based on the following estimated disease protection factors (proportion of infections protected from severe disease): ▪ EHL-mAb: 0.08 ((ICU admissions and death only) estimated based on efficacy against very severe lower respiratory tract illness (LRTI)) ▪ MV infants: 0.35 (estimated based on efficacy against medically attended severe RSV-associated LRTI) ▪ MV pregnant woman: 0.15 (estimated based on efficacy against RSV LRTI)	
	Waning	Waning immunity estimated by fitting a function to efficacy over time data against medically attended RSV-associated LRTI (EHL-mAb and MV infants) and RSV-related acute respiratory infection (MV pregnant women) ▪ EHL-mAb – proportion protected (mean, 95% CrI) ▪ at 150 days after administration – 0.587 (95% CrI 0.341 – 0.755) ▪ at 365 days after administration – 0.148 (95% CrI 0.015 – 0.338) ▪ MV infants – proportion protected (mean, 95% CrI) ▪ at 180 days after birth – 0.318 (95% CrI 0.078 – 0.499) ▪ at 365 days after birth – 0.093 (95% CrI 0.001 – 0.237) ▪ MV pregnant women – proportion protected (mean, 95% CrI) ▪ at 150 days after vaccination – 0.447 (95% CrI 0.171 – 0.636) ▪ at 365 days after vaccination – 0.137 (95% CrI 0.007 – 0.308)	
	Costs included	**<u>Type of cost</u>** **Direct costs** Medical costs ▪ GP consultations (£36) ▪ ED visits ▪ Hospital admissions ▪ ICU admissions	**<u>Measurement and valuation</u>** **Direct costs** Medical costs ▪ Cost per GP consultation ▪ Cost per ED attendance ▪ Cost per hospitalisation admission episode by duration of stay (short and long) and

		Intervention costs ▪ Combined cost of purchasing and administration (CCPA) of each dose of intervention (£5 to £200) **Indirect costs** N/A	age (<15yrs and ≥15yrs old) ▪ Cost per ICU admission episode by age (<15yrs and ≥15yrs old) Intervention costs ▪ Cost per vaccine dose (palivizumab, assumed all doses in infant's first season are given as 50mg dose) ▪ Combined cost of purchasing and administration (CCPA) of each dose of intervention
	Effects included	**<u>Type of Effects</u>** **Direct effects** ▪ Symptomatic cases ▪ GP-attended cases ▪ Hospital admissions ▪ ED visits ▪ ICU admissions ▪ Deaths **Indirect effects** ▪ Indirect protection	**<u>Measurement and valuation</u>** **Direct effects** ▪ Incidence of each effect by age group and vaccination strategy ▪ Proportional reduction of each effect by age group and vaccination strategy **UK specific estimates for the QALY loss per effect:** ▪ Symptomatic infection/GP consultation by age (<5yrs and ≥5yrs old): ○ <5 years: 2.336×10^{-3} (95% CI: 0.269×10^{-3} to 9.255×10^{-3}) ○ ≥5 years: 1.448×10^{-3} (95% CI: 0.135×10^{-3} to 5.928×10^{-3}) ▪ Hospitalisation/ICU admission by age: ○ <5 years: 4.098×10^{-3} (95% CI: 0.624×10^{-3} to 13.141×10^{-3}) ○ ≥5 years: 2.990×10^{-3} (95% CI: 0.346×10^{-3} to 11.387×10^{-3}) ▪ Discounted QALY loss due to death estimated using health-related quality of life (HR-QoL) and life expectancy by age. **Indirect effects**

			▪ Indirect protection was incorporated into the model.
Economic results	**Type of summary ratio**	Incremental Net Monetary Benefit ▪ The optimal programme was defined as the one with the highest incremental net monetary benefit (INMB) assuming an ICER WTP threshold of £20,000 per QALY.	
	Overall payer perspective result	At an ICER WTP threshold of £20,000 per QALY: ▪ If EHL-mAb is priced above £84 combined cost of purchasing and administration (CCPA), then a seasonal maternal vaccine programme is optimal between £36 to £80 CCPA, and a year-round programme is optimal up to £35 CCPA.If the maternal vaccine is priced above £80, then a seasonal EHL-mAb programme is optimal up to £55 to £83 CCPA, and a seasonal EHL-mAb with a catch-up programme is optimal up to £55 CCPA. ▪ The year-round EHL-mAb programme is dominated by the seasonal EHL-mAb with an annual catch-up programme across all CCPAs. ▪ If both products are priced below £30 then the EHL-mAb is optimal. ▪ If both products are priced above £30 then both programmes are similarly cost-effective.	
	Overall societal perspective result	**N/A**	
Epidemiological results		Measured the reduction in the incidence of symptomatic cases, GP consultations, ED visits, hospital admissions, ICU admissions and deaths by intervention programme and age group. (Details in Supplementary file 2, table 2)	
Authors conclusions	This study concludes that the extended half-life monoclonal antibody and the maternal vaccine could substantially reduce the burden of RSV disease in the infant population in England and Wales. It also estimates the optimally cost-effective intervention at various intervention price points.		

Key: CCPA - Combined cost of purchasing and administration; CI – confidence interval; CrI – credible interval; ED – emergency department; EHL – extended half-life monoclonal antibody; EVPI – expected value of perfect information; GP – general practitioner; ICER - incremental cost-effectiveness ratio; ICU – intensive care unit; INMB - Incremental Net Monetary Benefit; LRTI – lower respiratory tract infection; N/A – not applicable; NHS – National Health Service in England and Wales ; QALY- quality-adjusted life year; RSV - respiratory syncytial virus; wGA – weeks gestational age; WTP – willingness to pay; Yrs - years.

	Author name	Ishiwada N et al.

General study characteristics	**Year of publication** **DOI**	2024 https://doi.org/10.1007/s40121-024-01000-6
	Region or country	Japan
	Type of economic evaluation	Cost-utility analysis
	Population	Infants
	Funding	Pfizer Japan Inc.
Model characteristics	**Model type**	Markov model, decision tree structure Model cycle: monthly rolling cohort of infants aged <1 year with 12-monthly cohorts split by gestational age: ▪ full-term (≥ 37 weeks gestational age (wGA)) ▪ preterm (≤ 27 wGA, 28–31 wGA, and 32–36 wGA)
	Perspective	Health system and societal
	Time horizon	One year for all health outcomes except RSV-related death (lifetime)
	Comparator	Palivizumab for: ▪ infants with risk factors born ≤31 wGA, 32-26 wGA and ≥37 wGA ▪ infants without risk factors born ≤31 wGA and 32-35 wGA. Risk factors for RSV disease include bronchopulmonary dysplasia (BPD), congenital heart disease (CHD), Down's syndrome, or a compromised immune system.
	Discount rates	2% for both costs and effects
	Sensitivity analysis	One-way sensitivity analysis (model parameters were examined at lower and upper bounds of ±25%)
Intervention	**Strategies**	Strategy 1 includes: ▪ RSVpreF for pregnant women (24 to 36wGA) (year-round) ▪ Palivizumab for: ○ infants with risk factors born ≤31 wGA, 32 to 26 wGA and ≥37 wGA ○ infants without risk factors born ≤31 wGA ○ infants without risk factors born 32 to 36 wGA to unvaccinated mothers or within 2 weeks after maternal vaccination Strategy 2 includes: ▪ RSVpreF for pregnant women (24 to 36wGA) (year-round) ▪ Palivizumab for: ○ infants with risk factors born ≤31 wGA ○ infants with risk factors born 32 to 26 wGA and ≥37 wGA to unvaccinated mothers or within 2 weeks after maternal vaccination ○ infants without risk factors born ≤31 wGA

		○ infants without risk factors born 32 to 36 wGA to unvaccinated mothers or within 2 weeks after maternal vaccination	
	Dosing schedule	Single dose	
	Type of immunisation	Maternal vaccine (MV) - RSVpreF Monoclonal antibody (mAb) - Palivizumab	
	Age at immunisation	RSVpreF -24 to 36 wGA Palivizumab - at birth (once a month throughout the RSV season (up to 6 doses))	
	Coverage rate	RSVpreF – 80% equally year-round (based on the maternal vaccination rate against COVID-19 in Japan) Palivizumab ▪ weighted average of 46.2% applied for population aged ≤36 wGA (0% for 36wGA and 90% for ≤35wGA)95% for high-risk infants	
Model input parameters	**Efficacy/effectiveness**	RSVpreF: ▪ Against hospitalisation - Full term (≥37 wGA)-88.1%, Preterm (32-36 wGA)-73.4%, Preterm (28-31 wGA)-0%, Preterm (≤27 wGA)-0%, High-risk-0% ▪ Against ED - Full term (≥37 wGA)-47.6%, Preterm (32-36 wGA)-39.6%, Preterm (28-31 wGA)-0%, Preterm (≤27 wGA)-0%, High-risk-0% ▪ Against Outpatient - Full term (≥37 wGA)-47.6%, Preterm (32-36 wGA)-39.6%, Preterm (28-31 wGA)-0%, Preterm (≤27 wGA)-0%, High-risk-0% Palivizumab: 56%	
	Waning	RSVpreF: Up to 180 days waning based on RCT data. After 180 days, the VE was assumed to decrease linearly in the next 3 months until effectiveness rate reaches 0% by 9 months (270 days)	
	Costs included	**<u>Type of cost</u>** **Direct costs** Medical cost ▪ Hospitalisation ▪ Outpatient ▪ ED	**<u>Measurement and valuation</u>** **Direct costs** Medical cost ▪ Hospitalisation, ED and outpatient) per episode by age group (<1, 1-<2, 2-<6, 6-<12 months)

		Intervention cost ▪ Intervention price ($182 to $334) ▪ Administration cost **Indirect costs** Productivity loss (adults) ▪ Caregiver absence from work during nursing ▪ Recipients visiting hospital for MV ▪ Caregivers bringing infants to appointment to receive mAb	Intervention cost ▪ price per dose (a range of vaccine prices were explored) ▪ administration cost per dose (based on applicable national medical service fees) **Indirect costs** Productivity loss: ▪ Calculated based on general adult population work force participation rate and average daily wage ▪ Caregiver absence from work during nursing: ○ percentage of infants with primary caregiver in the workforce ○ percentage of caregivers with full time employment ○ caregiver work loss days (per episode) by healthcare setting (hospitalisation, ED, outpatient) ○ average daily wage for full time employed caregiver ▪ Recipient visiting hospital for intervention or taking infants to ○ work day loss ○ percentage of population impacted
	Effects included	**<u>Type of Effects</u>** **Direct effects** ▪ Hospitalisation ▪ ED encounters ▪ Outpatient visits ▪ Deaths **Indirect effects** N/A	**<u>Measurement and valuation</u>** **Direct effects** ▪ incidence of infection, hospitalisation and ED visits per 1000 person years ▪ probability of infection by month ▪ proportion of cases hospitalised by monthly age group ▪ case-fatality rate due to RSV per 100 cases by healthcare setting (hospitalisations, ED and outpatient)

			▪ relative risk of death due to RSV by wGA group QALY loss ▪ Hospitalised - 0.0157 ▪ ED - 0.0061 ▪ Outpatient - 0.0061 Baseline utility ▪ Infants (0-11mths): 1.0 ▪ 1-17 year olds: 1.0 ▪ 18–99-year-olds: calculated using EQ-5D-5L scores Caregiver disutility not considered in base case
Economic results	**Type of summary ratio**	ICER (incremental cost per QALY)	
	Overall payer perspective result	Scenario 1: ICER- JPY 4,998,847/QALY (US $38,043/QALY) Scenario 2: Dominant (more effective and less costly at a RSVpreF vaccine price of JPY 23,948 (US $182).	
	Overall societal perspective result	Scenario 1: ICER- JPY 4,638,509/QALY (US $35,301/QALY) Scenario 2: Dominant (more effective and less costly at a RSVpreF vaccine price of JPY 23,948 (US $182).	
Epidemiological results		Impact on RSV associated hospitalisations, ED visits, outpatient episodes and deaths reported.	
Authors conclusions	Compared with palivizumab only, a combined prophylaxis of year-round RSVpreF vaccination of pregnant women and palivizumab prescription for infants was cost-effective at the threshold value of JPY 5 million/QALY when the unit price of RSVpreF vaccine was no more than JPY 23,948 (US $182).		

Key: ED – emergency department; ICER- incremental cost-effectiveness ratio; MV – maternal vaccine; mAb – monoclonal antibody; QALY- quality-adjusted life year; RSV - respiratory syncytial virus; RSVpreF – respiratory syncytial virus prefusion F vaccine; US – United States; JPY - Japanese Yen; wGA – weeks gestational age

General study characteristics	**Author name** **Year of publication** **DOI**	Keiffer A et al. 2024 https://doi.org/10.1007/s40121-024-01037-7
	Region or country	United Kingdom

	Type of economic evaluation	Cost-utility analysis
	Population	Infants under one year of age
	Funding	Industry – AstraZeneca and Sanofi
Model characteristics	**Model type**	Static decision-analytic model ▪ Previously published model used in the US setting ▪ Tracks the UK infant cohort by month of birth during their first RSV season ▪ Stratified cohort (three subpopulations) by RSV-related lower respiratory tract disease (LRTD) risk: — (1) late preterm and term infants (born ≥ 35 weeks gestational age (wGA)) — (2) preterm infants (born ≥ 29 wGA and <35 wGA, not eligible for palivizumab), and — (3) palivizumab-eligible infants (born <29 wGA or those with chronic lung disease (CLD) or congenital heart disease (CHD)
	Perspective	NHS payer
	Time horizon	One RSV season for all health events except: ▪ Recurrent wheezing – 3 years ▪ Premature deaths – lifetime
	Comparator	▪ Current Standard of Practice which recommends palivizumab for the high-risk infant population only (i.e. those born <29 wGA or those with chronic lung disease (CLD) or chronic heart disease (CHD)), consisting of: ▪ a "seasonal" approach where infants born during the season receive monthly palivizumab administrations from birth until the end of the RSV season, and ▪ a "catch-up" approach in which infants born before the RSV season receive up to five monthly palivizumab administrations throughout the RSV season. Palivizumab coverage rate: informed to reflect the sales in UK annually (data reported as on file) ▪ 70% (95% CI: 56 to 84%)
	Discount rates	Risk of recurrent wheezing and associated management cost: 3.5% per annum for 2 years.

	Sensitivity analysis	Deterministic ▪ Assumed deviation in parameter estimates was 20%, except for treatment efficacy which was extracted from clinical trial results.
Intervention	**Strategies**	Strategy 1: Immunisation with palivizumab as outlined under comparator above Strategy 2: ▪ seasonal approach for all infants (including preterm and palivizumab-eligible) born during the RSV season, administering nirsevimab at birth ▪ catch-up approach for all infants (including preterm and palivizumab-eligible) born before the RSV season, administering nirsevimab during their regular National Immunisation Programme immunisation appointment (at weeks 8, 12, or 16 after birth) closest to, but no later than, the beginning of the RSV season.
	Dosing schedule	Nirsevimab – one dose
	Type of immunisation	▪ Extended half-life monoclonal antibody (EHL-mab) - nirsevimab
	Age at immunisation	Nirsevimab – at birth or during their regular National Immunisation Programme immunisation appointment (at weeks 8, 12, or 16 after birth) closest to, but no later than, the beginning of the RSV season.
	Coverage rate	Nirsevimab: uptake assumed to be similar to the primary series vaccinations in infants under 5 years old ▪ all groups: 91% (95% CI: 72.8 to 100%)
Model input parameters	**Efficacy/effectiveness**	Efficacy of nirsevimab against RSV-related health events in term and preterm infants not eligible for palivizumab based on RCT data. For infants born extremely preterm with CHD/CLD, authors assumed non-inferiority of nirsevimab versus palivizumab for this group. Palivizumab efficacy data was informed by a network meta-analysis of three RCTs assessing the prevention of hospitalisation associated with palivizumab versus placebo: Monthly Palivizumab efficacy - % (95% CI)

		▪ Efficacy against RSV ED and PC visits: 51.0% (40.8 to 61.2%) ▪ Efficacy against RSV hospitalisations: 51.0% (40.8 to 61.2%) Mean Nirsevimab efficacy - % (95% CI) ▪ Efficacy against RSV ED and PC visits (by subpopulation): — Palivizumab eligible - 51.0% (40.8 to 61.2%) — Preterm - 86.2% (68.0 to 94.0%) — Term - 74.5% (49.6 to 87.1%) ▪ Efficacy against RSV hospitalisations (by subpopulation): — Palivizumab eligible - 51.0% (40.8 to 61.2%) — Preterm - 83.2% (67.8 to 92.0%) — Term - 83.2% (67.8 to 92.0%) ▪ Efficacy against all-cause LRTD hospitalisations (by subpopulation): — Palivizumab eligible - N/A — Preterm - 58.04% — Term - N/A	
	Waning	Palivizumab- protection duration of one month after each dose, no protection after this period Nirsevimab-efficacy sustained through 150 days after administration (5 months), no residual efficacy after this period	
	Costs included	**<u>Type of cost</u>** **Direct costs** Medical costs ▪ Primary care visit ▪ ED visit ▪ Hospitalisation (standard paediatric ward) ▪ ICU admission ▪ Recurrent wheezing (year1, year2 and year3) ▪ All-cause LRTD hospitalisations (excluding RSV hospitalisations) Intervention ▪ Cost of EHL-mAb inclusive of administration	**<u>Measurement and valuation</u>** **Direct costs** Medical costs (assumed to be constant across subpopulations) ▪ Cost per hospitalisation event ▪ Cost per ICU admission ▪ Cost per ED visit ▪ Cost per primary care visit ▪ Cost of o recurrent wheezing in year 1 o recurrent wheezing in year 2 o recurrent wheezing in year 3 Intervention costs

		Indirect costs N/A	▪ Cost of EHL-mAb inclusive of administration ○ Estimated the maximum economically justifiable price of nirsevimab including administration costs at a WTP threshold of £20,000/QALY and £30,000/QALY saved, respectively.
	Effects included	**<u>Type of Effects</u>** **Direct effects** ▪ Primary care visit ▪ Hospitalisation (standard paediatric ward) ▪ ICU admission ▪ ED visit ▪ Recurrent wheezing (year1, year2 and year3) ▪ All-cause LRTD hospitalisations (excluding RSV hospitalisations) **Indirect effects** N/A	**<u>Measurement and valuation</u>** **Direct effects** ▪ Risk of primary care visit by age group (0-5m, 6-11m) ▪ Risk of hospitalisation based on risk status and ICU admission based on risk status: ○ Palivizumab eligible ○ Preterm ○ Term QALY loss Non-medically attended: 0.0036 Ambulatory care: 0.0063 Hospitalisation: 0.0101
Economic results	**Type of summary ratio**	Incremental cost per QALY gained	

	Overall payer perspective result	Strategy 2 (seasonal + catch-up for all infants with nirsevimab) was estimated to save 2,203 QALYs and £117 million in costs, compared with current Standard of Practice (palivizumab for the high-risk infant population only). The economically justifiable price of nirsevimab (including administration costs) was estimated at between £243 and £274 at WTP thresholds of £20,000 and £30,000 per QALY saved, respectively.
	Overall societal perspective result	N/A
Epidemiological results		Measured the reductions in the following events: ▪ Hospitalisations (standard ward) ▪ ICU admissions ▪ ED visits ▪ PC visits ▪ Non-medically attended events ▪ RSV-related deaths ▪ All-cause LRTD hospitalisations ▪ Recurrent wheezing across 3 years
Authors conclusions	This study concluded that a universal infant immunisation programme based on nirsevimab could considerably alleviate the health and economic implications of RSV infections among infants entering their first RSV season in the UK, compared with immunising only high-risk infants with palivizumab. The study estimated that nirsevimab based strategy could be cost-effective at a value between £243 and £274, assuming willingness-to-pay (WTP) thresholds of £20,000 and £30,000 per QALY gained, respectively.	

