Sanofi Oy:n kommentti Palkon 19.03.2024 laatimaan suositusluonnokseen koskien Nirsevimabi- valmistetta respiratory syncytial –viruksen (RSV) aiheuttaman alempien hengitysteiden infektion estossa

Liite 1. Yhteenveto nirsevimabia koskevista tosielämän tiedoista

Across Europe and Worldwide, countries are currently implementing and recommending Nirsevimab as part of all-infant immunisation strategies, to reduce the burden of RSV in all infants and on their respective healthcare systems.

Below is a summary of these implementations – highlighting the significant impact Nirsevimab has had, in reducing hospitalisations, admissions, and overall burden of RSV in infants, healthcare systems, and more.

Immunisation programmes using nirsevimab have already launched in Europe (France, Spain, Luxembourg) and the US, and are achieving impressive coverage rates (ranging from 84% to 100% dependent on the region and infant population) due to the high acceptability of nirsevimab among HCPs, parents and caregivers and ease of administration due to its presentation as a fully liquid pre-filled syringe.

Spain – Galicia: Currently available data indicate coverage rates of 93% in infants born during the RSV season (receiving nirsevimab at birth), 86% to 94% in infants receiving a catch-up dose at the beginning of the season, and 100% in infants born with risk factors [Nirse-Gal, 2024 & Dirección Xeral de Saúde Pública,; 2024]. A reduction of 89% in RSV hospitalization in infants below 6 months (target for Nirsevimab immunization) was observed when compared to expected rates.

France: Real-world data have confirmed that the efficacy of nirsevimab against bronchiolitis is ≥80%, with a very significant reduction observed in cases in infants aged < 3 months [Infovac-France; 2024].

USA: In this multisite analysis of 699 infants hospitalised with ARI during their first RSV season, receipt of nirsevimab was 90% effective against RSV-associated hospitalisation at a median of 45 days from receipt of nirsevimab to ARI symptom onset [Moline, H.L. et al.; 2024]. This early effectiveness estimate supports existing recommendations for the prevention of severe RSV disease in infants in their first RSV season [Moline, H.L. et al.; 2024].

Luxembourg: Data indicate a coverage rate of 84% for infants receiving nirsevimab at birth [Ernst, C et al.; 2024]. In 2023, 241 children under 5 years of age were hospitalised with a laboratory-confirmed RSV infection (i.e. cases), compared with 389 cases in 2022, representing decreases of 38% (389 vs 241) in cases under 5 years of age and 69% (232 vs 72) in cases of infants under 6 months old [Ernst, C et al.; 2024].

Overall, the Real-World Evidence (RWE) from Galicia and Catalonia in Spain, the CDC in the US and others – solidify the significant role Nirsevimab has, in reducing the burden of RSV in all infants, decreasing hospitalisation rates due to RSV, and overall lessening the substantial impact RSV has every

Winter season, worldwide.

Other countries and regions have recently announced their intention to implement immunisation programs for infants, and their decisions and recommendations are also featured below.

PUBLISHED DATA:

1.1 Galicia, Spain (Nirsegal Study)

The NIRSE-GAL study is a joint effort between the public health authorities of Galicia [Nirse-Gal; 2024 & Dirección Xeral de Saude Pública, Xunta de Galicia; 2024], particularly with the epidemiology unit and research and academic institutions (Instituto de Investigación Sanitaria de Santi-ago de Compostela), and with the Genetic, vaccines, Infectious Diseases and Paediatrics research group (GENVIP) [Nirse-Gal; 2024 & Dirección Xeral de Saude Pública, Xunta de Galicia; 2024].

The primary objective of the study is to evaluate the effectiveness of nirsevimab on hospitalisation for Respiratory Syncytial Virus (RSV) related to lower respiratory tract infections (LRTI) during the RSV season (which starts on October 1st and ends on March 1st) in 3 groups of children [Nirse-Gal; 2024 & Dirección Xeral de Saude Pública, Xunta de Galicia; 2024]:

- Seasonal: Infants born during RSV season, i.e. from 25th September 2023 to 31 March 2024
- Catch-up: Infants younger than 6 months at the start of RSV season, i.e. born between 1 April and 24 September 2023
- High-risk children younger than 24 months at the start of RSV season, i.e. between 1 October 2021 and 31 March 2023 (previously included in immunization with palivizumab).

NIRSE-GAL study | evolution of Immunization Coverage with Nirsevimab (nirsegal.es)

Results Overview

1.1.1. Cumulative hospitalisation rate in infants during the 1st RSV season (for those immunised with Nirsevimab)

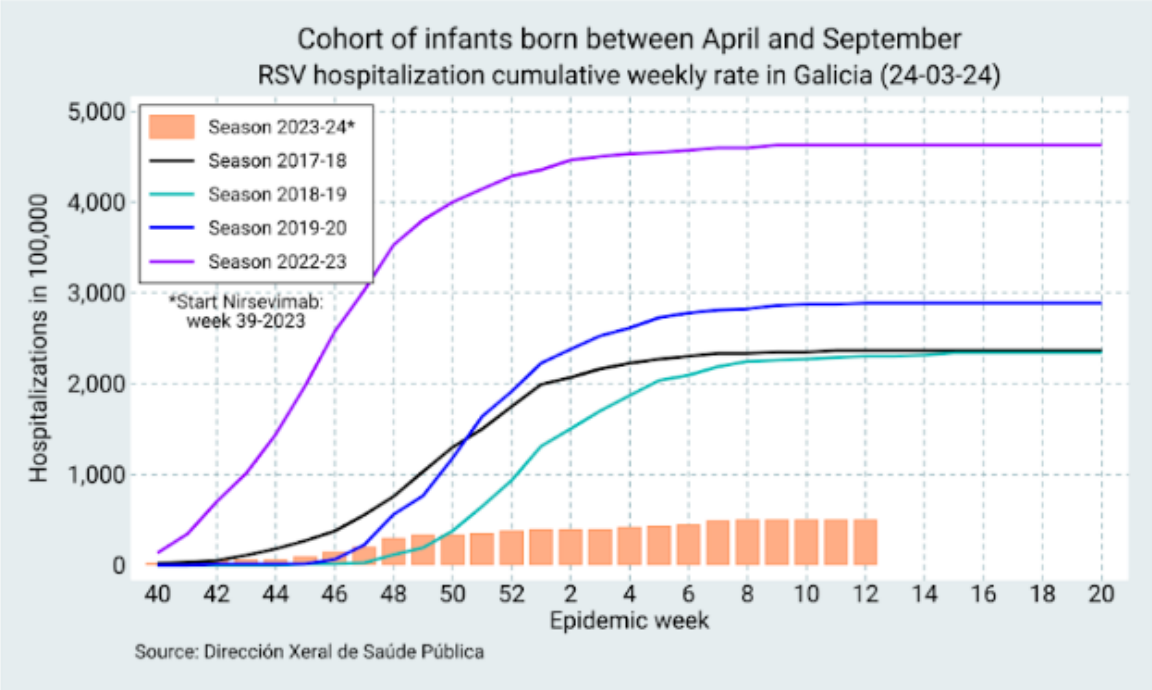

Figure 1. Cumulative weekly RSV hospitalisation rate in Galicia, by season, up to 24-03-2024. **Catch-up cohort** of infants born between April and September [Nirse-Gal.; 2024]