Key: CHD – congenital heart disease; CLD – chronic lung disease; CI – confidence interval; ED – emergency department; EHL – extended half-life monoclonal antibody; ICU – intensive care unit; JCVI - Joint Committee on Vaccination and Immunisation; LRTD – lower respiratory tract disease; MA – medically attended; NHS – National Health Service; PC – primary care; QALY- quality-adjusted life year; RCT – randomised controlled trial; RSV - respiratory syncytial virus.

General study characteristics	**Author name** **Year of publication** **DOI**	Li X et al 2022 10.1093/infdis/jiac064
	Region or country	Norway
	Type of economic evaluation	Cost utility analysis
	Population	Infants and Pregnant women

	Funding	European Union Funding – EU Horizon 2020 research and innovation programme and the European Federation of Pharmaceutical Industries and Associations
Model characteristics	**Model type**	Static Cohort Model ▪ A previously published model – Multi-Country Model Application for RSV Cost-Effectiveness policy (MCMARCEL) ▪ Model tracks monthly birth cohorts of children from birth to 5 years old ▪ Events in the model- Symptomatic RSV, Primary care visits, Hospital outpatient visits, Hospital admissions, Deaths among hospitalised, Long term consequences among hospitalised – Recurrent wheezing, recurrent wheezing and asthma
	Perspective	Healthcare payer perspective
	Time horizon	Base case: Birth to 5 years old In scenario analysis, recurrent wheezing and asthma events were followed up to 13 years old
	Comparator	No RSV disease prevention strategy
	Discount rates	4% cost and effects
	Sensitivity analysis	Probabilistic sensitivity analysis Two-way price sensitivity analysis was performed for EHL-mAb and MV (5 equidistant values from NOK 100 to 900 per intervention)
Intervention	**Strategies**	31 strategies modelled Year round programmes ▪ MV: year round maternal vaccination in the third trimester of pregnancy ▪ EHL-mAb: monoclonal antibody administered at birth through the year Seasonal monoclonal antibody programmes ▪ A single month programme or any combination of consecutive months during the RSV season (Oct to April) (n=28 strategies) o Jan only; Feb only; March only; April only; Oct only; Nov only; Dec only o Oct-Nov; Oct-Dec; Oct-Jan; Oct-Feb; Oct-March; Oct-April o Nov-Dec; Nov-Jan; Nov-Feb; Nov-March; Nov-April o Dec-Jan; Dec-Feb; Dec-March; Dec-April o Jan-Feb; Jan-March; Jan-April o Feb-March; Feb-April o March-April ▪ Seasonal "catch-up" programme that would administer EHL-mAb at birth to infants born during the RSV season (October to April) AND offer EHL-mAb to infants <6 months born outside the season (May to September), administered at the beginning of the RSV season (October)

	Dosing schedule	MV: 1 dose administered in the third trimester of pregnancy EHL-mAb: 1 dose at birth or for catch-up <6 months of age.	
	Type of immunisation	Maternal vaccine (MV) – hypothetical vaccine/failed candidate vaccine (novavax) (excluded from rest of extraction) EHL-mAb – nirsevimab (only EHL-mAb extracted from here)	
	Age at immunisation	MV: 1 dose administered in the third trimester of pregnancy EHL-mAb: 1 dose at birth or for catch-up <6 months of age.	
	Coverage rate	Rotavirus vaccine is the first infant vaccine in the national immunisation schedule, offered at 6 weeks of age. For simplicity, the rotavirus coverage of 92% used as proxy for both MV and EHL-mAb.	
Model input parameters	**Efficacy/effectiveness**	EHL-mAb recorded, MV excluded (hypothetical vaccine) Mean Efficacy against hospital admission or hospital outpatient visit ▪ 62.3% (95% CI: 12.1 to 98.0) ▪ Phase 3 results of EHL-mAb Mean Efficacy against primary care visit ▪ 74.5% (95% CI: 53.2 to 90.3) ▪ Phase 2b data of EHL-mAb used in the scenario analysis.	
	Waning	Duration of protection 5 months ▪ In base case assumed fixed ▪ Varied to 6 months in scenario analysis	
	Costs included (per strategy)	**<u>Type of cost</u>** **Direct costs** Medical costs ▪ Cost per hospitalisation ▪ Cost per hospital outpatient visit ▪ Cost per primary care visit ▪ Cost per emergency outpatient clinic (EOC) visit ▪ Recurrent wheezing and asthma treatment cost Intervention costs ▪ Intervention cost per dose: NOK 500 (€51)	**<u>Measurement and valuation</u>** **Direct costs** Medical costs ▪ Diagnosis-related group (DRG) unit cost multiplied by the weight of the DRG code for each RSV hospital visit. ▪ Average hospital cost per visit estimated by ○ encounter type (inpatient or outpatient) ○ age (age 0 months and age 1 year). ▪ Average cost per respiratory tract infection (RTI) primary care visit by

		▪ Delivery cost per dose ▪ Annual programme implementation costs **Indirect costs** Productivity Loss ▪ Cost of productivity loss due to RSV-infected child	○ encounter type (GP or emergency outpatient clinics) ○ age (0-1 year, 1-2 years, 2-5 years) ▪ Weighted average cost for a RTI primary care visit per age calculated ○ assumed average cost of RSV-related primary care visit would be the same ▪ Physician primary care reimbursement fees sourced from Norwegian administration data. ○ multiplied by a factor of two as per Norwegian pharmacoeconomics guidelines. ▪ Recurrent wheezing and asthma annual treatment cost per patient (0-12 years old, used in scenario analysis) ○ assumed as the cost of 5.5 primary care visits and one beta agonist inhaler based on a Dutch study Intervention costs ▪ Intervention cost per dose (assumption, varied in sensitivity analysis) ▪ Nurse time required for EHL-mAb administration (based on a rotavirus vaccine study) ▪ Annual programme implementation costs (based on rotavirus vaccine economic evaluation) **Indirect costs** Productivity loss ▪ Age 0-1 year - No work day loss for parents accounting maternal/paternal leave ▪ Age 1-5 year- No productivity loss

			considered (as the protection duration is less than one year)
	Effects included (per strategy)	**<u>Type of Effects</u>** **Direct effects** ▪ RSV coded hospital inpatient visits ▪ RSV coded hospital outpatient visits ▪ RSV coded mortality ▪ Respiratory tract infection primary care visits ▪ RSV-related primary care visits ▪ Recurrent wheezing/asthma given RSV hospitalisations in infants under 1 year-old (scenario analysis only) **Indirect effects** N/A	**<u>Type of Effects</u>** **Direct effects** ▪ RSV coded hospital inpatient visits ▪ RSV coded hospital outpatient visits ▪ RSV coded mortality (no preventable deaths assumed in base case) ▪ RSV-related primary care visits ○ for those aged less than 6 months and 6 months and older ▪ Age-specific proportion of respiratory tract infection primary care visits ○ monthly intervals from 0 to 5 months of age ▪ Probability of recurrent wheezing/asthma given RSV hospitalisation in infants under 1 year old ○ by yearly age groups from 0 to 4 years old, and 4 years to 13 years old. QALY loss ▪ hospital admission or hospital outpatient visit: 0.0039 (0.0002 to 0.0123) ▪ primary care visit: 0.0035 (0.0006 to 0.0088) ▪ recurrent wheezing/asthma per year: 0.0392 (0.0116 to 0.0632) ▪ QALY measured by EQ5D-3L-Y questionnaire in children under 5 with RSV infection
Economic results	**Type of summary ratio**	Lowest expected net loss (equivalent to incremental cost per QALY gained)	

	Overall payer perspective result	At NOK500 (€51) per dose, the Nov-Feb programme is preferred when the WTP threshold is below NOK 390,000 and the Oct-March programme is preferred when the WTP is above NOK 500,000 When the price per dose is NOK100, the catch-up is the most cost effective programme for all WTP thresholds considered When the price per dose is NOK900, no programme is cost effective for WTP values up to NOK 300,000 per QALY gained.
	Overall societal perspective result	N/A
Epidemiological results		**Outcomes:** ▪ RSV cases in children under 5 years ▪ RSV hospitalisations ▪ RSV hospital outpatient visits ▪ RSV deaths ▪ RSV disease results in average of 48 undiscounted QALY losses (0-59 months)
Authors conclusions	This study concluded that, assuming an equal price of NOK 500 per dose and EHL-mAb's efficacy and duration of protection in the real world would be in line with phase 3 data, a seasonal EHL-mAb programme is the cost-effective programme (eg Nov-Feb, Oct-Feb, or Oct-March, depending on the WTP value. When considering higher disease burden (accounting for long term consequences of asthma and recurrent wheeze), longer EHL-mAb programmes become cost effective, including the EHL-mAb catch up programme. Seasonal programmes are sensitive to the timing of the RSV season in each country.	

Key:; CI – confidence interval; EHL-mAb – extended half-life monoclonal antibody; EQ-5D-5L - EuroQol 5-Dimensions 5-Levels; ICER- incremental cost-effectiveness ratio; MV – maternal vaccine; N/A – not applicable; NOK – Norwegian Krone; QALY- quality-adjusted life year; RSV - respiratory syncytial virus; WTP – willingness to pay

General study characteristics	**Author name** **Year of publication** **DOI**	Li X et al. 2023 https://doi.org/10.1016/j.jval.2022.11.014
	Region or country	Europe
	Type of economic evaluation	Model comparison study – cost utility analysis

	Population	Infants and pregnant women
	Funding	European Union grant funding
Model characteristics	**Model type**	Static model n=3 ▪ Stochastic, multicohort decision tree, tracks infants aged in months and time in calendar months (University of Antwerp) ▪ Deterministic, decision tree, tracks full-term infants over pre-defined months (Novavax) ▪ Deterministic, multicohort markov, monthly cycle, tracks infants age in months and time in calendar months (Sanofi Pasteur) Dynamic model n=2 ▪ Deterministic, compartmental transmission model, age structured (SIRS – susceptible infected recovered susceptible) population (Sanofi Pasteur) ▪ Deterministic, compartmental transmission model, age structured (SEIRS – susceptible exposed infected recovered susceptible) population (London School of Hygiene and Tropical Medicine)
	Perspective	Health payer perspective Societal perspective
	Time horizon	Static model n=3 ▪ 1 year time horizon for each Dynamic model n=2 ▪ Deterministic, compartmental (SIRS) population (Sanofi Pasteur) – Steady State over 10 years ▪ Deterministic, compartmental (SEIRS)population (London School of Hygeine and Tropical Medicine) – 10 years
	Comparator	No intervention
	Discount rates	3% per annum for costs and health outcomes Static: Discrete, annually Dynamic SIRS: continuous using an exponential function

		Dynamic SEIRS: discrete, monthly
	Sensitivity analysis	One-way sensitivity analysis in which upper and lower ranges used for input parameter (Supplementary Table 6) Scenario analyses performed: ▪ Seasonal strategy, low coverage (30%) ▪ Seasonal strategy, high coverage (70%) ▪ Year-round strategy, low efficacy (52% against hospitalisation, 52.3% against primary care visit) ▪ Year-round strategy, high efficacy (90% against hospitalisation, 81.2% against primary care visit) ▪ Year-round strategy, short duration (duration of protection until 120 days) ▪ Year-round strategy, long duration (duration of protection until 240 days) ▪ Year-round, high hospital visits (50% increase to hospitalisation rate) ▪ Year-round, low hospital visits (50% decreased to hospitalisation rate)
Intervention	**Strategies**	The strategies included MV and EHL-mAb. As MV data was based off the discontinued Novavax study and vaccine, only EHL-mAb information has been extracted from this point onwards. EHL-mAb strategies included: ▪ Year round programme of EHL-mAb for infants at birth ▪ Seasonal programme of EHL-mAb protecting infants at birth during October to April ▪ Seasonal programme with catch up of seasonal EHL-mAb uptake plus a EHL-mAb catch-up programmes, where infants <6 months born outside of the season (May to September) would be administered the EHL-mAb at the beginning of the RSV season (October)
	Dosing schedule	1 dose
	Type of immunisation	Maternal vaccine (M) –failed candidate vaccine (novavax) (excluded from rest of extraction) Extended half-life acting monoclonal antibody (EHL-mAb) – nirsevimab
	Age at immunisation	At birth or those aged <6 months (catch up) MV: not stated
	Coverage rate	EHL-mAb: 94% coverage based on infant rotavirus vaccine coverage. MV: 67% (year-round) and 44% (seasonal)
	Efficacy/effectiveness	Data based on RCT results for EHL-mAb

<table>
<tr><td rowspan="3">Model input parameters</td><td></td><td colspan="2">Efficacy against hospital admission or hospital outpatient visit

▪ 78% (95% CI: 52 to 90)
Efficacy against primary care visit

▪ 70% (95% CI: 52.3 to 81.2)</td></tr>
<tr><td>Waning</td><td colspan="2">Duration of protection 150 days based on RCT results for EHL-mAb. This was varied in the scenario analysis

Static models-

UA, SPS- all or nothing approach with a stepwise function for duration: full protection then no protection

NV- all or nothing with a stepwise function for 150 days

Dynamic models-

SPD-all or nothing with a stepwise function for 150 days (individuals moving out of the protected compartment after 5 months)

LSHTM-All or nothing with an exponential decline function for individuals moving out of the “protected” compartment over time EHL-mAb: 150 days (median 103 days)</td></tr>
<tr><td>Costs included</td><td><u>Type of cost</u>
Direct costs
Medical costs

▪ Hospitalisation
▪ Hospital outpatient visit
▪ Primary care visit
▪ ICU admission
▪ Length of stay in hospital
▪ Length of stay in ICU
Patient borne costs
▪ Transportation for parents per hospitalisation or ICU admission</td><td><u>Measurement and valuation</u>
Direct costs
Medical costs

▪ Dutch reference costs for
○ hospitalisation per day
○ each hospital outpatient visit
○ each primary care visit
○ ICU admission per day and ambulance transfer for those admitted to ICU
▪ Length of stay in hospital and ICU based on a Dutch study

Patient-borne costs</td></tr>
</table>

		Intervention costs ▪ Single-dose EHL-mAb ▪ Delivery cost per dose ▪ Programme implementation costs (one off) **Indirect costs** ▪ Cost of productivity loss ▪ Workdays lost due to RSV-infected child	▪ Cost of transportation for parents per hospitalisation or ICU admission per Kilometre o mean distance travelled based on a Dutch study Intervention costs ▪ Cost per dose of EHL-mAb (assumption) ▪ Delivery cost per EHL-mAb dose o assumption, based on a Dutch study ▪ One-off programme implementation costs (assumption) o seasonal o year-round **Indirect costs** ▪ Cost of productivity loss salary loss paid work per day o loosely based on the Organisation for Economic Co-operation and Development (OECD) salary data ▪ Workdays lost due to RSV-infected child (assumptions) o 1 day paid work lost per primary care or hospital outpatient visit o number of days paid work lost equal to length of stay per hospitalisation or ICU admission
	Effects included	**<u>Type of Effects</u>** **Direct effects** ▪ RSV related Primary care visits ▪ Age specific proportion of respiratory tract infection (RTI) primary care visits	**<u>Measurement and valuation</u>** **Direct effects** ▪ RSV related Primary care visits for each hospitalisation by age less than 6 months or 6 months and older.