1.1.2. Cumulative hospitalisation rate in infants during the 2nd RSV season (those NOT eligible for Nirsevimab)

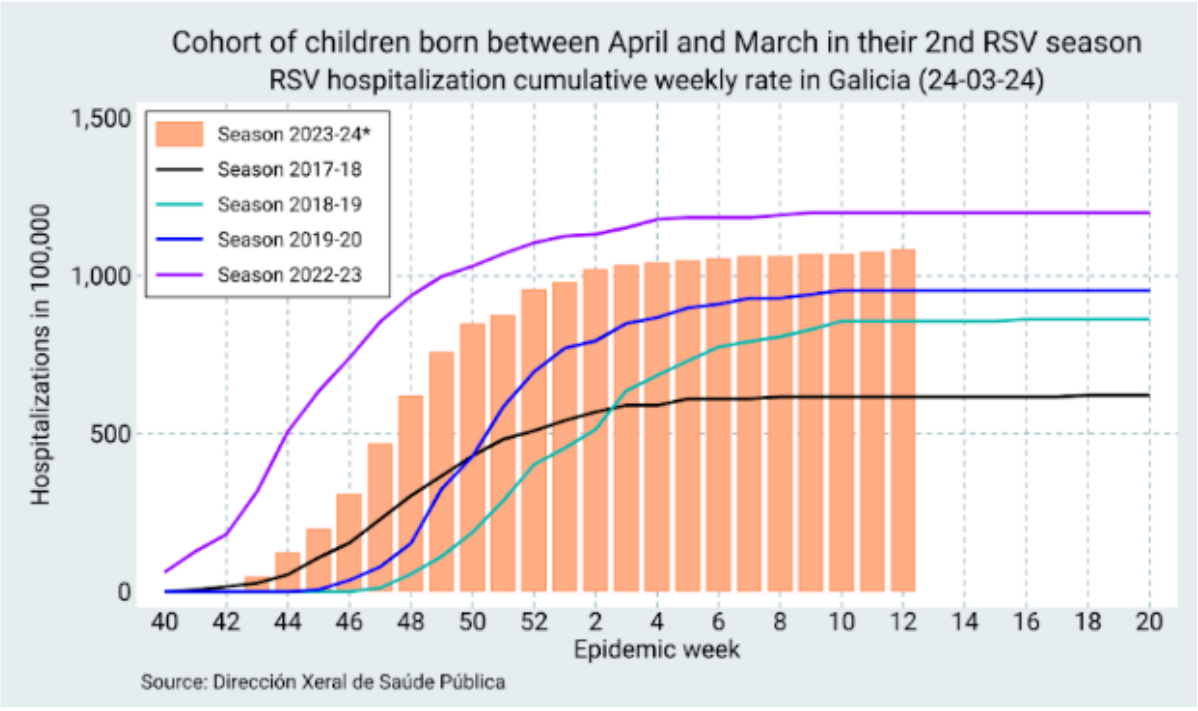

Figure 2. Cumulative weekly RSV hospitalisation rate in Galicia, by season, up to 24-03-2024. **Cohort of infants in their 2nd RSV season** [Nirse-Gal.; 2024].

1.1.3. Vaccination Coverage

A. <u>Immunised in campaign</u>: infants born after September 25 (up to 24-03-2024) = **92.6% -** with a total of 6,672 immunised infants

B. <u>Catch-up vaccinated</u>: infants born between April 1 and September 24 (up to 10-03-2024) = **85.0% -** with a total of 6,237 immunised infants

Note: 348 out of 360 high-risk children (96.7%) were immunised.

1.1.4. Evolution of the RSV epidemic wave

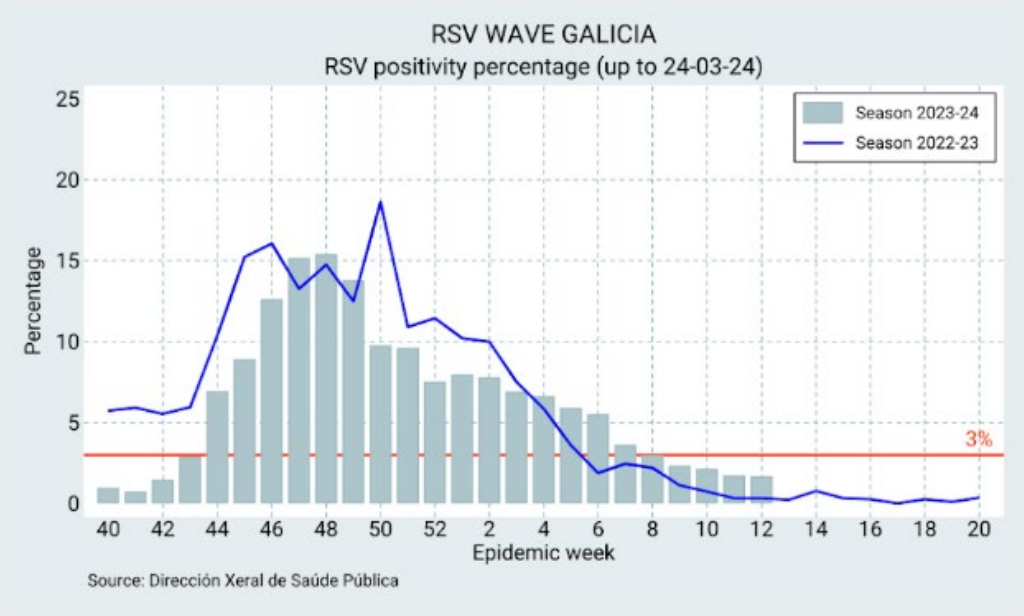

Figure 3. Total population positivity percentage (RSV) in Galicia, in seasons 2022-23 and 2023-24 up to 24-03-2024 [Nirse-Gal.; 2024].

Virus circulation is measured by positivity percentage to all samples sent to the microbiology laboratories of the Galician Health Service [Nirse-Gal.; 2024]. The data shows that the current 2023-24 RSV season percentage positivity has been similar to the 2022-23 RSV Season. [Boletín Epidemiolóxico de Galicia,; 2023].

1.1.5. **RSV Hospitalisation: Infants immunised with Nirsevimab**

a) Cohort of infants born between April and September

For current season 2023-24, it includes catch-up (infants born between April 1 and September 24, 2023); for the comparison with previous seasons, data was collected from infants born between April 1 and September 30 of the start of season year [Nirse-Gal.; 2024].