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<td>

RSV-coded Hospital outpatient visits
RSV-coded Hospitalisations (non ICU)
Proportion of ICU admission per RSV hospital admission
RSV-coded Deaths

Indirect effects

N/A
</td>
<td>

Age specific proportion of RTI primary care visits by month of age (0 to 5 months of age)
RSV-coded Hospital outpatient visits per 1,000 persons per year (by age in 1 month intervals and by calendar month)
RSV-coded Hospitalisations (by age in 1 month intervals and by calendar month)
Proportion of ICU admission per RSV hospital admission by age group
RSV-coded Deaths per 1,000 persons per year (by age in 1 month intervals and by calendar month)

QALY loss

Medically attended (MA) episode (including hospital): 0.0038 (0.0005 to 0.0128)
Non-MA episode: 0.0030 (0.0003 to 0.010)

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<tr>
<td>Economic results</td>
<td>Type of summary ratio</td>
<td colspan="2">Incremental cost per QALY gained</td>
</tr>
<tr>
<td></td>
<td>Overall payer perspective result</td>
<td colspan="2">ICER per QALY gained for mAb programme compared with no intervention:
<table>
<tr><td>Model</td><td>Year-round</td><td>Seasonal</td><td>Seasonal plus catch-up</td></tr>
<tr><td>University Antwerp (static)</td><td>€71,522</td><td>Dominant</td><td>€14,460</td></tr>
<tr><td>Novavax (static)</td><td>€69,419</td><td>Dominant</td><td>N/A</td></tr>
<tr><td>Sanofi (static)</td><td>€61,626</td><td>Dominant</td><td>€14,240</td></tr>
<tr><td>Sanofi (dynamic)</td><td>€101,282</td><td>€10,867</td><td>€38,168</td></tr>
<tr><td>LSHTM (dynamic)</td><td>€54,272</td><td>€36,376</td><td>€33,548</td></tr>
</table>
</td>
</tr>
</table>

ICER per QALY gained for MV programme compared with no intervention:

Model	Year-round	Seasonal
University Antwerp (static)	€402,349	€198,717
Novavax (static)	€463,979	€182,852
Sanofi (static)	€366,437	€142,378
Sanofi (dynamic)	€1,973,816	€1,733,256
LSHTM (dynamic)	€178,322	€131,423

Overall societal perspective result

ICER per QALY gained for mAb programme compared with no intervention:

Model	Year-round	Seasonal	Seasonal plus catch-up
University Antwerp (static)	€11,658	Dominant	Dominant
Novavax (static)	Dominant	Dominant	Dominant
Sanofi (static)	€1635	Dominant	Dominant
Sanofi (dynamic)	€34,327	Dominant	Dominant
LSHTM (dynamic)	€35,205	€15,342	€16,705

ICER per QALY gained for MV programme compared with no intervention:

Model	Year-round	Seasonal
University Antwerp (static)	€332,952	€129,280
Novavax (static)	€375,702	€94,579

		Sanofi (static)	€34,327	€73,568
		Sanofi (dynamic)	€1,901,299	€1,651,046
		LSHTM (dynamic)	€162,266	€115,186
Epidemiological results		Outcomes: (provided within season and year round, by age group) ▪ RSV primary care visits ▪ Hospital outpatient visits ▪ Non-ICU hospitalisations ▪ ICU admissions ▪ Deaths ▪ RSV infections and proportion resulting in MA cases in children <5 years ▪ Non-MA symptomatic infections ▪ Asymptomatic infections		
Authors conclusions	This model comparison study concluded that both static and dynamic models could produce similar output for EHL-mAb because the community impact on RSV transmission by reducing infants' infectivity through EHL-mAb likely remains limited. There are important differences between the 2 modelling approaches, as well as within dynamic models, especially regarding non-MA symptomatic RSV burden and waning of EHL-mAb and MV protection. The impact of uncertainty around these 2 aspects should be explored when evaluating RSV interventions. The dynamic models showed herd immunity in children <6 months, especially for MV, and a potential age shift. This needs to be considered and weighted in the choice of static versus dynamic models, depending on the intervention under study.			

Key: CEA – cost effectiveness analysis; CI – confidence interval; EHL-mAb – extended half-life monoclonal antibody; ICER- incremental cost-effectiveness ratio; ICU – intensive care unit; LSHTM - London School of Hygiene and Tropical Medicine; MA – medically attended; MV – maternal vaccine; NV – Novovax; QALY- quality-adjusted life year; RSV - respiratory syncytial virus; RTI – respiratory tract infection; SEIRS - susceptible exposed infected recovered susceptible; SIRS - susceptible infected recovered susceptible; SPD - Sanofi Pasteur dynamic; SPS - Sanofi Pasteur static; UA – University of Antwerp.

General study characteristics	**Author name** **Year of publication** **DOI**	Nourbaksh S et al. 2021 https://doi.org/10.1016/j.eclinm.2021.101141
	Region or country	Canada
	Type of economic evaluation	Cost utility analysis
	Population	Infants and pregnant women (only infants extracted)
	Funding	National funding (Canadian Institute of Health Research and the Public Health Agency of Canada)
Model characteristics	**Model type**	Discrete event agent-based simulation model that consisted of age distribution, infant health status, and household composition and size. The infant population was categorised in three age groups: 0 to 2 months, 3 to 5 months, and 6 to 11 months of age. The model also included older age groups: 12 to 23 months, 24 to 35 months, 36 to 47 months, and 5 to 18 years of age.
	Perspective	Healthcare system perspective
	Time horizon	1 Year (including RSV season)
	Comparator	3 baseline comparators: S1: No intervention S2: Palivizumab given to preterm infants (aged 0 to 5 months) and chronically ill infants under 1 years of age as 5 dose during the RSV season (January to June) S3: Extended half-life monoclonal antibody (EHL-mAb) given to preterm infants (aged 0 to 5 months) and chronically ill infants under 1 years of age as 5 dose during the RSV season (January to June)
	Discount rates	None applied
	Sensitivity analysis	No formal sensitivity analysis. To account for uncertainty in key model parameters in the scenarios run, a range of parameter values were sampled.
Intervention	**Strategies**	Strategy 1: No intervention (comparator) Strategy 2: Palivizumab for preterm infants aged 0 to 5 months and chronically ill infants aged <1 year (comparator)

<table>
<tr><td></td><td></td><td>Strategy 3: (nirsevimab) EHL-mAb for preterm infants aged 0 to 5 months and chronically ill infants aged <1 year (comparator)
Strategy 4: Maternal vaccine (not extracted)
Strategy 5: Maternal vaccine (not extracted)
Strategy 6: S2 + healthy full term infants included aged 0 to 2 months
Strategy 7: S3 + healthy full term infants included aged 0 to 2 months</td></tr>
<tr><td rowspan="3"></td><td>Dosing schedule</td><td>Palivizumab strategies: monthly administration of one dose for a total of 5 doses during a season
Nirsevimab strategies: a single dose given during the RSV season
Maternal vaccine strategy: not extracted (see above)</td></tr>
<tr><td>Type of immunisation</td><td>Monoclonal antibody (mAb) - palivizumab
Extended half-life monoclonal antibody (EHL-mAb) - nirsevimab
Maternal vaccine (MV) (based off discontinued ResVax (Novavax) so not extracted)</td></tr>
<tr><td>Age at immunisation</td><td>Palivizumab: preterm infants 0-5 months old, chronically ill infants <1 year-old, healthy full term infants 0-2 months old.
Nirsevimab: preterm infants 0-5 months old, chronically ill infants <1 year-old, healthy full term infants 0-2 months old.</td></tr>
<tr><td></td><td>Coverage rate</td><td>Not reported</td></tr>
<tr><td>Model input parameters</td><td>Efficacy/effectiveness (Table 1)</td><td>Average efficacy of the interventions
<table>
<tr><td></td><td colspan="2">Efficacy % (95% CI)</td></tr>
<tr><td></td><td>Palivizumab</td><td>Nirsevimab</td></tr>
<tr><td colspan="3">Outpatient visits</td></tr>
<tr><td>Preterm/chronically ill 0-2 months</td><td>48% (14 to 80)</td><td>47% (20 to 80)</td></tr>
<tr><td>Preterm/chronically ill 3-5 months</td><td>48% (14 to 80)</td><td>47% (20 to 80)</td></tr>
<tr><td>Preterm/chronically ill 6-11 months</td><td>48% (14 to 80)</td><td>47% (20 to 80)</td></tr>
<tr><td>Healthy 0-2 months</td><td>48% (14 to 80)</td><td>47% (20 to 80)</td></tr>
<tr><td colspan="3">Paediatric ward</td></tr>
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</table>

<table>
<tr><td></td><td></td><td colspan="3"><table>
<tr><td>Preterm/chronically ill 0-2 months</td><td>20 to 90%</td><td>20 to 90%</td></tr>
<tr><td>Preterm/chronically ill 3-5 months</td><td>20 to 90%</td><td>20 to 90%</td></tr>
<tr><td>Preterm/chronically ill 6-11 months</td><td>20 to 67%</td><td>20 to 67%</td></tr>
<tr><td>Healthy 0-2 months</td><td>23.5%</td><td>23.5%</td></tr>
<tr><td colspan="3">ICU</td></tr>
<tr><td>Preterm/chronically ill 0-2 months</td><td>63.9%</td><td>63.9%</td></tr>
<tr><td>Preterm/chronically ill 3-5 months</td><td>63.9%</td><td>63.9%</td></tr>
<tr><td>Preterm/chronically ill 6-11 months</td><td>63.9%</td><td>63.9%</td></tr>
<tr><td>Healthy 0-2 months</td><td>43.9%</td><td>43.9%</td></tr>
</table></td></tr>
<tr><td></td><td>Waning</td><td colspan="3">Duration of protection
Palivizumab
Preterm/chronically ill infants 30 days
Healthy infants 30 days
Nirsevimab
Preterm/chronically ill infants 150 days
Healthy infants 150 days</td></tr>
<tr><td></td><td>Costs included</td><td><u>Type of cost</u>
Direct costs
Medical cost
RSV case – outpatient visit
RSV case – paediatric ward
RSV case – ICU
Intervention costs
Immunisation cost per dose
Administration fee
Wastage</td><td><u>Measurement and valuation</u>
Direct costs
Medical cost
Average cost of RSV cases included physician consultation, treatment, paediatric ward and or ICU admission, transportation (including parental accommodation)
average cost of RSV case – outpatient visit (CAD$)
average cost of RSV case – paediatric ward (CAD$)
average cost of RSV case – ICU</td></tr>
</table>

		Indirect costs N/A	(CAD$) Intervention costs ▪ Age specific immunisation cost per dose based on weight (CAD$) ○ 0-2 months:1065 ○ 3-5 months: 1567 ○ 6-11 months: 2048 ▪ Assumed same cost for EHL-mAb ▪ Cost per dose includes administration fee of CAD$50 and 5% wastage rate
	Effects included	**<u>Type of Effects</u>** **Direct effects** ▪ Length of stay - pediatric ward ▪ Length of stay – ICU ▪ Proportion of ICU out of regional admissions (without palivizumab) ▪ Proportion of ICU out of tertiary transfers (with palivizumab)	**<u>Measurement and valuation</u>** **Direct effects** ▪ Length of stay per RSV patient (in days) grouped by age 0 to 2 months, 3 to 5 months and 6 to 11 months old. ▪ Proportion of ICU admissions (%) grouped by health status: preterm/chronically ill and healthy groups QALY Disutility weights (assumed to be the same for healthy and preterm/chronically ill infants): ▪ Without previous infection or outpatient visit: 0.05 ▪ With previous infection: 0.12 ▪ Outpatient visit: 0.16 ▪ Paediatric ward: 0.41 ▪ ICU: 0.60
Economic results	**Type of summary ratio**	Incremental cost per QALY gained	
	Overall payer perspective result	Mild RSV Season ▪ S2 (Palivizumab high risk) compared with S1 (no intervention) (95% CI) ○ QALYs gained 0.0840 (0.0780 to 0.0898) ○ ICER (95% CI) 1,011,139 (1,007,586 to 1,026,033) $/QALY gained	

		▪ S3 (nirsevimab high risk) compared with S1 (no intervention) o QALYs gained 0.0814 (0.0757 to 0.0867) o ICER (95% CI) -883,539 (-885,162 to -881,099) $/QALY gained ▪ S6 (palivizumab including healthy) compared with S2 (palivizumab high risk) o QALY gained 0.8905 (0.8318 to 0.9451) o ICER (95% CI) 441,023 (440,315 to 444,423) $/QALY gained ▪ S7 (nirsevimab including healthy) compared with S3 (nirsevimab high risk) o QALY gained 0.8906 (0.8324 to 0.9452) o ICER (95% CI) 39,414 (39314 to 40017) $/QALY gained Moderate RSV season ▪ S2 (Palivizumab high risk) compared with S1 (no intervention) (95% CI) o QALYs gained 0.1660 (0.1581 to 0.1736) o ICER (95% CI) 13,926 (12,669 to 15,755) $/QALY gained ▪ S3 (nirsevimab high risk) compared with S1 (no intervention) o QALYs gained 0.1661 (0.1580 to 0.1734) o ICER (95% CI) -931,845 (-932,832 to -930,793) $/QALY gained ▪ S6 (palivizumab including healthy) compared with S2 (palivizumab high risk) o QALY gained 1.7660 (1.6903 to 1.8387) o ICER (95% CI) 208,015 (207848 to 208376) $/QALY gained ▪ S7 (nirsevimab including healthy) compared with S3 (nirsevimab high risk) o QALY gained 1.7677 (1.6931 to 1.8416) o ICER (95% CI) 5,255 (5222 to 5307) $/QALY gained Severe RSV season ▪ S2 (Palivizumab high risk) compared with S1 (no intervention) (95% CI) o QALYs gained 0.2484 (0.2382 to 0.2582) o ICER (95% CI) -290,034 (-292097 to -288699) $/QALY gained ▪ S3 (nirsevimab high risk) compared with S1 (no intervention) o QALYs gained 0.2511 (0.2402 to 0.2610) o ICER (95% CI) -905256 (-906069 to -904322) $/QALY gained ▪ S6 (palivizumab including healthy) compared with S2 (palivizumab high risk) o QALY gained 2.6181 (2.5276 to 2.7058) o ICER (95% CI) 129726 (129379 to 129840) $/QALY gained ▪ S7 (nirsevimab including healthy) compared with S3 (nirsevimab high risk) o QALY gained 2.6195 (2.5281 to 2.7078) o ICER (95% CI) -7049 (-7072 to -7007) $/QALY gained
	Overall societal perspective result	**<u>N/A</u>**

Epidemiological results		Outcomes ▪ RSV incidence ▪ RSV-associated hospital admissions Outcomes were reported by patient groups and by mild season, moderate season and severe season.
Authors conclusions	The study concluded that EHL-mAb would substantially reduce costs of programme delivery compared with palivizumab. Utilising a single dose mAb reduces logistical challenges and would likely increase uptake. Switching from palivizumab to nirsevimab in RSV immunisation programmes would be cost effective or even cost saving depending on severity of the RSV season without increasing RSV associated hospitalisations.	

Key: CAD – Canadian Dollar; CI – confidence interval; EHL-mAb – extended half-life monoclonal antibody; ICER- incremental cost-effectiveness ratio; ICU – intensive care unit; N/A – not applicable; QALY- quality-adjusted life year; RSV - respiratory syncytial virus.
Note: Mild season defined as 30-50% of households infected with RSV having at least one infant under 1 year of age. Moderate season defined as 50-70% of households infected with RSV having at least one infant under 1 year of age. Severe season defined as 70-90% of households infected with RSV having at least one infant under 1 year of age

General study characteristics	**Author name** **Year of publication** **DOI**	Shoukat A et al 2023 https://doi.org/10.1016/j.lana.2023.100629
	Region or country	Canada
	Type of economic evaluation	Cost-utility analysis
	Population	Infants and pregnant women
	Funding	Supported by the Canadian Immunisation Research Network (CIRN) and the Canadian Institutes of Health Research (CIHR).
Model characteristics	**Model type**	Discrete event simulation model with 12 monthly birth cohorts followed through the first year of their life. Categorised as ▪ preterm (<29 weeks gestational age (wGA) 29 to 32 wGA, or 33 to 36 wGA) ▪ term (≥37 wGA) infants. Additional major risk factors for RSV disease outcomes in the model included:

		▪ congenital heart disease (CHD) ▪ chronic lung disease (CLD)
	Perspective	Healthcare and societal
	Time horizon	1 year from birth
	Comparator	No intervention
	Discount rates	1.5% for costs and QALY loss
	Sensitivity analysis	Probabilistic Secondary scenario analyses were run with varying coverage and efficacy profiles.
Intervention	**Strategies**	Six strategies L1 – nirsevimab for preterm infants ≤32 wGA and infants with CLD or CHD L2 – nirsevimab for preterm infants ≤36 wGA and infants with CLD or CHD L3 – nirsevimab for preterm infants ≤36 wGA, infants with CLD or CHD, and term infants born during the RSV season L4 – nirsevimab for the birth cohort MI – maternal immunisation as a year round programme, LMI – combined programme including year round maternal immunisation of pregnant women followed by administration of nirsevimab to infants at high risk of severe RSV disease (i.e. preterm infants ≤32 wGA and infants with CLD or CHD) during the RSV season
	Dosing schedule	Single dose
	Type of immunisation type	Extended half-life acting monoclonal antibody (EHL-mAb)– Nirsevimab Maternal vaccine (MV) – RSVpreF vaccine
	Age at immunisation	Infants -at birth or at start of RSV season Pregnant women - in last trimester before 33 wGA
	Coverage rate	EHL-mAb (Nirsevimab) ▪ Base case - 100%

		MV (RSVpreF) ▪ Base case - 100%	
Model input parameters	**Efficacy/effectiveness**	Approach to efficacy in base case: sigmoidal decay to disaggregate the constant efficacy values for up to 10 months, maintaining the same mean efficacy for the first 5 months (for nirsevimab) and 3 months (for RSVpreF) (note, initial efficacy rates are higher and rates after the 5 and 3 month periods are lower, declining to 0% by month 10) Mean nirsevimab efficacy rates over 150 day period after administration (95% CI) ▪ MA RSV LRTI: 79.5% (65.9 to 87.7%) ▪ Hospitalisation: 77.3% (50.3 to 89.7%) ▪ Very severe RSV LRTI (used against ICU admission): 86% (62.5 to 94.8%) Mean RSVpreF efficacy rates over 90 days after birth (95% CI) ▪ MA RSV LRTI: 57.1% (14.7 to 79.8%) ▪ Hospitalisation: 67.9% (34.6 to 84.2%) ▪ Severe MA RSV LRTI (used against ICU admission): 81.8% (40.6 to 96.3%)	
	Waning	Decline in vaccine efficacy was estimated over a 10 month period using a sigmoidal decay function. The mean efficacy rates above were maintained for the first 150 after administration and 90 days after birth, for nirsevimab and RSVpreF, respectively. Efficacy was assumed 0% by 10 months.	
	Costs included	**Type of cost** **Direct costs** Medical costs ▪ Office visit ▪ ED visit ▪ Paediatric ward (Hospitalisation) ▪ 30 days of follow up for hospitalised infants ▪ ICU ▪ Wheezing Intervention costs ▪ Price per dose ▪ Administration cost	**Measurement and valuation** **Direct costs** Medical costs ▪ Cost per office visit (CAD$) ▪ Cost per ED visit (CAD$) ▪ Cost per paediatric ward day (hospitalisation) (CAD$) ▪ Cost of follow up at 30 days per hospitalised infant (CAD$) ○ Categorised by age at hospitalisation ▪ Cost per ICU day (CAD$) ▪ Cost of wheezing per visit (CAD$)

		Patient-borne costs ▪ Out-of-pocket expenses **Indirect costs** ▪ Productivity loss (parents) ▪ Loss of life due to RSV- related infant mortality	Intervention costs ▪ Price per dose (CAD$)- varied between CAD $50 and CAD $1000 ▪ Administration cost per dose (CAD$)- CAD $15 Patient-borne costs ▪ Out-of-pocket expenses (indirect costs not borne by the health system and included in societal perspective only) **Indirect costs** ▪ Cost of out-of-pocket expenses per day of hospital stay (including transportation, over-the-counter medications, meals, child care and other costs) (CAD$) ▪ Cost of workdays lost per day for working parents (assumed total workdays lost were equal to the length of stay for hospitalised infants and one day for infants who required outpatient care) (CAD$) ▪ Cost of loss of life per death (using the annual personal income and discounted QALY loss) (CAD$)
	Effects included	**<u>Type of Effects</u>** **Direct effects** ▪ MA (office or ED visit) RSV LRTI ▪ Hospitalisation ▪ ICU admission ▪ Wheezing ▪ RSV-related mortality **Indirect effects** N/A	**<u>Measurement and valuation</u>** **Direct effects** ▪ Annual incidence of MA-RSV cases per 100,000 population ▪ Rates of MA-RSV LRTI by age group (<29 days, 29 to 89 days, 90 days to < 6months, 6 months to <1year) ▪ ICU admission rates among hospitalised cases by wGA ▪ Maximum number of MA RSV events per infant during first year of life ▪ Minimum time-interval between the events

			if two occurred ▪ Hospitalisation rates for infants with MA RSV LRTI based on age at incidence and wGA ▪ Probability of experiencing wheezing episode post hospitalisation during the first year of life ▪ RSV-related mortality for hospitalised infants by wGA group with and without CHD or CLD QALY loss ▪ Duration of symptomatic RSV disease among outpatient cases : 5 to 8 days ▪ Length of stay in paediatric ward ○ ≤32 wGA 6.1 ○ ≥33 wGA 3.9 ▪ Length of stay in ICU ○ ≤32 wGA 9.5 ○ ≥33 wGA 5.2 ▪ Duration of a wheezing episode : 5.2 to 9 days Disutilities ▪ Without RSV - 0.05 ▪ Outpatient - 0.16 ▪ Paediatric ward - 0.41 ▪ ICU - 0.60 ▪ Wheezing - 0.04
Economic results	**Type of summary ratio**	Incremental cost per QALY gained	
	Overall payer perspective result	**Base-case** ICER $/QALY gained (95% CI)	

Strategy	Max price per dose	ICER $/QALY gained (95% CI)
L1	610	49,577 (-14,712 to 125,242)
L2	370	45,924 (-2,959 to 103,322)
L3	295	34,331 (-1,682 to 72,362)
L4	215	4,200 (-34,697 to 43,384)
MI	185	41,321 (6,800 to 78,174)
LMI	Nirsevimab: 615 RSVpreF: 140	3,853 (-30,616 to 38,887)
LMI	Nirsevimab: 215 RSVpreF: 155	18,913 (-16,004 to 54,135)

Overall societal perspective result

Base-case

Strategy	Max price per dose	ICER $/QALY gained (95% CI)
L1	700	47,467 (-18,071 to 128,490)
L2	450	49,618 (-3,025 to 110,691)
L3	380	28,634 (-13,811 to 73,395)
L4	285	46,749 (597 to 95,262)

<table>
<tr><td></td><td></td><td>
<table>
<tr><td>MI</td><td>235</td><td>25,815 (-13,217 to 66,816)</td></tr>
<tr><td>LMI</td><td>Nirsevimab: 705

RSVpreF: 180</td><td>5,797 (-33,894 to 46,014)</td></tr>
<tr><td>LMI</td><td>Nirsevimab: 290

RSVpreF: 195</td><td>15,511 (-23,306 to 56,333)</td></tr>
</table>
</td></tr>
<tr><td>Epidemiological results</td><td></td><td>▪ Reductions in RSV related outpatient care
▪ Reductions in RSV related inpatient care
▪ Reductions in RSV related infant mortality</td></tr>
<tr><td>Authors conclusions</td><td colspan="2">This simulation study shows that prevention strategies against RSV disease in infants using nirsevimab and RSVpreF could be cost effective. Passive immunisation of all infants experiencing their first RSV season would require a PPD under $290 to become costeffective without considering the monetary loss of life due to RSV-related infant mortality. However, this programme would incur a higher budget impact to the healthcare system than a cost-effective strategy that combines year-round maternal vaccination with seasonal administration of nirsevimab to infants who are currently eligible for palivizumab.</td></tr>
</table>

Key: CAD – Canadian Dollar; CHD – congenital heart disease; CLD – chronic lung disease; CI – confidence interval; ED – emergency department; EHL-mAb – extended half-life monoclonal antibody; ICER- incremental cost-effectiveness ratio; ICU – intensive care unit; LRTI – lower respiratory tract infections; MA – medically attended; MV maternal vaccine; N/A – not applicable; PPD – price per dose; QALY- quality-adjusted life year; RSV - respiratory syncytial virus; RSVpreF – respiratory syncytial virus prefusion F vaccine; wGA – weeks gestational age.

A5.3 Older adult data extraction tables

General study characteristics	**Author name** **Year of publication** **DOI**	Hutton DW et al. 2024 https://doi.org/10.1016/j.vaccine.2024.126294
	Region or country	USA
	Type of economic evaluation	Cost-utility analysis
	Population	Adults aged 60 years and older
	Funding	US Centers for Disease Control and Prevention
Model characteristics	**Model type**	Decision-analytic simulation model of RSV infection and disease burden: ▪ monthly health outcomes ▪ health states included vaccination related adverse events (systemic reactions, injection-site reactions, serious adverse events) and illness related events (outpatient, emergency department, and hospital admission). For hospitalised adults, RSV-attributable deaths were simulated.
	Perspective	Societal perspective
	Time horizon	2 years for all health outcomes except RSV-related death (lifetime)
	Comparator	No vaccination
	Discount rates	3% (health outcomes and costs)
	Sensitivity analysis	One way deterministic sensitivity analyses Probabilistic sensitivity analyses Scenario analyses
Intervention	**Strategies**	Vaccination with either GSK RSV vaccine (RSVPreF3) or Pfizer RSV vaccine (RSVpreF) of adults by age groups

		▪ Base case: ≥ 65 years ▪ Secondary analyses: ≥60 years, 60 to <65 years, 65 to < 70 years, 70 to <75 years, ≥ 75 years
	Dosing schedule	One dose Assumed uptake started in September and plateaued by January
	Type of immunisation	GSK RSV vaccine (RSVPreF3) and Pfizer RSV vaccine (RSVpreF)
	Age at immunisation	≥ 65 years (base case) (see strategies)
	Coverage rate	20% (monthly uptake followed the timing observed for influenza vaccination from 2019 to 2021. Low uptake was to account for limited uptake of newly-recommended vaccines)
Model input parameters	**Efficacy/effectiveness**	Modelled vaccine efficacy estimates informed by RCT data. i Modelled efficacy estimates % (range for sensitivity analysis) RSVPreF3, 0 to 7 months ▪ MA RSV LRTD (ED and hospitalisation): 87.5% (58.9 to 97.6%) ▪ MA RSV ARI (outpatient): 79.0% (54.3 to 91.5%) RSVpreF, 0 to 7 months ▪ MA RSV LRTD (ED and hospitalisation): 84.6% (32.0 to 98.3%) ▪ MA RSV ARI (outpatient): 65.2% (36.0 to 82.0%) Definition differed between RSVpreF3 and RSVpreF vaccines. RSVPreF3: ▪ LRTD defined as two or more lower respiratory symptoms (new or increased sputum, cough, and dyspnoea) or signs (new or increased wheezing, crackles or rhonchi detected during chest auscultation, respiratory rate ≥20 respirations per minute, low or decreased oxygen saturation (<95% or ≤90% if baseline was <95%), and need for oxygen supplementation) for ≥24 hours, including one or more lower respiratory signs, or three or more lower respiratory symptoms for ≥24 hours. ▪ Medically attended RSV-associated LRTD defined as LRTD plus attention at one or more inpatient or outpatient healthcare services. RSVpreF: ▪ RSV LRTD with three or more lower respiratory signs or symptoms lasting >1 day. Lower respiratory signs and symptoms included new or worsened cough, sputum production, wheezing, shortness of breath, and tachypnea.

		▪ Medically attended RSV-associated LRTD was defined as LRTD prompting any healthcare visit (any outpatient or inpatient visit such as hospitalisation, emergency department visit, urgent care visit, home healthcare services, primary care physician office visit, pulmonologist office visit, specialist office visit, other visit, or telehealth contact)	
	Waning	Waning efficacy estimates informed by RCT data. % (Range for sensitivity analysis) GSK RSVPreF3, 8 to 18 months (after 18 months efficacy is assumed to decay linearly to 0% by 24 months) ▪ MA RSV LRTD (ED and hospitalisation): 52.9% (0.0 to 81.2%) ▪ MA RSV ARI (outpatient): 27.8% (0.0 to 60.4%) RSVpreF, 8 to 14 months (after 14 months, efficacy is assumed to decay linearly to 0% by 24 months) ▪ MA RSV LRTD (ED and hospitalisation): 75.0% (0.0 to 97.4%) ▪ MA RSV ARI (outpatient): 55.0% (0.0 to 82.0%)	
	Costs included	**<u>Type of cost</u>** **Direct costs** Medical costs ▪ Hospitalisation ▪ Emergency department visits ▪ Outpatient visit ▪ Nursing home care for subset of hospitalised patients Intervention costs ▪ Vaccine per dose: $280 for GSK RSVPreF3 and $295 for Pfizer RSVpreF (sourced from the manufacturers announced wholesale acquisition costs) ▪ Administration per dose: $16.96 (sourced from the Medicare & Medicaid Services Physician Fee Schedule) ▪ Serious adverse event **Indirect costs**	**<u>Measurement and valuation</u>** **Direct costs** Medical costs ▪ Cost per hospitalisation by age group (60-64 years, 70-74 years, ≥74 years) ▪ Cost per emergency department visit by age group (60-64 years, 70-74 years, ≥74 years) ▪ Cost per outpatient visit (60-64 years, 70-74 years, ≥74 years) Intervention costs ▪ Cost per dose (Pfizer/GSK) ▪ Cost per administration ▪ Cost per serious adverse event **Indirect costs** Patient productivity loss ▪ Daily productivity by age group (60-64 years, 70-74 years, ≥74 years) ▪ Days of lost productivity due to RSV

		Patient productivity loss due to: ▪ RSV-related morbidity ▪ RSV-related premature mortality ▪ Vaccine-related adverse events ▪ Patient time	disease by outpatient and ED (based on influenza) ▪ Days of lost productivity due to RSV disease hospitalisation (length of hospitalisation + 2 days) ▪ Days of lost productivity due to RSV disease death (based on age-based annual mortality and life expectancy from life tables all discounted at 3% per year) ▪ Days of productivity lost from serious adverse event ▪ Patient time (vaccination related visit physician/pharmacy)
	Effects included	**<u>Type of Effects</u>** **Direct effects** ▪ Outpatient case ▪ Emergency department visit ▪ Hospital admission / ICU stay ▪ Death ▪ Vaccine-related adverse events o systemic reaction o injection-site reaction o outpatient visit for systemic reaction / injection-site reaction o hypothetical serious adverse event **Indirect effects** N/A	**<u>Measurement and valuation</u>** **Direct effects** ▪ Incidence of medically attended outpatient case, hospital admission, of emergency department visit and RSV related mortality per 100,000 population by age group ▪ Probability of ICU stay ▪ Length of hospitalisation and ICU stay (days) ▪ Probabilities of adverse events by vaccine type and reaction type QALY ▪ QALY loss per case due to o outpatient RSV-0.0185 o hospitalised RSV-0.0193 ▪ QALY loss per case due to adverse events o systemic reactions by age group (50 to 64 years and ≥65 years) o injection-site reaction o serious adverse event

			Baseline utility values reported by age group ○ 60 to <65 years- 0.82 (95% CI:0.62-1.0) ○ 65 to <75 years- 0.8 (95% CI: 0.59-1.0) ○ ≥75 years-0.75 (95% CI: 0.56-1)
Economic results	**Type of summary ratio**	Incremental cost per QALY gained	
	Overall payer perspective result	N/A	
	Overall societal perspective result	ICER per QALY gained by age group and vaccine ≥60 years: ▪ GSK RSVPreF3 vaccine - $196,842 per QALY gained ▪ Pfizer RSVpreF vaccine - $176,557 per QALY gained ≥65 years: ▪ GSK RSVPreF3 vaccine - $162,138 per QALY gained ▪ Pfizer RSVpreF vaccine - $146,543 per QALY gained ≥70 years: ▪ GSK RSVPreF3 vaccine - $134,742 per QALY gained ▪ Pfizer RSVpreF vaccine - $122,296 per QALY gained ≥75 years: ▪ GSK RSVPreF3 vaccine - $101,567 per QALY gained ▪ Pfizer RSVpreF vaccine - $92,664 per QALY gained ≥80 years: ▪ GSK RSVPreF3 vaccine - $110,830 per QALY gained ▪ Pfizer RSVpreF vaccine - $100,726 per QALY gained ICER per QALY by 5-year age subgroups for each vaccine	

		60 to <65 years: ▪ GSK RSVPreF3 vaccine - $385,829 per QALY gained ▪ Pfizer RSVpreF vaccine - $331,486 per QALY gained 65 to <70 years: ▪ GSK RSVPreF3 vaccine - $253,967 per QALY gained ▪ Pfizer RSVpreF vaccine - $225,521 per QALY gained 70 to <75 years: ▪ GSK RSVPreF3 vaccine - $233,472 per QALY gained ▪ Pfizer RSVpreF vaccine - $207,453 per QALY gained 75 to <80 years: ▪ GSK RSVPreF3 vaccine - $92,438 per QALY gained ▪ Pfizer RSVpreF vaccine - $84,652 per QALY gained ≥80 years: ▪ GSK RSVPreF3 vaccine - $110,830 per QALY gained ▪ Pfizer RSVpreF vaccine - $100,726 per QALY gained Sensitivity analyses: there was high correlation between vaccine costs and ICERs. To achieve an ICER of <$100,000 per QALY gained: ▪ Required GSK vaccine cost per dose for adults ≥65 years: <$195 ▪ Required GSK vaccine cost per dose for adults ≥60 years: <$165 ▪ Required Pfizer vaccine cost per dose for adults ≥65 years: <$222 ▪ Required Pfizer vaccine cost per dose for adults ≥60 years: <$190
Epidemiological results		RSV outcomes reported by strategy, vaccine , and targeted age group Number and % of cases averted, and NNV)reported ▪ NNV to avert one hospitalisation ranged between 364 and 395 for all adults ≥65 years old. ▪ NNV decreased with increasing age – the NNV to avert one hospitalisation was 244 for adults ≥75 years old
Authors conclusions	Reducing RSV disease burden by vaccinating adults aged ≥65 years with a single dose of a licensed RSV vaccine may be considered cost-effective, particularly for the oldest age groups.	

	It was noted that lower vaccine acquisition costs and efficacy that persists beyond two RSV seasons would make vaccination more cost effective. Additional work is needed to evaluate cost effectiveness of RSV vaccination, including long-term safety surveillance, and evaluation in different risk strata, which may include adults younger than 60 years.

Key: ARI- acute respiratory infection; CI – confidence interval; ED – emergency department; ICER- incremental cost-effectiveness ratio; ICU- intensive care unit; GSK - GlaxoSmithKline plc; MA – medically attended; LRTD – lower respiratory tract disease; N/A – not applicable; NNV - number needed to vaccinate; QALY- quality-adjusted life year; RCT – randomized controlled trial; RSV - respiratory syncytial virus.