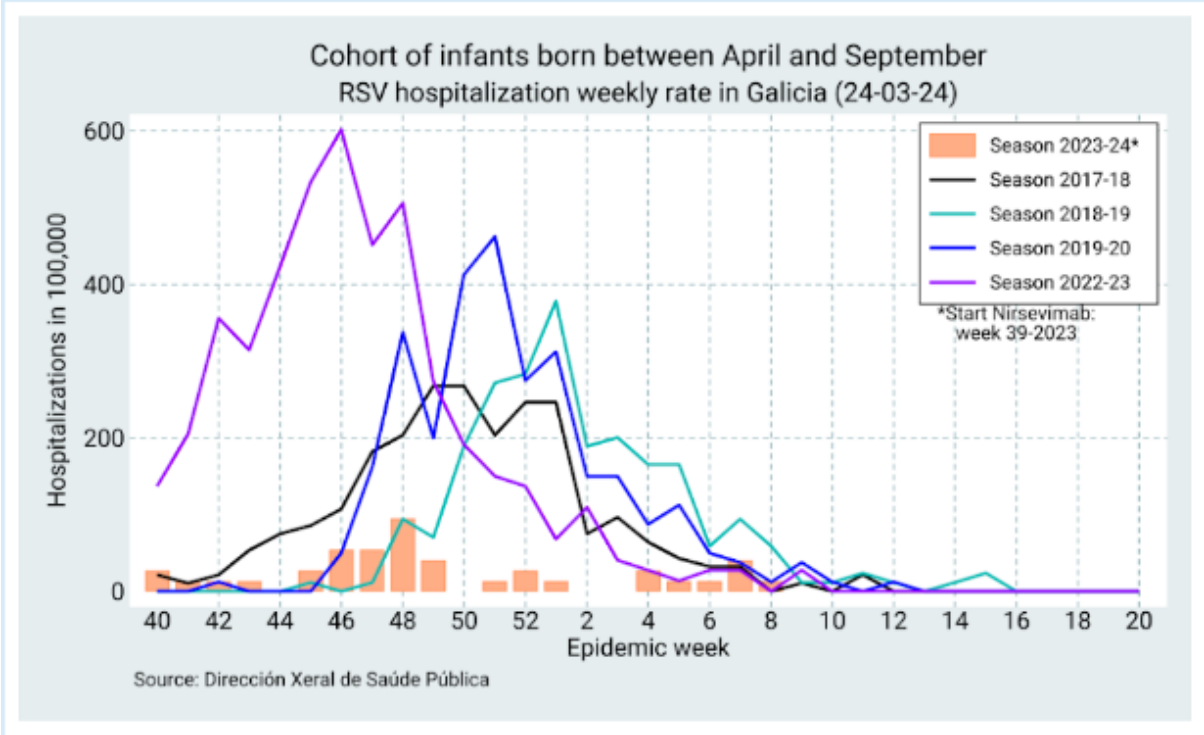

Figure 4. Weekly RSV hospitalisation rate in Galicia, by season, up to 24-03-2024. Cohort of infants born between April and September [Nirse-Gal.; 2024].

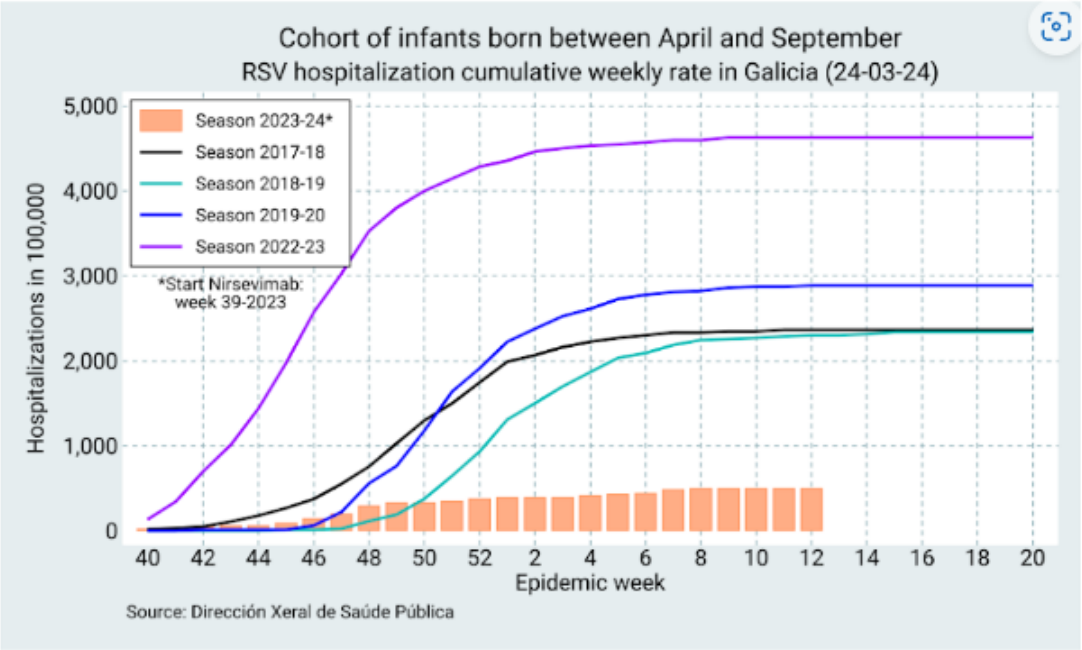

Figure 5. Cumulative weekly RSV hospitalisation rate in Galicia, by season, up to 24-03-2024. Cohort of infants born between April and September [Nirse-Gal.; 2024].

b) Infants under 2 months of age

For the current season, this group is dynamic and will begin with a high proportion of catch-up infants; as weeks go by, the percentage of infants immunised at birth will increase, until reaching 100% on 25 November (epidemiological week 47) [Nirse-Gal.; 2024].