General study characteristics	**Author name** **Year of publication** **DOI**	Moghadas SM 2023 https://doi.org/10.1093/cid/ciad658
	Region or country	USA
	Type of economic evaluation	Cost-effectiveness analysis (including cost-utility analysis)
	Population	Adults 60 years and older
	Funding	Academia
Model characteristics	**Model type**	Discrete event simulation model (with decision tree) ▪ population of 100,000 adults stratified into age groups: 60 to 64, 65 to 69, 70 to 74, 75 to 79, 80 to 84, and ≥ 85 years ▪ Individuals characterised by presence of 0, 1–3, and ≥4 comorbidities chronic medical conditions Health states included: Symptomatic RSV infection, outpatient care (office visits, emergency department visits), inpatient care (hospitalisation, ICU admission), mechanical ventilation, death.
	Perspective	Societal
	Time horizon	Primary analysis: One RSV season post vaccination Secondary analysis: Two RSV seasons
	Comparator	No vaccination
	Discount rates	3% (for costs and outcomes)
	Sensitivity analysis	Sensitivity analysis not undertaken

Intervention	**Strategies**	Strategy 1 (S1) Vaccination of older adults aged 60 years and older with 66% vaccine coverage Strategy 2 (S2) Vaccination of older adults aged 60 years and older with 100% vaccine coverage
	Dosing schedule	Single dose beginning in September and achieving target coverage within 2 months
	Type of immunisation	GSK RSV vaccine (RSVPreF3) and Pfizer RSV vaccine (RSVpreF) (RSVPreF3 only, RSVpreF only or a combination of RSVPreF3 and RSVpreF (50% probability of receiving one of these vaccines)
	Age at immunisation	60 years and older
	Coverage rate	S1: 66% coverage S2: 100% coverage (Target coverage assumed reached within 2 months)
Model input parameters	**Efficacy/effectiveness**	Modelled vaccine efficacy (VE) estimated informed by RCT data. Estimates reflect the initial VE at start of season 1. RSVPreF3 ▪ outpatient care - 82.6% (95% CI: 57.9%–94.1%) ▪ hospitalisation - 94.1% (95% CI: 62.4%–99.9%) RSVpreF ▪ outpatient care - 65.1% (95% CI: 35.9%–82.0%) ▪ hospitalisation - 88.9% (95% CI: 53.6%–98.7%) Definitions for RSVPreF3 and RSVpreF outcomes: RSVPreF3 ▪ outpatient care was based on VE for medically attended RSV-related LRTD ▪ hospitalisation was based on VE for severe RSV LRTD RSVpreF ▪ outpatient care was based on medically attended RSV LRTD ▪ hospitalisation was based on VE for severe RSV-related LRTD
	Waning	Season 2 efficacy estimates (two approaches to modelling) RSVPreF3

		▪ outpatient care – 67.2% (48.2-80.0) ▪ hospitalisation – 78.8% (52.6-92.0) RSVpreF ▪ outpatient care - 48.9% (13.7-70.5) ▪ hospitalisation - 78.6% (23.2-96.1) Approach 1) Sigmoidal decline in immunity over 24 months. Season 2 efficacy estimates reflect the mean efficacy over 18 month follow up periods (season 1 and season 2) after an initial efficacy described above. Efficacy declines to 0% by 24 months. Approach 2) Linear decline in immunity with fixed efficacy estimate during follow up periods (season 1: 0 to 8 months; season 2: 12 to 18 months). Immunity wanes linearly between seasons and linearly to 0% from 18 months to 24 months.	
	Costs included	**<u>Type of cost</u>** **Direct costs** Medical cost ▪ Outpatient (Office visits and ED visits) ▪ Hospitalisation ▪ ICU visit with/without MV Intervention ▪ Vaccine per dose: $50 - 500 (cost varied to determine the price range within which vaccination would be cost-effective) ▪ Administration per dose: $25 (based on administration costs of seasonal influenza vaccination) **Indirect costs** ▪ Market and non-market productivity loss due to RSV-related outcomes including death	**<u>Measurement and valuation</u>** **Direct costs** Medical costs ▪ Cost per office visit ▪ Cost per ED visit ▪ Cost per day of hospitalisation (general ward) ▪ Cost per ICU visit (with/without MV) ▪ Length of hospitalisation in general ward/ICU (days) ▪ Length of stay in general ward before ICU admission (days) ▪ Length of stay in general ward post-ICU (days) Intervention costs ▪ Cost per dose of RSV vaccines (varied between $50 and $500) ▪ Administration cost (average based on seasonal influenza)

			Indirect costs ▪ For working adults, both market and non-market productivity losses included ▪ For those out of the labor force, only non-market productivity loss included ▪ Annual market and non-market productivity ($) (by age) ▪ Duration of RSV-related disease (days) ▪ Productivity years lost due to death (by age) ▪ For productivity loss due to death, an annual productivity growth rate of 1% was applied
	Effects included	**<u>Type of Effects</u>** **Direct effects** ▪ Outpatient (Office visit and ED visit) ▪ ED visit ▪ Hospitalisation (general ward) ▪ ICU with/without MV ▪ Adverse events of vaccination **Indirect effects** N/A	**<u>Measurement and valuation</u>** **Direct effects** ▪ Duration of symptomatic disease in days (medically attended and non-medically attended cases) ▪ Median time interval in days between onset of symptoms and hospital admission ▪ Length of hospital admission in days (general ward/prior to ICU/ICU/post-ICU) ▪ Duration of adverse events in days QALY Baseline utility values reported by age-group o 60-64 years-0.77 o 65-69 years-0.76 o 70-74 years-0.74 o 75-79 years-0.70 o 80-84 years-0.63 o 85+ years-0.51

<table>
<tr><td></td><td></td><td></td><td>Utility scores
non-MA RSV cases during the symptomatic illness-0.88
outpatient care (office or ED visit)-0.76
hospitalized non-ICU patients-0.1
hospitalized ICU patients-0.88
Average QALY loss due to death reported by age group
60-64 years-9.47
65-69 years-7.79
70-74 years-5.93
75-79 years-4.49
80-84 years-2.97
85+ years-1.49</td></tr>
<tr><td rowspan="3">Economic results</td><td>Type of summary ratio</td><td colspan="2">Net monetary benefit, ICER (incremental cost per QALY gained)</td></tr>
<tr><td>Overall payer perspective result</td><td colspan="2">N/A</td></tr>
<tr><td>Overall societal perspective result</td><td colspan="2">Cost effectiveness estimates for vaccination programmes with RSVPreF3 only, RSVpreF only, and combination of RSVPreF3 and RSVpreF over one RSV season in a population of 100,000 adults aged 60 years and older at a WTP of $95,000 results:

<table>
<tr><th>Programme scenario</th><th>Maximum PPD, $</th><th>ICER</th></tr>
<tr><td colspan="3">S1 sigmoidal vaccine efficacy profile</td></tr>
<tr><td>RSVPreF3</td><td>127</td><td>93981</td></tr>
<tr><td>RSVpreF</td><td>118</td><td>94651</td></tr>
<tr><td>Combined</td><td>122</td><td>94234</td></tr>
<tr><td colspan="3">S1 linear vaccine efficacy profile</td></tr>
<tr><td>RSVPreF3</td><td>132</td><td>94035</td></tr>
<tr><td>RSVpreF</td><td>117</td><td>94664</td></tr>
<tr><td>Combined</td><td>126</td><td>94848</td></tr>
</table></td></tr>
</table>

		S2 sigmoidal vaccine efficacy profile RSVPreF3: 126 / 93968 RSVpreF: 115 / 94471 Combined: 112 / 95004 **S2 linear vaccine efficacy profile** RSVPreF3: 130 / 93978 RSVpreF: 116 / 93906 Combined: 123 / 94081 Note: in the combined programme of RSVPreF3 and RSVpreF, it was assumed that the PPD would be the same for both vaccines.
Epidemiological results		Number needed to vaccinate to avert one outcome reported Outcomes: Reductions in outpatient care, hospitalisation and deaths reported
Authors conclusions	Vaccination against RSV-associated LRTD could be cost-effective and reduce the burden of illness substantially among older adults. Additional evidence of vaccine effectiveness at the population level would be required to alleviate uncertainty on longer-term health benefits and cost-effectiveness of vaccination beyond a single RSV season.	

Key: CI- confidence interval; ED – emergency department; GSK - GlaxoSmithKline plc; ICER- incremental cost-effectiveness ratio; ICU- intensive care unit; MA – medically attended; LRTD – lower respiratory tract disease; MV – mechanical ventilation; N/A – not applicable; PPD - price per dose; QALY- quality-adjusted life year; RSV - respiratory syncytial virus; WTP – willingness to pay.

General study characteristics	**Author name** **Year of publication** **DOI**	Shoukat A et al. 2024 https://doi.org/10.1016/j.vaccine.2024.02.041
	Region or country	Canada
	Type of economic evaluation	Cost utility analysis
	Population	Adults aged 60 years and older
	Funding	Not reported (financial support for individual authors acknowledged)

Model characteristics	**Model type**	Discrete-event simulation model: • Decision tree structure • Population of 100,000 individuals stratified by age group (60 to 64, 65 to 69, 70 to 74, 75 to 79, 80 to 84, ≥85 years) and whether community dwelling or living in long-term care home (LTCH) • Health states included: Symptomatic RSV infection, outpatient care, inpatient care, mechanical ventilation, death.
	Perspective	Health system and societal
	Time horizon	2 RSV seasons (post vaccination)
	Comparator	No vaccination
	Discount rates	1.5% (both costs and outcomes)
	Sensitivity analysis	Deterministic sensitivity analyses
Intervention	**Strategies**	i. Strategy 1 (S1): vaccination for residents of LTCHs only ii. Strategy 2 (S2): vaccination for community-dwelling adults and residents of LTCHs
	Dosing schedule	Single dose with vaccination beginning in September (target coverage met within 4 weeks for S1 and within 8 weeks for S2)
	Type of immunisation	GSK RSV vaccine (RSVPreF3) and Pfizer RSV vaccine (RSVpreF)
	Age at immunisation	60 years and older
	Coverage rate	S1: 90% for residents of LTCHs (target coverage assumed reached within 4 weeks) S2: 90% for residents of LTCHs and 74% for community-dwelling adults (2022-23 seasonal influenza vaccination coverage used, target coverage assumed reached within 8 weeks)
Model input parameters	**Efficacy/effectiveness**	Modelled vaccine efficacy (VE) estimates informed by RCT data. Initial vaccine estimates for season 1: RSVPreF3 ▪ outpatient care – 82.6% ▪ hospitalisation – 94.1% RSVpreF ▪ outpatient care – 65.1% ▪ hospitalisation – 88.9%

		Definitions for RSVPreF3 and RSVpreF outcomes: RSVPreF3 ▪ outpatient care was based on VE for medically attended RSV-related LRTI ▪ hospitalisation was based on VE for severe RSV-related LRTD RSVpreF ▪ not explicitly stated as to whether VE estimates were based on outcome other than outpatient care ▪ hospitalisation was based on VE for severe RSV-related LRTD	
	Waning	Modelled VE waning estimates informed by RCT data. Temporal decay for VE included both sigmoidal and linear waning profiles. Season 2 efficacy estimates: RSVPreF3 ▪ outpatient care 56.1% ▪ hospitalisation 64.2% RSVpreF ▪ outpatient care 48.9% ▪ hospitalisation 78.6% Approach 1) Sigmoidal decline in immunity over 24 months. Season 2 efficacy estimates reflect the mean efficacy over 18 month follow up periods (season 1 and season 2) after an initial efficacy described above. Efficacy declines to 0% by 24 months. Approach 2) Linear decline in immunity with fixed efficacy estimate during follow up periods (season 1: 0 to 8 months; season 2: 12 to 18 months). Immunity wanes linearly between seasons and linearly to 0% from 18 months to 24 months.	
	Costs included	**<u>Type of cost</u>** **Direct costs**	**Measurement and valuation** **Direct costs**

		Medical ▪ Physician visit ▪ ED visit ▪ Hospital stay in general ward ▪ ICU admission with/without mechanical ventilation ▪ Hospital overhead Intervention ▪ Vaccine per dose: CAD $50 - 300 (cost varied to determine the price range within which a vaccination would be cost-effective) ▪ Administration per dose: CAD $15 (sourced and adjusted from a previously published paper on influenza vaccines) **Indirect costs** ▪ Loss of both market and non-market productivity for community-dwelling older adults o RSV related illness o RSV related mortality	Medical costs ▪ Outpatient cost per physician/ emergency department visit ▪ Cost per day of general hospital ward stay ▪ Cost per day of ICU stay (with/without mechanical ventilation) ▪ Hospital overhead per admission Intervention costs ▪ Vaccine price-per-dose (varied via a range) ▪ Administration cost per dose of vaccine (adjusted from 2017 Canadian estimates) **Indirect costs** ▪ Productivity losses estimated using Human Capital Approach with the following data: o annual market and non-market productivity ($) - assumed 1% growth in median annual income for market productivity per year o potential years of labour force participation for working adults (by age) o health productivity lost due to death (by age)
	Effects included	**<u>Type of Effects</u>** **Direct effects** ▪ Symptomatic disease ▪ Outpatient o Physician office visit o ED visit ▪ Inpatient o Hospitalisation in general ward o Hospitalisation in ICU with/without mechanical ventilation	**<u>Measurement and valuation</u>** **Direct effects** ▪ Duration of symptomatic disease per day for o non-medically attended RSV case o medically attended RSV outpatient case ▪ Time interval in days between symptom onset and hospital admission ▪ Length of stay in days in hospital

		○ In hospital RSV-related mortality **Indirect effects** N/A	(with/prior to/post ICU) ▪ Length of stay in days in ICU (with/without mechanical ventilation) ▪ Proportion of medically attended RSV cases with ED visit (≥60 years) ▪ Physician visit prior to hospital admission (≥60 years) ▪ Proportion of hospitalisations from LTCHs (≥60 years) ▪ Age distribution of hospitalised patients (60 to 69, 70 to 79, ≥80 years) ▪ Proportion with ICU admission (≥60 years) ▪ Proportion of ICU patients using MV (≥60 years) ▪ In hospital mortality rate (by age group: 60 to 69, 70 to 79, ≥80 years) **QALY loss** Utility values ▪ Age specific baseline utility values reported: ○ 60-64 years 0.77 ○ 65-69years- 0.76 ○ 70-74 years- 0.74 ○ 75-79 years- 0.70 ○ 80-84 years- 0.63 ○ 85+years-0.51 ▪ Utility weights associated with RSV outcomes: ○ Non-medically attended case-0.88 ○ OPD (office of ED visit)-0.76 ○ Hospitalisation (non-ICU)-0.35 ○ ICU-0.1
Economic results	**Type of summary ratio**	Net Monetary Benefit (NMB) and ICER (incremental cost per QALY gained)	

<table>
<tr><td></td><td></td><td></td></tr>
<tr><td></td><td>Overall payer perspective result</td><td>Cost effectiveness for vaccination programmes with RSVPreF3 only and RSVpreF only in a population of 100,000 adults aged 60 years and older at a WTP of CAD $50,000 per QALY gained over 2 RSV seasons:
<table>
<tr><th>Programme scenario</th><th>Maximum PPD, CAD $</th><th>ICER</th></tr>
<tr><td colspan="3">S1 with sigmoidal vaccine efficacy profile</td></tr>
<tr><td>RSVPreF3</td><td>139</td><td>49653</td></tr>
<tr><td>RSVpreF</td><td>137</td><td>49806</td></tr>
<tr><td colspan="3">S1 with linear vaccine efficacy profile</td></tr>
<tr><td>RSVPreF3</td><td>163</td><td>49984</td></tr>
<tr><td>RSVpreF</td><td>177</td><td>49977</td></tr>
<tr><td colspan="3">S2 with sigmoidal vaccine efficacy profile</td></tr>
<tr><td>RSVPreF3</td><td>69</td><td>49669</td></tr>
<tr><td>RSVpreF</td><td>68</td><td>49788</td></tr>
<tr><td colspan="3">S2 with linear vaccine efficacy profile</td></tr>
<tr><td>RSVPreF3</td><td>81</td><td>49457</td></tr>
<tr><td>RSVpreF</td><td>87</td><td>49931</td></tr>
</table></td></tr>
<tr><td></td><td>Overall societal perspective result</td><td>Cost effectiveness for vaccination programmes with RSVPreF3 only and RSVpreF only in a population of 100,000 adults aged 60 years and older at a WTP of CAD $50,000 per QALY gained over 2 RSV seasons:
<table>
<tr><th>Programme scenario</th><th>Maximum PPD, CAD $</th><th>ICER</th></tr>
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<tr><td>RSVpreF</td><td>177</td><td>49977</td></tr>
<tr><td colspan="3">S2 with sigmoidal vaccine efficacy profile</td></tr>
<tr><td>RSVPreF3</td><td>119</td><td>49478</td></tr>
<tr><td>RSVpreF</td><td>114</td><td>49711</td></tr>
</table></td></tr>
</table>

		S2 with linear vaccine efficacy profile RSVPreF3 — 139 — 49698 RSVpreF — 143 — 49175
Epidemiological results		Reductions in inpatient care, outpatient care and death reported
Authors conclusions	A publicly-funded program to vaccinate residents of LTCHs against RSV disease would be cost-effective depending on PPD; extending the programme to community-dwelling older adults could be cost-effective and substantially reduce the direct and indirect health and economic burden of RSV disease.	

Key: CAD – Canadian dollar; ED – emergency department; ICER - incremental cost-effectiveness ratio; ICU - intensive care unit; LRTD – lower respiratory tract disease; LTCH – long term care home; MV-mechanical ventilation; PPD - price per dose; QALY- quality-adjusted life year; RSV - respiratory syncytial virus; WTP – willingness to pay.

General study characteristics	**Author name** **Year of publication** **DOI**	Tuite AR et al. 2024 https://doi.org/10.1503/cmaj.240452
	Region or country	Canada
	Type of economic evaluation	Cost-utility analysis
	Population	Adults aged 50 years and older
	Funding	Government Centre for Immunization Programs, Public Health Agency of Canada
Model characteristics	**Model type**	Static individual-based model ▪ Multi-aged closed population of 100,000 people ▪ Individuals characterised by presence of 1 or more chronic medical conditions ▪ Monthly time steps ▪ Health states included: o at risk for medically attended RSV (MA-RSV) o healthcare provider visit o emergency department (ED) visit

		○ hospital admission ○ hospital admission with ICU admission ○ recovery ○ death
	Perspective	Health-system and societal
	Time horizon	3 years except lifetime for RSV-related mortality
	Comparator	No vaccination and each alternative strategy
	Discount rates	1.5% for costs and outcomes
	Sensitivity analysis	Probabilistic sensitivity analyses Scenario analyses
Intervention	**Strategies**	Age-only eligibility ▪ People aged ≥60yrs, ≥65yrs, ≥70yrs, ≥75yrs and ≥80yrs Age with medical risk eligibility ▪ People aged ≥60yrs, ≥65yrs, ≥70yrs, ≥75yrs and ≥80yrs with at least one chronic medical condition Age plus medical risk-only eligibility ▪ As above for age-only eligibility and people from 50 or 60 years of age with at least one chronic medical condition
	Dosing schedule	One dose in the first 2 months of model entry
	Type of immunisation	GSK RSV vaccine (RSVPreF3) and Pfizer RSV vaccine (RSVpreF)
	Age at immunisation	Various – at least 50 years old with a chronic medical condition and at least 60 years old without a chronic medical condition (see intervention strategies above)
	Coverage rate	Based on influenza vaccine uptake With chronic medical conditions, % ▪ 50 to 59 years – 58.6 ▪ 60 to 64 – 59.9 ▪ 65 to 69 – 65.2

		▪ 70 to 79 – 82.7 ▪ ≥80 years – 83.4 Without chronic medical conditions % ▪ 50 to 59 years – 36.7 ▪ 60 to 64 – 49.4 ▪ 65 to 69 – 61.1 ▪ 70 to 79 – 74.9 ▪ ≥80 years – 74.8
Model input parameters	**Efficacy/effectiveness**	Modelled vaccine efficacy (VE) estimates informed by RCT data (assumed effectiveness did not vary by age or chronic medical condition status) Mean VE for season 1: RSVPreF3 ▪ Outpatient – 82.6% ▪ Hospital admitted – 94.1% RSVpreF ▪ Outpatient – 65.1% ▪ Hospital admitted – 88.9% Definition differed between RSVpreF3 and RSVpreF vaccines RSVPreF3 ▪ outpatient care was based on VE for medically attended RSV-LRTD ▪ hospitalisation was based on VE for severe RSV LRTD RSVpreF ▪ outpatient care was based on VE for medically attended RSV LRTI with 2 or more symptoms ▪ hospitalisation was based on VE for medically attended RSV LRTI with 3 or more signs or symptoms
	Waning	Modelled VE waning estimates informed by RCT data. Data on average VE and average duration of follow-up were used to generate step functions, and protection was assumed to wane linearly between seasons. In the base case, VE was assumed to be 0 in season 3.

		Mean VE for season 2: RSVPreF3 ▪ Outpatient – 56.1% ▪ Hospital admitted – 64.2% RSVpreF season 2 ▪ Outpatient – 48.9% ▪ Hospital admitted – 78.6%	
	Costs included	**<u>Type of cost</u>** **Direct costs** Medical ▪ Outpatient case ▪ Hospitalisation Intervention ▪ Vaccine per dose: CAD $230 for GSK RSVPreF3 or Pfizer RSVpreF (sourced from a media report on the announced price of GSK RSVPreF3) ▪ Administration per dose: CAD $18 (sourced from a previously published paper on the pneumococcal vaccine) ▪ Wastage ▪ Adverse events following immunisation (AEFI) o severe local AE o severe systemic AE Patient ▪ Patient medication costs ▪ Transportation costs	**<u>Measurement and valuation</u>** **Direct costs** Medical costs ▪ Outpatient cost by setting (healthcare provider or emergency department) based on estimates for influenza ▪ Hospitalisation cost by mortality status during hospital stay Intervention costs ▪ Vaccination cost per dose and vaccine type based on public Canadian list prices ▪ Vaccine administration cost per dose (all ages) ▪ Vaccine wastage (5%) –based on WHO source ▪ AEFIs cost by age (<65 years and ≥65 years) and severity included o a healthcare provider visit o treatment costs Patient-borne costs ▪ Patient medication costs o co-pay per prescription by age (50 to 64 years) and ≥65 years) o over the counter medication for

		Indirect costs ▪ Patient productivity loss ▪ Caregiver productivity loss	medically attended case o prescription medication for medically attended case for <65 year olds o prescription medication for severe AEFI (local or systemic) for <65 years olds ▪ Patient transportation costs: o 2 way travel to vaccination or outpatient care (out of pocket) o travel to inpatient care. **Indirect costs** Patient productivity loss ▪ Productivity loss estimated using the human capital method due to: o RSV-attributable disease o AEFIs o death ▪ Duration of patient productivity loss assumed equivalent to the length of illness ▪ Time to receive vaccine, including travel and waiting time Caregiver productivity loss ▪ Caregiver time loss was assumed to be equivalent to length of illness multiplied by average (%) reduction in productivity for caregivers.
	Effects included	**<u>Type of Effects</u>** **Direct effects** ▪ Medically attended RSV disease with/without ED visit ▪ RSV-attributable hospitalisation ▪ ICU admission ▪ Death ▪ Severe local adverse event ▪ Severe systemic adverse event	**<u>Measurement and valuation</u>** **Direct effects** ▪ Annual incidence of medically attended RSV requiring outpatient healthcare provider visit per 100000 population (age group stratified) ▪ Annual incidence of medically attended RSV requiring emergency department visit per 100000 population (age group

		Indirect effects N/A	stratified) ▪ Annual incidence of RSV-attributable hospital admission per 100000 population (age group stratified) ▪ Proportion of patients admitted to hospital with RSV requiring ICU admission ▪ Proportion of RSV mortality per hospital admission **QALY** Baseline health utility by age based on EQ-5D-5L for the Canadian population QALY losses ○ outpatient, with/without ED visit (all ages)- 0.0056(0.0037–0.0075) ○ hospital admission (all ages)- 0.020(0.017–0.030) ○ serious local adverse event- 0.0003(0.0002–0.0004) ○ serious systemic adverse event - 0.0004 (0.0003–0.0005) ○ death (by age group) – 50-59yr: 20.26 – 60-64yr: 16.74 – 65-69yr: 14.29 – 70-74yr: 11.75 – 75-79yr: 9.38 – ≥80yr: 5.84
Economic results	**Type of summary ratio**	Incremental cost per QALY gained	
	Overall payer perspective result	For both vaccines, according to incremental analysis, a programme focused on vaccinating people with at least one chronic medical condition aged 70 years and older was the optimal strategy for a cost-effectiveness threshold of CAD $50,000 per QALY, with ICERs of CAD $49,439 (RSVPreF3) and CAD $46,542 (RSVpreF) per QALY compared with vaccinating people with at least one chronic medical condition aged 75 years and older.	

	Overall societal perspective result	For both vaccines, a programme focused on vaccinating people with at least one chronic medical condition aged 70 years and older was the optimal strategy for a cost-effectiveness threshold of CAD $50,000 per QALY, with ICERs of CAD $43,255 (RSVPreF3) and CAD $41,632 (RSVpreF) per QALY compared with vaccinating people with at least one chronic medical condition aged 75 years and older.
Epidemiological results		Outcomes reported by age group, case-risk group (outpatient, inpatient, death) and vaccine type: ▪ cases per 100,000 person-years ▪ cases (%) averted ▪ number needed to vaccinate For all strategies, number of cases averted was largest when vaccination included younger ages. Estimates of number needed to vaccinate to avert 1 outpatient visit, hospital admission, or death tended to be largest for the age- plus risk-based strategies and were smallest for risk-based strategies. For all strategies, number needed to vaccinate increased as the age cut-off for vaccination was lowered.
Authors conclusions	RSV vaccination programmes in some groups of older Canadian adults are expected to be cost-effective with programmes focusing on people with underlying medical conditions that place them at increased risk of severe RSV disease expected to provide the best value for money.	

Key: AE – adverse events; AEFI - adverse events following immunisation; CAD – Canadian dollar; ED – emergency department; EQ-5D-5L - EuroQol 5-Dimensions 5-Levels; ICER- incremental cost-effectiveness ratio; ICU- intensive care unit; LRTD – lower respiratory tract disease; MA – medically attended; N/A – not applicable; QALY- quality-adjusted life year; RCT – randomized controlled trial; RSV - respiratory syncytial virus; VE- vaccine effectiveness; yrs – years; WHO – World Health Organization.

General study characteristics	**Author name** **Year of publication** **DOI**	Wang Y et al. 2023 https://doi.org/10.3390/vaccines11101605
	Region or country	Hong Kong
	Type of economic evaluation	Cost-utility analysis
	Population	Adults aged 60 years and older
	Funding	Research grant (Academia) - Direct Grant for Research (The Chinese

		University of Hong Kong)
Model characteristics	**Model type**	Decision analytic model (decision tree) Disease pathways following vaccination included RSV infection, RSV-associated lower respiratory tract disease (LRTD), RSV-associated acute respiratory tract infection (ARI), outpatient care, self-managed care, hospitalisation and death.
	Perspective	Health system
	Time horizon	2 years
	Comparator	No vaccination and alternative strategy
	Discount rates	3% for both costs and effects
	Sensitivity analysis	One-way sensitivity analyses Probabilistic sensitivity analyses
Intervention	**Strategies**	▪ Vaccination with RSVPreF3 ▪ Vaccination with RSVpreF
	Dosing schedule	Single dose Timing not specified. Stated that the model timeframe aligned with the follow-up period of RSV vaccine efficacy studies, in which vaccines were administered prior to the start of the RSV season.
	Vaccination type	○ GSK RSV vaccine (RSVPreF3) and Pfizer RSV vaccine (RSVpreF)
	Age at vaccination	60 years and older
	Coverage rate	48.2% (adopted from data for seasonal influenza of Hong Kong in 2022–2023)
Model input parameters	**Efficacy/effectiveness**	Season 1 mean efficacy: % (95% CI) RSVPreF3 ▪ RSV-ARI - 79% (54.3-91.5) ▪ RSV-LRTD - 87.5% (58.9-97.6) RSVpreF ▪ RSV-ARI - 65.2% (36.0-82.0) ▪ RSV-LRTD - 84.6% (32.0-98.3)

	Waning	Season 2 mean efficacy: % (95% CI) RSVPreF3 ▪ RSV-ARI – 27.8% (0-60.4) ▪ RSV-LRTD – 52.9% (0-81.2%) RSVpreF ▪ RSV-ARI – 55.0% (3.4-82.0) ▪ RSV-LRTD – 75.0% (25.3-97.4)	
	Costs included	**<u>Type of cost</u>** **Direct costs** Medical costs ▪ Inpatient care (hospitalisation) ▪ Self-managed care ▪ Outpatient care Intervention ▪ Vaccine per dose: $270 for GSK RSVPreF3 and $200 for Pfizer RSVpreF (sourced from the 2023 US ACIP meeting) ▪ Treatment of vaccine-related severe adverse events **Indirect costs** N/A	**<u>Measurement and valuation</u>** **Direct costs** Medical costs ▪ Cost of inpatient care (hospitalisation) per day ▪ Cost of self-managed care per episode (cost of over the counter medicines) ▪ Cost of outpatient care per clinic visit (assumed one visit per episode of RSV and per vaccine-related adverse event) Intervention cost ▪ Vaccine price per dose ▪ Cost of Treatment of vaccine-related severe adverse events ○ assume one outpatient care visit per vaccine-related adverse event
	Effects included	**<u>Type of Effects</u>** **Direct effects**	**<u>Measurement and valuation</u>** **Direct effects**

<table>
<tr>
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<td>

RSV infection / RSV-ARI
Outpatient case
Self-managed care
RSV-associated hospitalisation
Death
Vaccine-related severe adverse events

Indirect effects
N/A
</td>
<td>

RSV attack rate
Proportion of ARI among RSV infections
RSV-associated hospitalisation and mortality rates (by age group)
Proportion of patients who sought medical care (by risk status)
Length of illness for outpatient/self-managed care in days
Length of hospitalisation in days
Probability of severe adverse events after vaccination (defined as grade 3 solicited local or systemic reactions) by vaccine type

QALY loss

Severe adverse events 0.000677

Utility values

Utility scores were extracted from European studies conducted using EQ-5D-5L

RSV uninfected -0.896
self-managed care for RSV 0.82 0.73–0.94
outpatient care for RSV 0.75 0.69–0.90
hospitalization for RSV 0.576 0.560–0.592

</td>
</tr>
<tr>
<td>Economic results</td>
<td>Type of summary ratio</td>
<td colspan="2">ICER (Incremental cost per QALY gained)</td>
</tr>
<tr>
<td></td>
<td>Overall payer perspective result</td>
<td colspan="2">ICERs for each vaccine strategy at four levels of US vaccine prices (RSVpreF: $200; RSVPreF3: $270):
<table>
<tr><td>Strategy</td><td>ICER vs next less costly option</td><td>ICER vs no vaccination</td></tr>
<tr><td colspan="3">25% US vaccine price</td></tr>
</table>
</td>
</tr>
</table>

<table>
<tr><td></td><td></td><td>
<table>
<tr><td>No vaccination</td><td>-</td><td>-</td></tr>
<tr><td>RSVpreF</td><td>26209</td><td>26209</td></tr>
<tr><td>RSVPreF3</td><td>Dominated</td><td>47485</td></tr>
<tr><td colspan="3">50% US vaccine price</td></tr>
<tr><td>No vaccination</td><td>-</td><td>-</td></tr>
<tr><td>RSVpreF</td><td>63441</td><td>63441</td></tr>
<tr><td>RSVPreF3</td><td>Dominated</td><td>104756</td></tr>
<tr><td colspan="3">75% US vaccine price</td></tr>
<tr><td>No vaccination</td><td>-</td><td>-</td></tr>
<tr><td>RSVpreF</td><td>100674</td><td>100674</td></tr>
<tr><td>RSVPreF3</td><td>Dominated</td><td>162027</td></tr>
<tr><td colspan="3">100% US vaccine price</td></tr>
<tr><td>No vaccination</td><td>-</td><td>-</td></tr>
<tr><td>RSVpreF</td><td>137907</td><td>137907</td></tr>
<tr><td>RSVPreF3</td><td>Dominated</td><td>219299</td></tr>
</table>
</td></tr>
<tr><td></td><td>Overall societal perspective result</td><td>N/A</td></tr>
<tr><td>Epidemiological results</td><td></td><td>For each strategy reported:
RSV infection
RSV-associated hospitalisation
RSV-associated mortality</td></tr>
<tr><td>Authors conclusions</td><td colspan="2">A single vaccination of ABRYSVO® or AREXVY® to adults aged 60 years and older appears to gain QALYs by reducing RSV-associated events over 2 years from the perspective of Hong Kong public healthcare providers. The cost-effectiveness of ABRYSVO® or AREXVY® is highly subject to vaccine price and RSV attack rate.</td></tr>
</table>

Key: ACIP - Advisory Committee on Immunization Practices; ARI – acute respiratory infection; CI- confidence interval; EQ-5D-5L - - EuroQol 5-Dimensions 5-Levels; ICER- incremental cost-effectiveness ratio; LRTD – lower respiratory tract disease; N/A – not applicable; QALY- quality-adjusted life year; RSV - respiratory syncytial virus; WTP – willingness to pay.

Appendix A6

Appendix A6.1 Input parameters for economic models

Description	Base-case value	Lower Range	Upper Range	Distribution	Source
Resource use parameters					
Probability GP visit for RSV					
Probability GP visit for RSV_age group 1	100%	100%	100%	Fixed	Assumed given notified case
Probability GP visit for RSV_age group 2	100%	100%	100%	Fixed	
Probability GP visit for RSV_age group 3	100%	100%	100%	Fixed	
Probability GP visit for RSV_age group 4	100%	100%	100%	Fixed	
Probability GP visit for RSV_age group 9	100%	100%	100%	Fixed	
Probability GP visit for RSV_age group 10	100%	100%	100%	Fixed	
Probability GP visit for RSV_age group 11	100%	100%	100%	Fixed	
Probability GP visit for RSV_age group 12	100%	100%	100%	Fixed	
Frequency of GP visit for RSV					
Frequency of GP visit for RSV_age group 1	2.70	2.5	2.9	Gamma	Hak et al. 2025[337]
Frequency of GP visit for RSV_age group 2	2.70	2.5	2.9	Gamma	
Frequency of GP visit for RSV_age group 3	2.70	2.5	2.9	Gamma	
Frequency of GP visit for RSV_age group 4	2.10	1.9	2.3	Gamma	
Frequency of GP visit for RSV_age group 9	2.00	1.1	3.1	Gamma	Expert opinion
Frequency of GP visit for RSV_age group 10	2.00	1.1	3.1	Gamma	
Frequency of GP visit for RSV_age group 11	4.00	2.3	6.2	Gamma	
Frequency of GP visit for RSV_age group 12	4.00	2.3	6.2	Gamma	
Probability prescription medication prescribed by GP for RSV					
Probability medication prescribed by GP for RSV_age group 1	49.7%	44.7%	54.7%	Beta	Hak et al. 2025[337]
Probability medication prescribed by GP for RSV_age group 2	49.7%	44.7%	54.7%	Beta	

Description	Base-case value	Lower Range	Upper Range	Distribution	Source
Probability medication prescribed by GP for RSV_age group 3	49.7%	44.7%	54.7%	Beta	
Probability medication prescribed by GP for RSV_age group 4	61.7%	55.4%	67.8%	Beta	
Probability medication prescribed by GP for RSV_age group 9	36.0%	32.4%	39.6%	Beta	Mao et al. 2023[329]
Probability medication prescribed by GP for RSV_age group 10	36.0%	32.4%	39.6%	Beta	
Probability medication prescribed by GP for RSV_age group 11	36.0%	32.4%	39.6%	Beta	
Probability medication prescribed by GP for RSV_age group 12	36.0%	32.4%	39.6%	Beta	
Probability GP visit card					
Probability GP visit card_age group 1	69.3%	29.2%	29.2%	Fixed	Health Service Executive: Primary Care Reimbursement Service - eligibility July 2025[336]
Probability GP visit card_age group 2	69.3%	3.2%	3.2%	Fixed	
Probability GP visit card_age group 3	69.3%	3.0%	3.0%	Fixed	
Probability GP visit card_age group 4	69.3%	3.1%	3.1%	Fixed	
Probability GP visit card_age group 9	3.8%	22.8%	22.8%	Fixed	
Probability GP visit card_age group 10	38.6%	22.8%	22.8%	Fixed	
Probability GP visit card_age group 11	26.9%	22.8%	22.8%	Fixed	
Probability GP visit card_age group 12	26.9%	22.8%	22.8%	Fixed	
Probability medical card					
Probability medical card_age group 1	20.6%	28.8%	28.8%	Fixed	Health Service Executive: Primary Care Reimbursement Service - eligibility July 2025[336]
Probability medical card_age group 2	20.6%	21.5%	21.5%	Fixed	
Probability medical card_age group 3	20.6%	29.0%	29.0%	Fixed	
Probability medical card_age group 4	20.6%	38.7%	38.7%	Fixed	
Probability medical card_age group 9	36.5%	77.2%	77.2%	Fixed	
Probability medical card_age group 10	53.4%	77.2%	77.2%	Fixed	
Probability medical card_age group 11	73.1%	77.2%	77.2%	Fixed	
Probability medical card_age group 12	73.1%	77.2%	77.2%	Fixed	