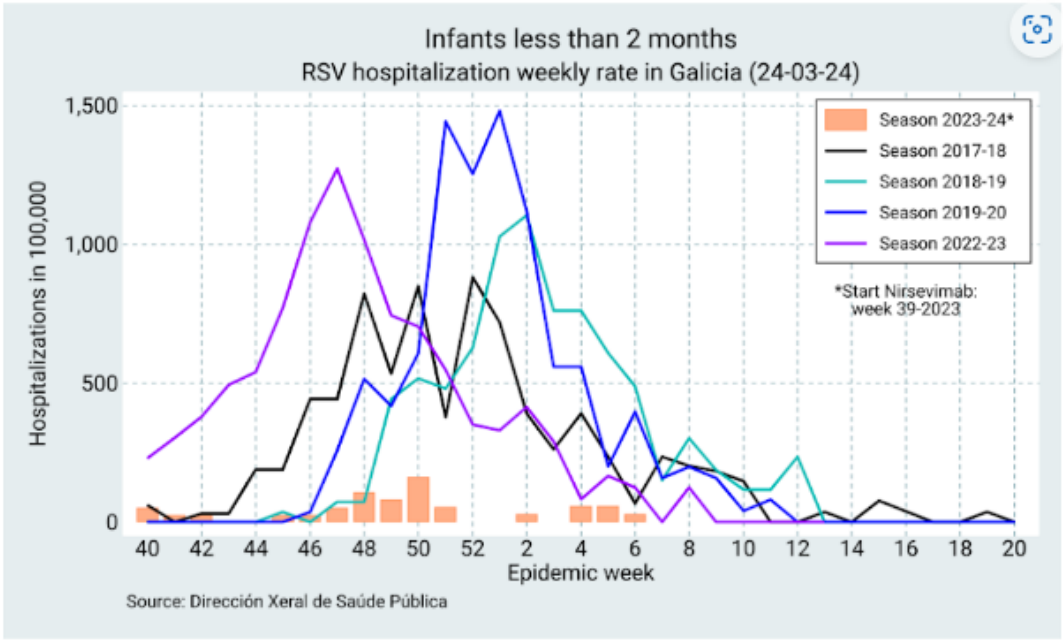

Figure 6. Weekly RSV hospitalisation rate in Galicia, by season, up to 24-03-2024. Infants less than 2 months

[Nirse-Gal.; 2024]

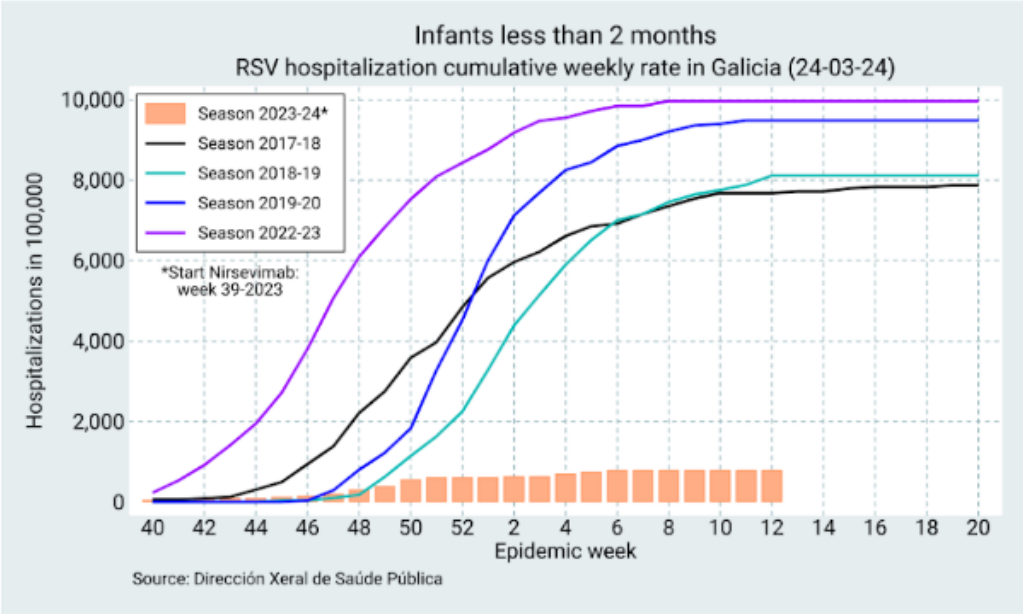

Figure 7. Cumulative weekly RSV hospitalisation rate in Galicia, by season, up to 24-03-2024. Infants less than 2 months [Nirse-Gal.; 2024].

c) Infants under 6 months of age

Also, for this group, at the beginning of the wave the majority of infants come from the catch-up group [Nirse-Gal.; 2024].

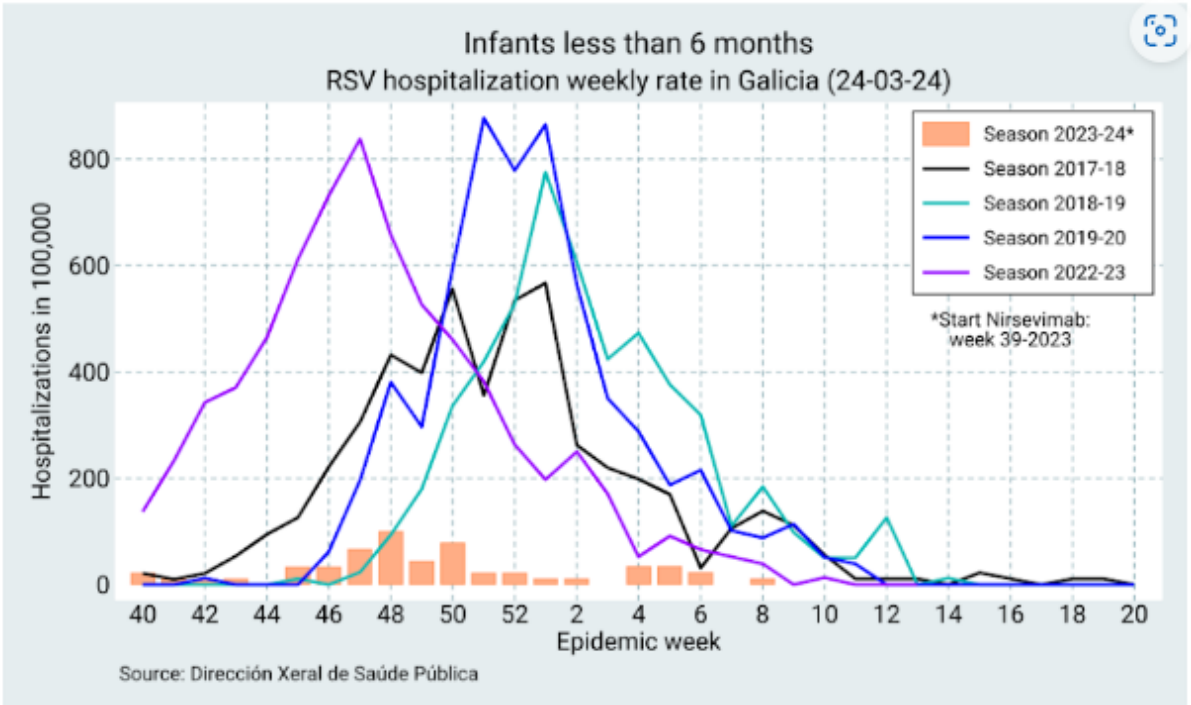

Figure 8. Weekly RSV hospitalisation rate in Galicia, by season, up to 24-03-2024. Infants less than 6 months [Nirse-Gal.; 2024]

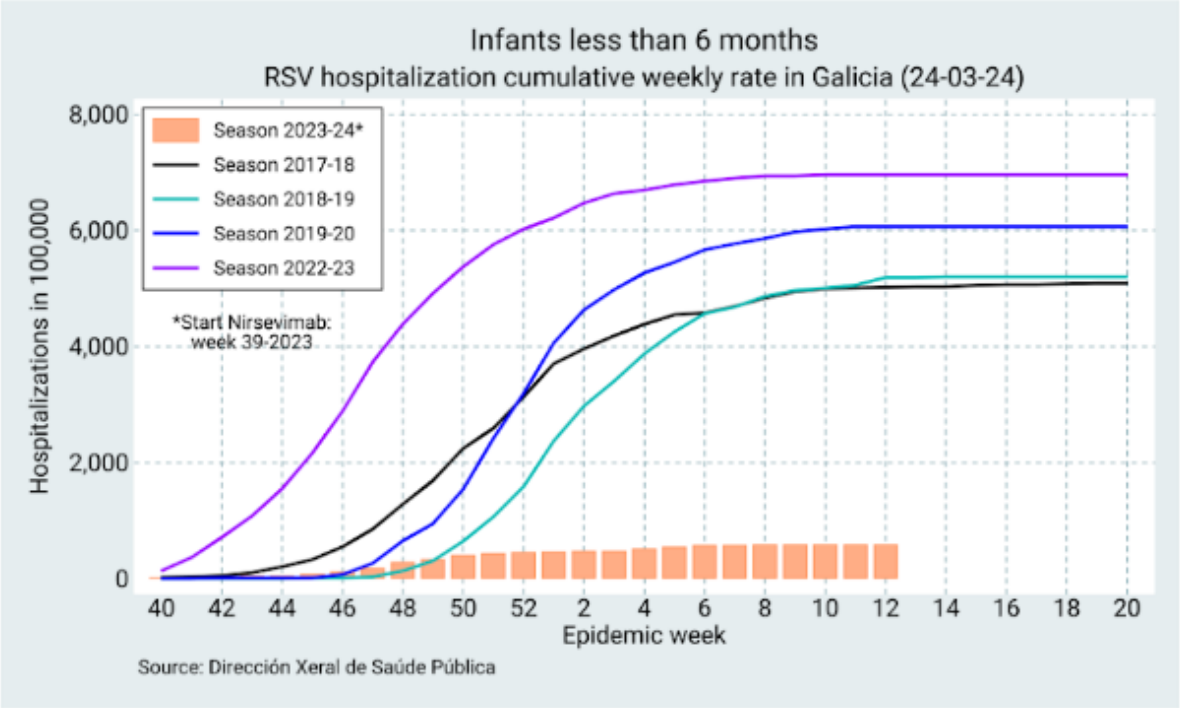

Figure 9. Cumulative weekly RSV hospitalisation rate in Galicia, by season, up to 24-03-2024. Infants less than 6 months [Nirse-Gal.; 2024].

1.1.6. **RSV Hospitalisation: Infants Not** Immunised with Nirsevimab

a) Cohort of infants born between April and March in their 2nd RSV season

For 2023-24 are infants born between 1 April 2022 and 31 March 2023. Same criteria was applied to the previous season's cohort [Nirse-Gal.; 2024].

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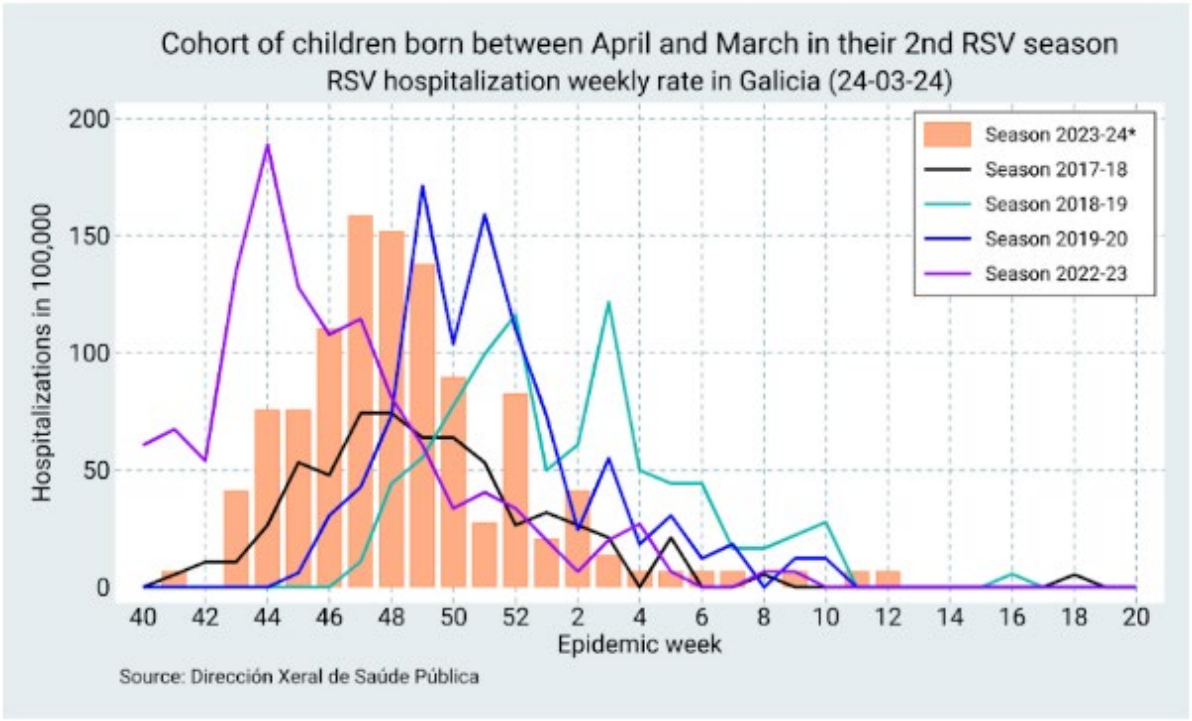


Figure 10. Weekly RSV hospitalisation rate in Galicia, by season, up to 24-03-2024. Cohort of infants born between April and March in their 2nd RSV season [Nirse-Gal.; 2024].