Description	Base-case value	Lower Range	Upper Range	Distribution	Source
Probability OTC medication recommended for RSV					
Probability OTC medication recommended for RSV_age group 1	51.0%	46.2%	55.8%	Beta	Hak et al. 2025[337]
Probability OTC medication recommended for RSV_age group 2	51.0%	46.2%	55.8%	Beta	
Probability OTC medication recommended for RSV_age group 3	51.0%	46.2%	55.8%	Beta	
Probability OTC medication recommended for RSV_age group 4	52.3%	47.8%	56.7%	Beta	
Probability OTC medication recommended for RSV_age group 9	100.0%	100.0%	100.0%	Fixed	Assumed
Probability OTC medication recommended for RSV_age group 10	100.0%	100.0%	100.0%	Fixed	
Probability OTC medication recommended for RSV_age group 11	100.0%	100.0%	100.0%	Fixed	
Probability OTC medication recommended for RSV_age group 12	100.0%	100.0%	100.0%	Fixed	
Probability ED for RSV					
Probability ED for RSV_age group 1	10.3%	7.6%	13.4%	Beta	Health Protection Surveillance Centre
Probability ED for RSV_age group 2	11.4%	10.4%	12.4%	Beta	
Probability ED for RSV_age group 3	11.5%	10.2%	12.8%	Beta	
Probability ED for RSV_age group 4	10.9%	7.8%	14.5%	Beta	
Probability ED for RSV_age group 9	7.5%	7.3%	7.6%	Beta	
Probability ED for RSV_age group 10	6.1%	1.0%	15.6%	Beta	
Probability ED for RSV_age group 11	7.4%	7.0%	7.8%	Beta	
Probability ED for RSV_age group 12	6.4%	5.5%	7.2%	Beta	
Probability hospitalisation for RSV					
Probability hospitalisation (severe RSV)_age group 1	13.1%	10.4%	16.1%	Beta	Health Protection Surveillance Centre
Probability hospitalisation (severe RSV)_age group 2	11.7%	11.0%	12.4%	Beta	
Probability hospitalisation (severe RSV)_age group 3	11.0%	10.2%	11.8%	Beta	
Probability hospitalisation (severe RSV)_age group 4	11.7%	9.6%	13.8%	Beta	
Probability hospitalisation (severe RSV)_age group 9	8.0%	7.3%	8.8%	Beta	
Probability hospitalisation (severe RSV)_age group 10	9.1%	7.1%	11.4%	Beta	

Description	Base-case value	Lower Range	Upper Range	Distribution	Source
Probability hospitalisation (severe RSV)_age group 11	9.2%	7.6%	11.0%	Beta	
Probability hospitalisation (severe RSV)_age group 12	9.1%	7.1%	11.2%	Beta	
Cost parameters					
Direct medical costs - RSV					
Cost of GP visit for RSV_public	€53.97	€43.72	€65.29	Gamma	Smith et al. 2021[339]
Cost of GP visit for RSV_private	€58.67	€47.53	€70.97	Gamma	
Cost of prescription medication for RSV public_age group 1	€5.70	€4.62	€6.89	Gamma	Health Service Executive Prescribing guidelines - Recommended treatment courses for URTI and LRTI presenting in primary care[340]
Cost of prescription medication for RSV public_age group 2	€5.70	€4.62	€6.89	Gamma	
Cost of prescription medication for RSV public_age group 3	€5.70	€4.62	€6.89	Gamma	
Cost of prescription medication for RSV public_age group 4	€8.23	€6.67	€9.95	Gamma	
Cost of prescription medication for RSV public_age group 9	€8.11	€6.57	€9.81	Gamma	
Cost of prescription medication for RSV public_age group 10	€8.11	€6.57	€9.81	Gamma	
Cost of prescription medication for RSV public_age group 11	€8.11	€6.57	€9.81	Gamma	
Cost of prescription medication for RSV public_age group 12	€8.11	€6.57	€9.81	Gamma	
Cost of prescription medication for RSV private_age group 1	€7.87	€6.37	€9.51	Gamma	Health Service Executive Prescribing guidelines - Recommended treatment courses for URTI and LRTI presenting in primary care[340]
Cost of prescription medication for RSV private_age group 2	€7.87	€6.37	€9.51	Gamma	
Cost of prescription medication for RSV private_age group 3	€7.87	€6.37	€9.51	Gamma	
Cost of prescription medication for RSV private_age group 4	€11.23	€9.10	€13.59	Gamma	
Cost of prescription medication for RSV private_age group 9	€10.31	€8.35	€12.47	Gamma	
Cost of prescription medication for RSV private_age group 10	€10.31	€8.35	€12.47	Gamma	
Cost of prescription medication for RSV private_age group 11	€10.31	€8.35	€12.47	Gamma	
Cost of prescription medication for RSV private_age group 12	€10.31	€8.35	€12.47	Gamma	
Cost of prescription medication for RSV public_BIA_age group 1	€5.70	€4.62	€6.90	Gamma	

Description	Base-case value	Lower Range	Upper Range	Distribution	Source
Cost of prescription medication for RSV public_BIA_age group 2	€5.70	€4.62	€6.90	Gamma	Health Service Executive Prescribing guidelines - Recommended treatment courses for URTI and LRTI presenting in primary care[340]
Cost of prescription medication for RSV public_BIA_age group 3	€5.70	€4.62	€6.90	Gamma	
Cost of prescription medication for RSV public_BIA_age group 4	€8.23	€6.67	€9.96	Gamma	
Cost of prescription medication for RSV public_BIA_age group 9	€8.26	€6.69	€9.99	Gamma	
Cost of prescription medication for RSV public_BIA_age group 10	€8.26	€6.69	€9.99	Gamma	
Cost of prescription medication for RSV public_BIA_age group 11	€8.26	€6.69	€9.99	Gamma	
Cost of prescription medication for RSV public_BIA_age group 12	€8.26	€6.69	€9.99	Gamma	
Cost of OTC medication for RSV_age group 1	€9.14	€7.40	€11.06	Gamma	Health Service Executive Prescribing guidelines - Recommended treatment courses for URTI and LRTI presenting in primary care[340]
Cost of OTC medication for RSV_age group 2	€9.14	€7.40	€11.06	Gamma	
Cost of OTC medication for RSV_age group 3	€9.14	€7.40	€11.06	Gamma	
Cost of OTC medication for RSV_age group 4	€8.82	€7.14	€10.67	Gamma	
Cost of OTC medication for RSV_age group 9	€19.87	€16.10	€24.04	Gamma	
Cost of OTC medication for RSV_age group 10	€19.87	€16.10	€24.04	Gamma	
Cost of OTC medication for RSV_age group 11	€19.87	€16.10	€24.04	Gamma	
Cost of OTC medication for RSV_age group 12	€19.87	€16.10	€24.04	Gamma	
Cost of ED for RSV_age group 1	€473.87	€383.85	€573.23	Gamma	Healthcare Pricing Office
Cost of ED for RSV_age group 2	€473.87	€383.85	€573.23	Gamma	
Cost of ED for RSV_age group 3	€473.87	€383.85	€573.23	Gamma	
Cost of ED for RSV_age group 4	€473.87	€383.85	€573.23	Gamma	
Cost of ED for RSV_age group 9	€473.87	€383.85	€573.23	Gamma	
Cost of ED for RSV_age group 10	€473.87	€383.85	€573.23	Gamma	
Cost of ED for RSV_age group 11	€473.87	€383.85	€573.23	Gamma	
Cost of ED for RSV_age group 12	€473.87	€383.85	€573.23	Gamma	
Cost of hospitalisation for severe RSV_age group 1	€11,346	€9,191	€13,725	Gamma	

Description	Base-case value	Lower Range	Upper Range	Distribution	Source
Cost of hospitalisation for severe RSV_age group 2	€9,738	€7,888	€11,779	Gamma	Hospital InPatient Enquiry System and Health Protection Surveillance Centre
Cost of hospitalisation for severe RSV_age group 3	€9,288	€7,524	€11,236	Gamma	
Cost of hospitalisation for severe RSV_age group 4	€8,977	€7,271	€10,859	Gamma	
Cost of hospitalisation for severe RSV_age group 9	€8,621	€6,984	€10,429	Gamma	
Cost of hospitalisation for severe RSV_age group 10	€9,466	€7,668	€11,451	Gamma	
Cost of hospitalisation for severe RSV_age group 11	€8,817	€7,142	€10,666	Gamma	
Cost of hospitalisation for severe RSV_age group 12	€8,791	€7,121	€10,634	Gamma	
Indirect costs - RSV - probability of productivity loss					
Probability of productivity loss for those with RSV_age group 1	0.0%	0.0%	0.0%	Fixed	Assumed 0% probability of productivity loss given age
Probability of productivity loss for those with RSV_age group 2	0.0%	0.0%	0.0%	Fixed	
Probability of productivity loss for those with RSV_age group 3	0.0%	0.0%	0.0%	Fixed	
Probability of productivity loss for those with RSV_age group 4	0.0%	0.0%	0.0%	Fixed	
Probability of productivity loss for those with RSV_age group 9	28.4%	0.0%	0.0%	Fixed	Estimated based on Q22025 CSO employment rates[343]
Probability of productivity loss for those with RSV_age group 10	17.2%	0.0%	0.0%	Fixed	
Probability of productivity loss for those with RSV_age group 11	7.7%	0.0%	0.0%	Fixed	
Probability of productivity loss for those with RSV_age group 12	3.4%	0.0%	0.0%	Fixed	
Probability of productivity loss for carers of those with RSV_age group 1	0.0%	0.0%	0.0%	Fixed	Assumed 0% due to statutory maternity benefit of 26 weeks
Probability of productivity loss for carers of those with RSV_age group 2	0.0%	0.0%	0.0%	Fixed	
Probability of productivity loss for carers of those with RSV_age group 3	56.0%	0.0%	0.0%	Fixed	Estimated based on CSO Census 2022 data (Children Under 15 Years of Age in Childcare)[344]
Probability of productivity loss for carers of those with RSV_age group 4	56.0%	0.0%	0.0%	Fixed	
Probability of productivity loss for carers of those with RSV_age group 9	0.0%	0.0%	0.0%	Fixed	Assumed no productivity loss for caregiver given age of person with RSV
Probability of productivity loss for carers of those with RSV_age group 10	0.0%	0.0%	0.0%	Fixed	

Description	Base-case value	Lower Range	Upper Range	Distribution	Source
Probability of productivity loss for carers of those with RSV_age group 11	0.0%	0.0%	0.0%	Fixed	
Probability of productivity loss for carers of those with RSV_age group 12	0.0%	0.0%	0.0%	Fixed	
Indirect costs - productivity loss (1 day) for RSV					
Productivity loss (1 day) for those with RSV_age group 1	€0.00	€0.00	€0.00	Fixed	Assumed not working given age
Productivity loss (1 day) for those with RSV_age group 2	€0.00	€0.00	€0.00	Fixed	
Productivity loss (1 day) for those with RSV_age group 3	€0.00	€0.00	€0.00	Fixed	
Productivity loss (1 day) for those with RSV_age group 4	€0.00	€0.00	€0.00	Fixed	
Productivity loss (1 day) for those with RSV_age group 9	€129.79	€105.14	€157.00	Gamma	Central Statistics Office 2024 Median weekly earnings[345]
Productivity loss (1 day) for those with RSV_age group 10	€129.79	€105.14	€157.00	Gamma	
Productivity loss (1 day) for those with RSV_age group 11	€129.79	€105.14	€157.00	Gamma	
Productivity loss (1 day) for those with RSV_age group 12	€129.79	€105.14	€157.00	Gamma	
Productivity loss (1 day) for caregivers of those with RSV_age group 1	€169.25	€137.10	€204.74	Gamma	Central Statistics Office 2024 Median weekly earnings[345]
Productivity loss (1 day) for caregivers of those with RSV_age group 2	€169.25	€137.10	€204.74	Gamma	
Productivity loss (1 day) for caregivers of those with RSV_age group 3	€169.25	€137.10	€204.74	Gamma	
Productivity loss (1 day) for caregivers of those with RSV_age group 4	€169.25	€137.10	€204.74	Gamma	
Productivity loss (1 day) for caregivers of those with RSV_age group 9	€0.00	€0.00	€0.00	Fixed	Assumed caregiving not required given age
Productivity loss (1 day) for caregivers of those with RSV_age group 10	€0.00	€0.00	€0.00	Fixed	
Productivity loss (1 day) for caregivers of those with RSV_age group 11	€0.00	€0.00	€0.00	Fixed	
Productivity loss (1 day) for caregivers of those with RSV_age group 12	€0.00	€0.00	€0.00	Fixed	
Work days lost due to illness					
Work days lost for those with non-severe RSV_age group 1	0	0	0	Fixed	Assumed zero given age
Work days lost for those with non-severe RSV_age group 2	0	0	0	Fixed	
Work days lost for those with non-severe RSV_age group 3	0	0	0	Fixed	

Description	Base-case value	Lower Range	Upper Range	Distribution	Source
Work days lost for those with non-severe RSV_age group 4	0	0	0	Fixed	
Work days lost for those with non-severe RSV_age group 9	5	4	6	Gamma	Assumed based on duration of infectiousness
Work days lost for those with non-severe RSV_age group 10	5	4	6	Gamma	
Work days lost for those with non-severe RSV_age group 11	5	4	6	Gamma	
Work days lost for those with non-severe RSV_age group 12	5	4	6	Gamma	
Work days lost for ED attendance for RSV_age group 1	2	0	0	Fixed	Calculated
Work days lost for ED attendance for RSV_age group 2	2	0	0	Fixed	
Work days lost for ED attendance for RSV_age group 3	1.5	0	0	Fixed	
Work days lost for ED attendance for RSV_age group 4	1.5	0	0	Fixed	
Work days lost for ED attendance for RSV_age group 9	3	0	0	Fixed	
Work days lost for ED attendance for RSV_age group 10	4	0	0	Fixed	
Work days lost for ED attendance for RSV_age group 11	4	0	0	Fixed	
Work days lost for ED attendance for RSV_age group 12	6	0	0	Fixed	
***Note: work days lost for those with non-severe RSV equals the number of days (n=7) with quality of life impact less 2 weekend days.					
***Note: work days lost for those attending ED (without admission) for RSV equals the number of days lost for non-severe RSV plus additional number of days for ED cases (equals the half the average length of stay in hospital).					
***Note: work days lost for those with severe (hospitalised) RSV equals the number of days lost for non-severe RSV plus the average length of stay in hospital.					
***Note: work days lost for caregivers of those with non-severe RSV equals the number of work days lost for patients with non-severe illness.					
***Note: work days lost for caregivers of those attending ED (without admission) for RSV equals the number of work days lost for patients with non-severe illness plus additional number of days for ED cases.					
***Note: work days lost for caregivers of those with severe (hospitalised) RSV equals the number of work days lost for caregivers of those with non-severe illness plus the average length of stay in hospital.					
Length of stay - hospitalised case of RSV					
Average length of stay hospitalised RSV case_ age group 1	4	3	5	Gamma	Healthcare Pricing Office, Hospital Inpatient Enquiry System[326]
Average length of stay hospitalised RSV case_ age group 2	4	3	5	Gamma	
Average length of stay hospitalised RSV case_ age group 3	3	2	4	Gamma	

Description	Base-case value	Lower Range	Upper Range	Distribution	Source
Average length of stay hospitalised RSV case_ age group 4	3	2	4	Gamma	
Average length of stay hospitalised RSV case_ age group 9	6	5	7	Gamma	
Average length of stay hospitalised RSV case_ age group 10	8	6	10	Gamma	
Average length of stay hospitalised RSV case_ age group 11	8	6	10	Gamma	
Average length of stay hospitalised RSV case_ age group 12	12	10	15	Gamma	
Quality of life parameters					
Baseline utilities					
Baseline utility_age group 1	0.98	0.98	0.98	Fixed	Assumed
Baseline utility_age group 2	0.98	0.98	0.98	Fixed	
Baseline utility_age group 3	0.98	0.98	0.98	Fixed	
Baseline utility_age group 4	0.98	0.98	0.98	Fixed	
Baseline utility_age group 9	0.879	0.879	0.879	Fixed	Hobbins et al. 2018[327]
Baseline utility_age group 10	0.879	0.879	0.879	Fixed	
Baseline utility_age group 11	0.841	0.841	0.841	Fixed	
Baseline utility_age group 12	0.841	0.841	0.841	Fixed	
RSV utilities					
Utility_RSV_age group 9	0.74	0.70	0.78	Beta	Mao et al. 2022[463]
Utility_RSV_age group 10	0.74	0.70	0.78	Beta	
Utility_RSV_age group 11	0.74	0.70	0.78	Beta	
Utility_RSV_age group 12	0.74	0.70	0.78	Beta	
Utility_ED_RSV_age group 9	0.74	0.70	0.78	Beta	Mao et al. 2022[463]
Utility_ED_RSV_age group 10	0.74	0.70	0.78	Beta	
Utility_ED_RSV_age group 11	0.74	0.70	0.78	Beta	
Utility_ED_RSV_age group 12	0.74	0.70	0.78	Beta	