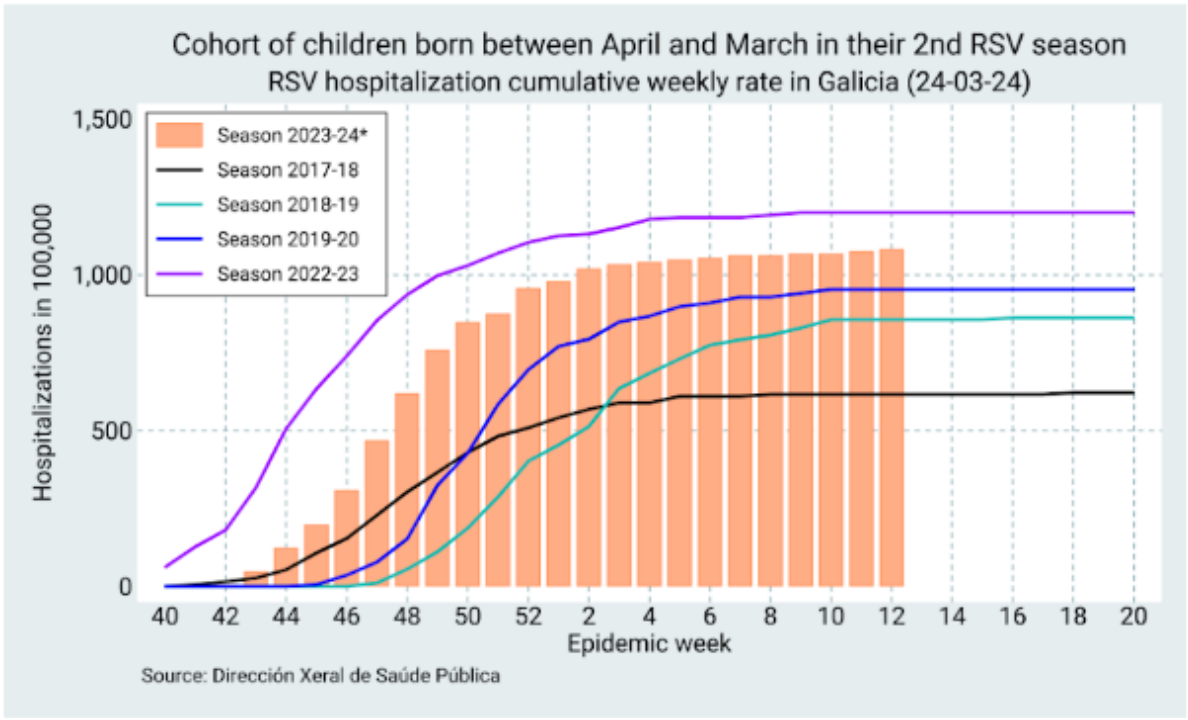


Figure 11. Cumulative weekly RSV hospitalisation rate in Galicia, by season, up to 24-03-2024. Cohort of infants born between April - March in 2nd RSV season [Nirse-Gal.; 2024].

b) Infants 1 to 4 years old

Infants between 1 and 4 years at the start of hospitalisation.

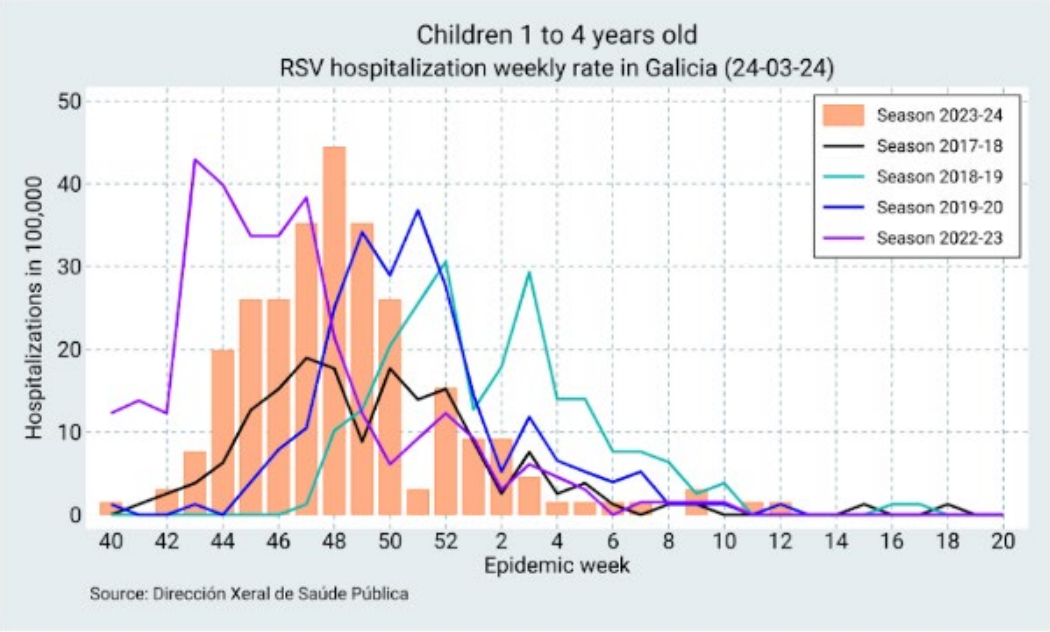


Figure 12. Weekly RSV hospitalisation rate in Galicia, by season, up to 24-03-2024. Infants 1 to 4 years old [Nirse-Gal.; 2024].

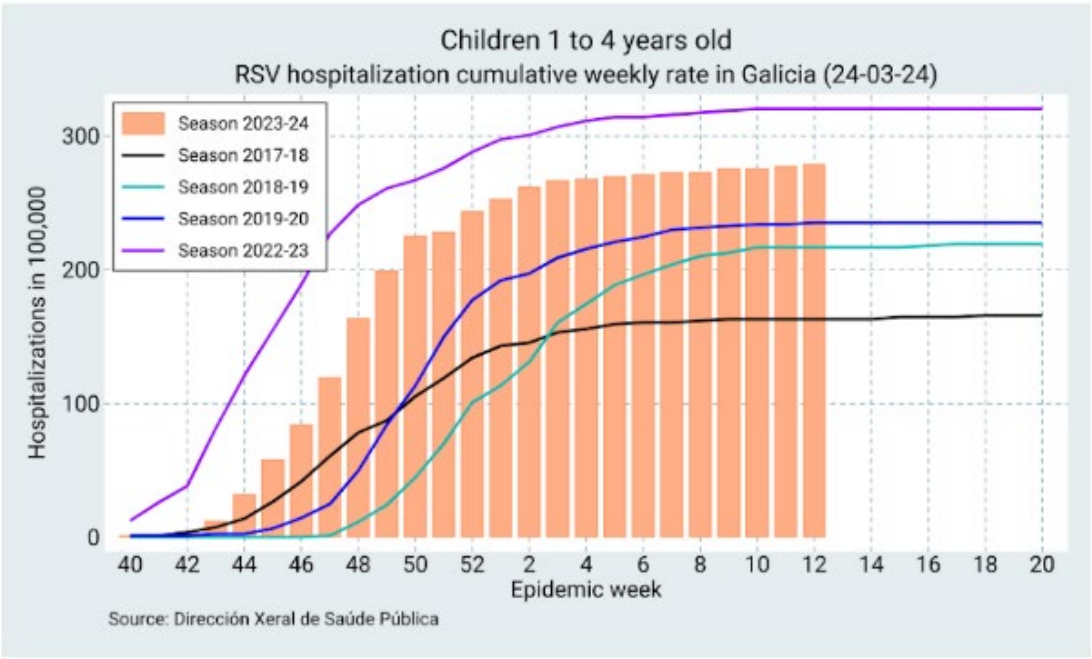
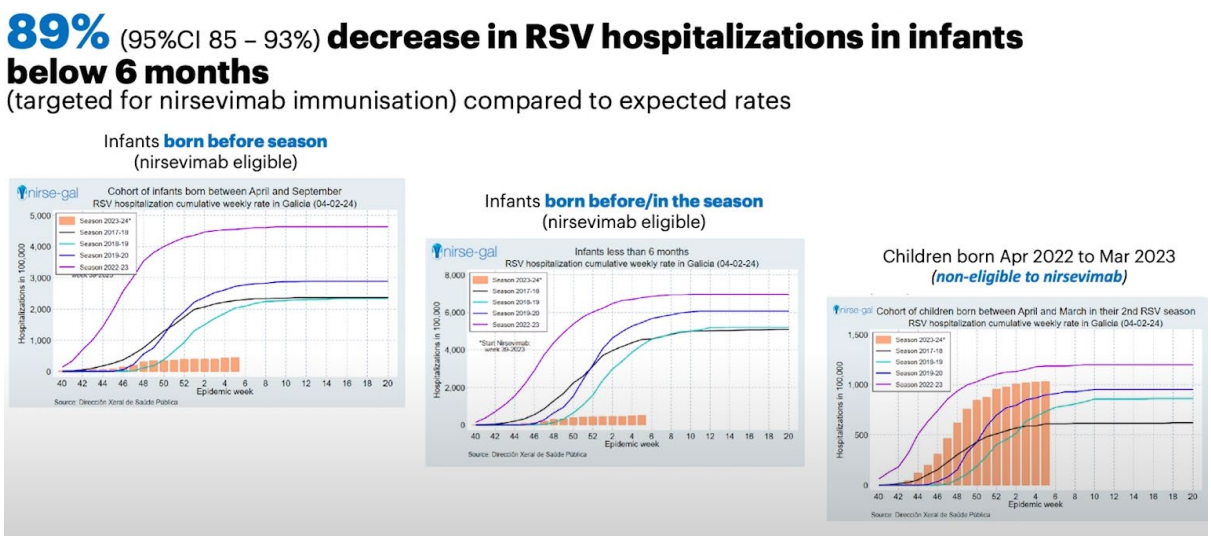