Description	Base-case value	Lower Range	Upper Range	Distribution	Source
Utility_hosp_RSV_age group 9	0.46	0.44	0.48	Beta	Chapter 5
Utility_hosp_RSV_age group 10	0.46	0.44	0.48	Beta	
Utility_hosp_RSV_age group 11	0.46	0.44	0.48	Beta	
Utility_hosp_RSV_age group 12	0.46	0.44	0.48	Beta	
QALY_loss_RSV_age_group_1 (GP)	0.006301	0.005479	0.007123	Gamma	Mao et al. 2023[329]
QALY_loss_RSV_age_group_2 (GP)	0.006301	0.005479	0.007123	Gamma	
QALY_loss_RSV_age_group_3 (GP)	0.006301	0.005479	0.007123	Gamma	
QALY_loss_RSV_age_group_4 (GP)	0.003811	0.000490	0.012649	Gamma	Hodgson et al. 2020[330]
QALY_loss_RSV_age_group_1 (ED)	0.008219	0.005479	0.007123	Gamma	Mao et al. 2023[329]
QALY_loss_RSV_age_group_2 (ED)	0.008219	0.005479	0.007123	Gamma	
QALY_loss_RSV_age_group_3 (ED)	0.008219	0.005479	0.007123	Gamma	
QALY_loss_RSV_age_group_4 (ED)	0.003811	0.000490	0.012649	Gamma	Hodgson et al. 2020[330]
QALY_loss_RSV_hosp_age_group_1	0.010137	0.009041	0.011781	Gamma	Mao et al. 2023[329]
QALY_loss_RSV_hosp_age_group_2	0.010137	0.009041	0.011781	Gamma	
QALY_loss_RSV_hosp_age_group_3	0.010137	0.009041	0.011781	Gamma	
QALY_loss_RSV_hosp_age_group_4	0.003811	0.000490	0.012649	Gamma	Hodgson et al. 2020[330]
Number of days of utility loss_non severe RSV	7	7	7	Fixed	
Number of days of utility loss_ED_RSV_age group 9	3	8	8	Fixed	Assumed 50% of hospitalised utility loss
Number of days of utility loss_ED_RSV_age group 10	4	8	8	Fixed	
Number of days of utility loss_ED_RSV_age group 11	4	9	9	Fixed	
Number of days of utility loss_ED_RSV_age group 12	6	9	9	Fixed	

Description	Base-case value	Lower Range	Upper Range	Distribution	Source
Immunisation programme parameters					
Immunisation programme cost parameters					
Cost of EHL-mAb - infant	€301.12	€243.92	€364.26	Gamma	Assumed
Cost of vaccine - maternal	€165.00	€133.66	€199.60	Gamma	Assumed
Cost of vaccine - adult	€165.00	€133.66	€199.60	Gamma	Assumed
Cost of mAb administration - infant @ catch-up	€19.73	€15.98	€23.87	Gamma	National Immunisation Office
Cost of vaccine administration - pregnant woman	€25.00	€20.25	€30.24	Gamma	Assumed based on existing contracted prices
Cost of vaccine administration - adult	€25.00	€20.25	€30.24	Gamma	
Cost of storage and distribution (per annum)	€600,000	€486,024	€725,801	Gamma	National Immunisation Office
Cost of pick and pack (per single dose pack)	€1.39	€1.13	€1.68	Gamma	
Cost of public health information campaign (infant programme)	€500,000	€405,020	€604,834	Gamma	
Cost of public health information campaign (adult programme)	€500,000	€405,020	€604,834	Gamma	
Cost of training (development of module)	€50,000	€40,502	€60,483	Gamma	
Cost of programme management (IT system for recording and monitoring uptake)	€1,000,000	€810,041	€1,209,669	Gamma	
Cost of programme manager (annual)	€137,488	€124,081	€151,572	Gamma	National Immunisation Office and HSE Salary Scales[334]
Cost of pharmacy technician (annual)	€73,909	€66,702	€81,480	Gamma	
Cost of (staff nurse) registered midwife (per 15 min. consultation)	€11.32	€9.17	€13.69	Gamma	
Other resource parameters					
Number of large maternity units	4	4	4	Fixed	National Immunisation Office
Number of medium maternity units	3	3	3	Fixed	
Number of small maternity units	12	12	12	Fixed	
Number of FTE pharmacy technicians_large maternity units	1	1	1	Fixed	
Number of FTE pharmacy technicians_medium maternity units	0.5	0.5	0.5	Fixed	
Number of FTE pharmacy technicians_small maternity units	0.25	0.25	0.25	Fixed	
Time required of pharmacy technicians (6mths)	0.5	0.5	0.5	Fixed	

Description	Base-case value	Lower Range	Upper Range	Distribution	Source
Eligible population					
Eligible population_age group 1 (BIA - year 1)	27,586	27,727	27,727	Fixed	Central Statistics Office[321]
Eligible population_age group 2 (BIA - year 1)	27,586	27,727	27,727	Fixed	
Eligible population_age group 9 (BIA - year 1)	257,176	251,332	251,332	Fixed	
Eligible population_age group 10 (BIA - year 1)	219,283	214,650	214,650	Fixed	
Eligible population_age group 11 (BIA - year 1)	176,206	169,164	169,164	Fixed	
Eligible population_age group 12 (BIA - year 1)	208,431	198,063	198,063	Fixed	
Immunisation coverage					
Immunisation coverage EHL-mAb seasonal_age group 1	82.6%	82.6%	82.6%	Fixed	Expert opinion and international uptake rates[332]
Immunisation coverage EHL-mAb catch-up	76.0%	76.0%	76.0%	Fixed	
Immunisation coverage_maternal_age group 1	62.0%	62.0%	62.0%	Fixed	
Immunisation coverage_age group 9	60.1%	60.1%	60.1%	Fixed	Health Protection Surveillance Centre - Seasonal Influenza Uptake Rates[333]
Immunisation coverage_age group 10	73.0%	73.0%	73.0%	Fixed	
Immunisation coverage_age group 11	88.4%	88.4%	88.4%	Fixed	
Immunisation coverage_age group 12	88.4%	88.4%	88.4%	Fixed	
Immunisation adverse events parameters					
Probability of solicited severe adverse event (adults only)	1.5%	0.5%	3.1%	Beta	Chapter 4 - Clinical Effectiveness & Safety
Number of days QALY loss for severe adverse event (adults only)	2	2	2	Fixed	Assumed
Epi parameters					
RSV risk parameters					
Relative risk RSV_EHL-mAb	0.310	0.245	0.392	Log Normal	Chapter 4 - Clinical Effectiveness & Safety
Relative risk RSV_hospitalisation_EHL-mAb (conditional on RSV)	0.541	0.199	1.470	Log Normal	
Relative risk RSV_maternal vaccine	0.510	0.381	0.682	Log Normal	

Description	Base-case value	Lower Range	Upper Range	Distribution	Source
Relative risk RSV_hospitalisation_maternal vaccine (conditional on RSV)	0.880	0.577	1.343	Log Normal	
Relative risk RSV_adult_vaccine_yr1	0.210	0.076	0.583	Log Normal	
Relative risk RSV_adult_vaccine_yr2	0.465	0.263	0.821	Log Normal	
Relative risk RSV_adult_vaccine_yr3	0.465	0.263	0.821	Log Normal	
Mortality parameters					
Life expectancy_age group 1	81	73	73	Fixed	CSO Irish Life Tables[328]
Life expectancy_age group 2	81	48	48	Fixed	
Life expectancy_age group 3	81	27	27	Fixed	
Life expectancy_age group 4	80	18	18	Fixed	
Life expectancy_age group 9	18	8	8	Fixed	
Life expectancy_age group 10	14	8	8	Fixed	
Life expectancy_age group 11	11	8	8	Fixed	
Life expectancy_age group 12	4	8	8	Fixed	
All-cause (less RSV) mortality risk_age group 1	1.04%	0.99%	0.99%	Fixed	CSO Mortality Data[464]
All-cause (less RSV) mortality risk_age group 2	0.08%	0.09%	0.09%	Fixed	
All-cause (less RSV) mortality risk_age group 3	0.08%	0.09%	0.09%	Fixed	
All-cause (less RSV) mortality risk_age group 4	0.02%	0.01%	0.01%	Fixed	
All-cause (less RSV) mortality risk_age group 9	1.12%	1.12%	1.12%	Fixed	
All-cause (less RSV) mortality risk_age group 10	1.93%	1.93%	1.93%	Fixed	
All-cause (less RSV) mortality risk_age group 11	3.40%	3.40%	3.40%	Fixed	
All-cause (less RSV) mortality risk_age group 12	10.24%	10.24%	10.24%	Fixed	
RSV mortality risk_age group 1	0.0006%	0.0006%	0.0006%	Fixed	Chapter 4 and HPSC
RSV mortality risk_age group 2	0.0000%	0.0000%	0.0006%	Fixed	
RSV mortality risk_age group 3	0.0000%	0.0000%	0.0006%	Fixed	

Description	Base-case value	Lower Range	Upper Range	Distribution	Source
RSV mortality risk_age group 4	0.0000%	0.0000%	0.0006%	Fixed	
RSV mortality risk_age group 9	0.0015%	0.0015%	0.0015%	Fixed	
RSV mortality risk_age group 10	0.0015%	0.0015%	0.0015%	Fixed	
RSV mortality risk_age group 11	0.0041%	0.0041%	0.0041%	Fixed	
RSV mortality risk_age group 12	0.0160%	0.0160%	0.0160%	Fixed	
Other parameters					
Model cycle length (days)	7	7	7	Fixed	
VAT	23%	23%	23%	Fixed	Revenue – Irish Tax and Customs[348]
Discount rate_costs	4%	3%	5%	Beta	HIQA 2025[317]
Discount rate_QALYs	4%	3%	5%	Beta	

Note: Age group 1 - 0 to 2 months; Age group 2 - 3 to 5 months: Age group 3 - 6 to 11 months; Age group 4 - 1 to 2 years; Age group 9 - 65 to 69 years; Age group 10 – 70 to 74 years; Age group 11 – 75 to 79 years: Age group 12 – 80 years and over.

Key: BIA – budget impact analysis; ED - emergency department; EHL-mAb – extended half-life monoclonal antibody; FTE – full-time equivalent; RSV respiratory syncytial virus; OTC - over-the-counter; QALYs – quality-adjusted life years; VE – vaccine efficacy.

Appendix A6.2 Medication included for estimating the average cost of prescription medication for infants, children and adults*

Treatment options for RSV	Description
Amoxicillin Antibiotic	Antibiotic - Adult
Doxycycline Antibiotic	Antibiotic - Adult
Clarithromycin Antibiotic	Antibiotic - Adult
Amoxicillin 125mg/5ml	Antibiotic - Infants up to 11 months
Amoxicillin 250mg/5ml	Antibiotic – Children from 12 months to 2 years
Clarithromycin 125mg/5ml	Antibiotic - Infants and children up to 2 years old
Phenoxymethylpenicillin 250mg/5ml	Antibiotic - Infants and children up to 2 years old
Ceflalexin 125mg/5ml	Antibiotic - Infants and children up to 2 years old
Prednisolone (Deltacortril®)	Oral steroid - Adults
Prednisolone (Prednesol®)	Oral steroid – Adults, infants and children up to 2 years old
Beclometasone	Inhaled steroid – Adults, infants and children up to 2 years old
Salbutamol	Bronchodilator – Adults, infants and children up to 2 years old
Fluticasone nasal spray	Nasal spray (steroid) - Adult
Mometasone nasal spray	Nasal spray (steroid) - Adult
Paracetemol	Analgesic/anti-pyretic - Adult
Ibuprofen	Analgesic/anti-pyretic - Adult

Note: The average cost of prescription medication has been estimated in line with published guidelines for Ireland.(465) It is noted that an increase in dispensing fees has been agreed under the Community Pharmacy Agreement 2025 (published in September 2025), with the new rates applicable from 1 September 2025. While these new rates have not been used in the estimates, as the guidelines referenced above have not yet been updated, it is acknowledged that the new rates will result in a minor increase in the average cost of prescription medication.
*The average cost of prescription medication for infants (per person) was estimated based on the composition of a prescription being bronchodilator (57%), antibiotic (22%), inhaled steroid (12%) and oral steroid (10%).

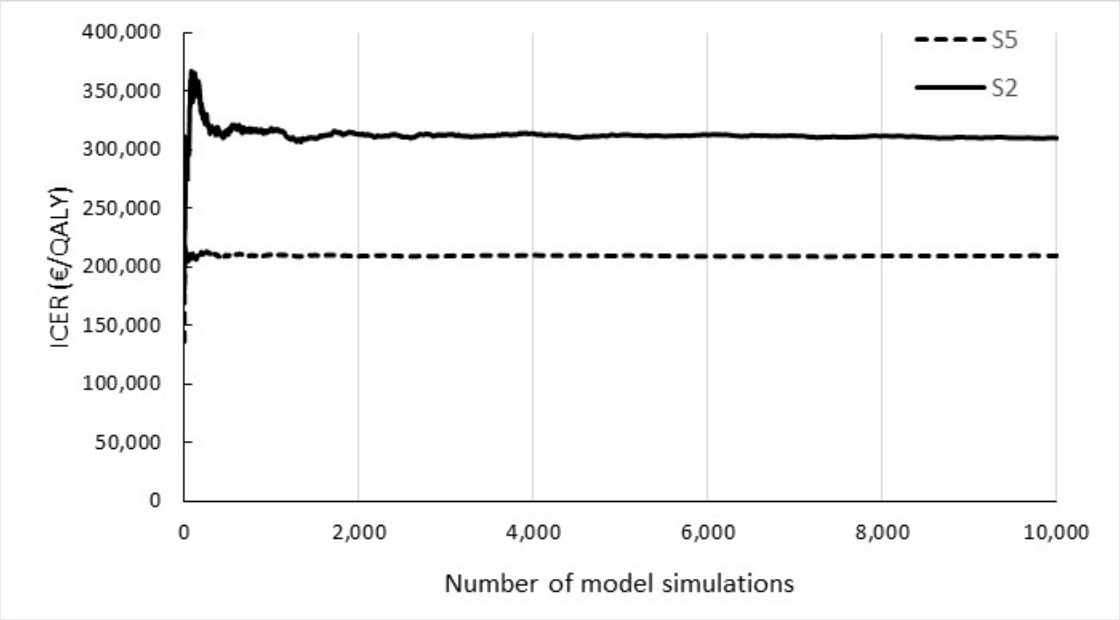
*The average cost of prescription medication for children (per person) from 1 to 2 years old was estimated based on the composition of a prescription being bronchodilator (44%), antibiotic (29%), inhaled steroid (16%) and oral steroid (12%).
*The average cost of prescription medication for adults (per person) was estimated based on the composition of a prescription being antibiotic (41%), analgesic (31%) and 'other' (28%).

Appendix A6.3 Medication included for estimating the average cost* of over-the-counter medication for infants, children and adults

Treatment options for RSV	Description
Infants	
Calpol® (under 6 years old)	Analgesic
Neurofen® (under 6 years old)	Anti-inflammatory
Adults	
Paracetemol	Analgesic/Antipyretic
Ibuprofen	Anti-inflammatory
Pseudoephedrine tablets	Decongestant
Pseudoephedrine nasal spray	Decongestant
Guaifenesin	Expectorant (cough bottle)
Dextromethorphan®	Anti-tussive (cough bottle)
Difflam® throat spray	Anti-sore throat
Strepsils plus®	Anti-sore throat

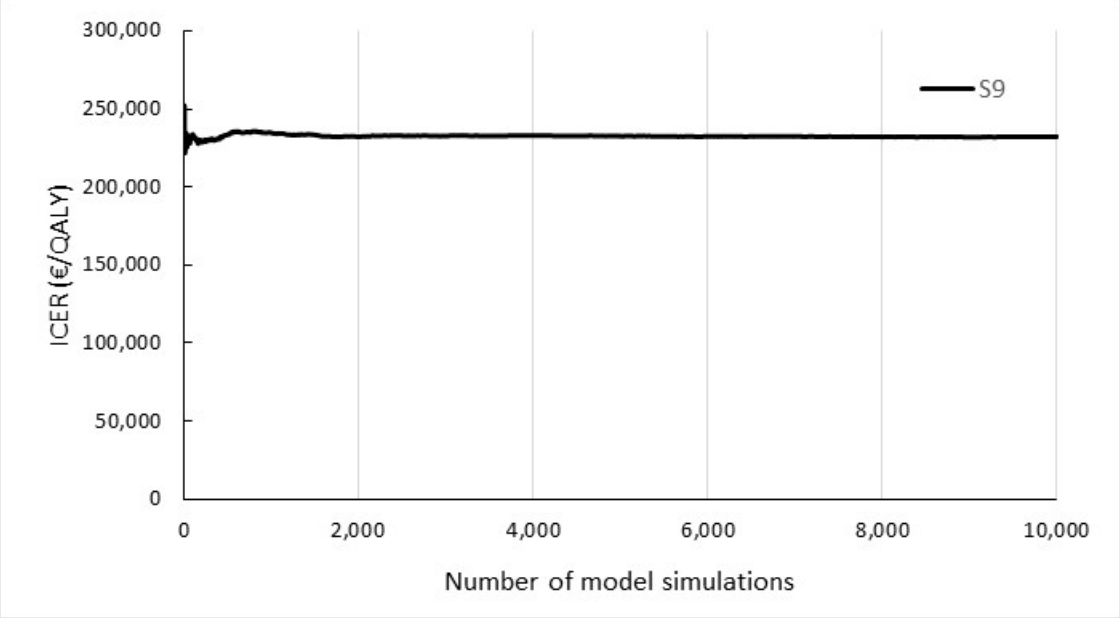
*The average cost of over the counter medication for infants (per person) was estimated based on the composition of the medication being analgesic (82%) and anti-inflammatory (18%).
*The average cost of over the counter medication for children (aged 1 to 2 years) (per person) was estimated based on the composition of the medication being analgesic (75%) and anti-inflammatory (25%).
*The average cost of over the counter medication for adults (per person) was estimated based on the composition of a prescription being cough preparation (24%), decongestant (22%), antipyretic (21%), anti-sore throat (19%) and anti-inflammatory (14%).

Appendix A6.4 Convergence testing for infant-based RSV immunisation strategies



Key: ICER - incremental cost-effectiveness ratio; QALY – quality-adjusted life year; S2 – Strategy 2 (seasonal EHL-mAb plus catch-up EHL-mAb); S5 – Strategy 5 (seasonal maternal vaccine and EHL-mAb plus catch-up EHL-mAb).

Appendix A.5 Convergence testing for adult-based RSV immunisation strategies



Key: ICER - incremental cost-effectiveness ratio; QALY – quality-adjusted life year; S9 – Strategy 9 (adults aged 80 years and over in year one and aged 80 years thereafter).

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