Figure 13. Cumulative weekly RSV hospitalisation rate in Galicia, by season, up to 24-03-2024. Infants 1 to 4 years old [Nirse-Gal.; 2024].

RWE experience continues to show an encouraging and positive picture of the acceptability and ease of implementation of nirsevimab

Currently available data from the above NIRSEGAL study from the Andalucía and Galicia regions of Spain indicate coverage rates of 93% in infants born during the RSV season (receiving nirsevimab at birth), 86% to 94% in infants receiving a catch-up dose at the beginning of the season, and 100% in infants born with risk factors [Nirse-Gal, 2024 & Dirección Xeral de Saúde Pública; 2024].

A reduction of 89% in RSV hospitalization in infants below 6 months (target for Nirsevimab immunization) was observed when compared to expected rates. [Martinon-Torres et al. ESWI Respiratory Virus Summit 2024 | ESWI 5th of March 2024 Brussels & online]



1.2. **Catalonia, Spain**

The effectiveness of Nirsevimab immunoprophylaxis against RSV-related outcomes in both Hospital and Primary Care settings was evaluated in Catalonia, Spain. This retrospective cohort study in infants in Catalonia, is available as a pre-print article in The Lancet.

Among 26,525 infants, a dose of nirsevimab led to significant effectiveness, with reductions of 87.6% and 90.1% in hospital and ICU admissions for bronchiolitis due to RSV, respectively [Coma, E et al.; 2024].

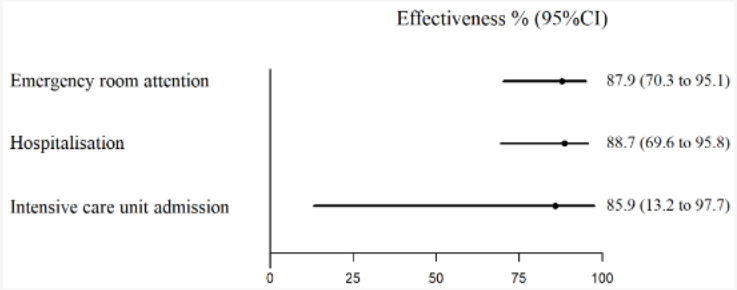
Moreover, substantial decreases were observed in less severe outcomes, including primary care attended bronchiolitis (48.1%), RSV infections (68.9%), viral pneumonia (60.7%), and hospital emergency visits for bronchiolitis (55.4%) [Coma, E et al.; 2024].

Effectiveness of Nirsevimab Immunoprophylaxis Against Respiratory Syncytial Virus-Related Outcomes in Hospital and Primary Care Settings: A Retrospective Cohort Study in Infants in Catalonia (Spain) by Ermengol Coma, Montse Martinez-Marcos, Eduardo Hermosilla, Jacobo Mendioroz Peña, Anna Reñé, Francesc Fina-Aviles, Aida Perramon, Clara Prats, Gloria Cereza, Pilar Ciruela, Valentí Pineda, Andrés Antón, Gemma Ricós-Furió, Antoni Soriano-Arandes, Carmen Cabezas :: SSRN

1.3. Navarra, Spain

- In 1177 infants studied, the risk of hospitalisation for RSV was 8.5% (8/94) among non-immunized infants vs 0.7% (8/1083) in those that were immunized
- 88.7% effectiveness against RSV hospitalization and similar figures were observed for ER and ICU admission.
- 1 hospitalization prevented for every 15.3 immunized infants immunized at birth of infants born between October and December 2023 (babies born in season)

Figure 3. Effectiveness of nirsevimab in preventing laboratory-confirmed respiratory syncytial virus cases.



Vaccines | Free Full-Text | Effectiveness of Nirsevimab Immunoprophylaxis Administered at Birth to Prevent Infant Hospitalisation for Respiratory Syncytial Virus Infection: A Population-Based Cohort Study (mdpi.com)

1.4. Three other regions, Spain

A multicentre hospital-based active surveillance in nine hospitals located in three autonomous regions in Spain (Murcia, Valencia, Valladolid).

- Nirsevimab population-based coverage ranged between 78.7% and 98.6%, depending on the hospital

- Nirsevimab effectiveness was 69.3% (95% CI: 36.4–86.2), 86.9% (95% CI: 77.1–92.9) and 97.0% (95% CI: 87.7–99.6) in Valencia, Murcia and Valladolid, respectively

Eurosurveillance | Early estimates of nirsevimab immunoprophylaxis effectiveness against hospital admission for respiratory syncytial virus lower respiratory tract infections in infants, Spain, October 2023 to January 2024

1.5. Luxembourg

Similarly, data from Luxembourg indicate a coverage rate of 84% (with some variation from 66% to 94% depending on maternity ward) for infants receiving nirsevimab at birth [Ernst, C et al.; 2024]. In 2023, 241 children under 5 years of age were hospitalised with a laboratory-confirmed RSV infection (i.e. cases), compared with 389 cases in 2022, representing decreases of 38% (389 vs 241) in cases under 5 years of age and 69% (232 vs 72) in cases of infants under 6 months old [Ernst, C et al.; 2024]. The length of hospital stay was significantly reduced from a mean of 5.1 days (SD:5.4) in 2022 compared to 3.2 days (SD:2.5) in 2023 ($p<0.001$). This significant reduction was most marked among infants < 6 months old (5.6 days in 2022 vs 3.4 days in 2023, $p<0.001$) compared to children ≥ 12 months old (4.2 days in 2022 vs 3.2 days in 2023, $p=0.17$), who were not the main target of the immunisation campaign [Ernst, C et al.; 2024]. The total number of RSV-related hospitalisation days decreased from 1,984 in 2022 to 771 in 2023 ($p<0.001$) [Ernst, C et al.; 2024].

- During the study period, the mean age of children was significantly higher in 2023 (14.4 months; SD: 12.9) compared to 2022 (7.8 months; SD: 10.1; $p<0.001$) (figure 15)
- In 2022, the largest age group of admission was up to the age of 6 months (59.6%; 232/389), whereas they accounted for 29.9% (72/241) of admissions ($p<0.001$) in 2023. (figure 15)
- Among the 241 children under 5 years of age hospitalised with an RSV infection in 2023, 213 (88.4%) were not immunised with nirsevimab (figure 15)
- Among 72 hospitalised infants up to 6 months of age, 47 (65.3%) were not immunised (figure 15)

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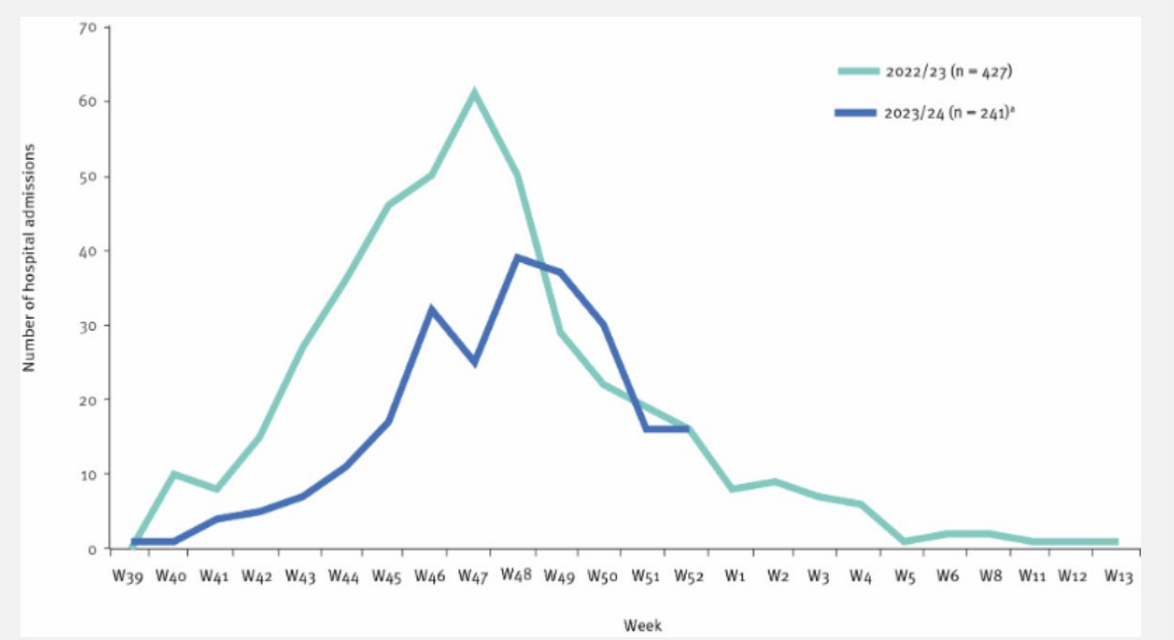

Figure 14. RSV hospital admission of children under 5 years of age by week in Luxembourg's national paediatric hospital, Luxembourg, 2022–2023 (n = 668) [Ernst, C et al.; 2024].

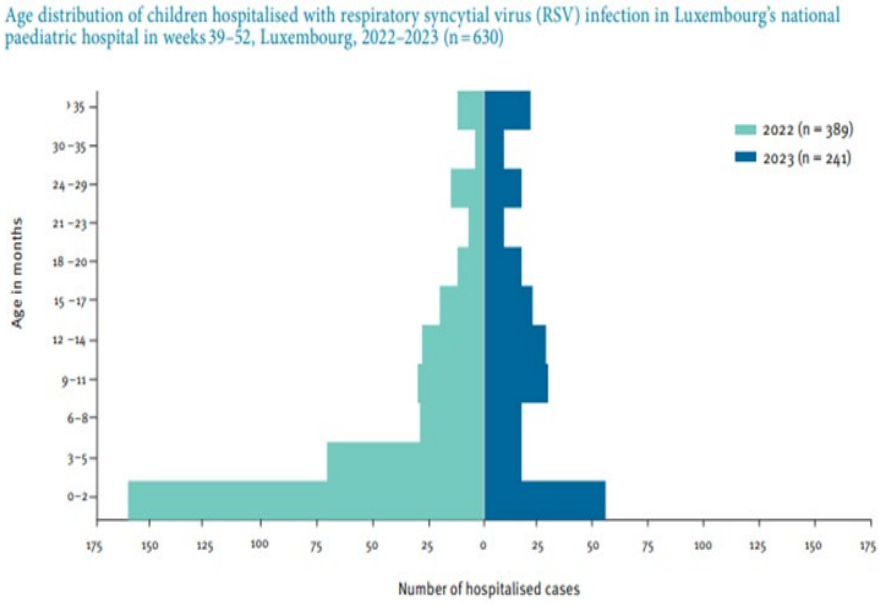

Figure 15. Age distribution of children hospitalised with RSV infection in Luxembourg's national paediatric hospital in weeks 39–52, Luxembourg, 2022–2023 (n = 630).

Eurosurveillance | Impact of nirsevimab prophylaxis on paediatric respiratory syncytial virus (RSV)-related hospitalisations during the initial 2023/24 season in Luxembourg

1.6. France

Since June 2017, AFPA (French Association of Ambulatory Pediatrics) and ACTIV (Association Clinique et Thérapeutique Infantile du Val de Marne) have set up a national monitoring network for pediatric infectious diseases. This network is based on the automated extraction of data from more than a hundred AFPA investigators.

Real-world data from this sentinel group in France have confirmed that the efficacy of nirsevimab against bronchiolitis is ≥80%, with a very significant reduction observed in cases in infants aged < 3 months [Infovac-France; 2024].

https://www.infovac.fr/reseau-pari-bronchiolites

France have collected data on the number of bronchiolitis cases (figures translated below) [Infovac-France; 2024].

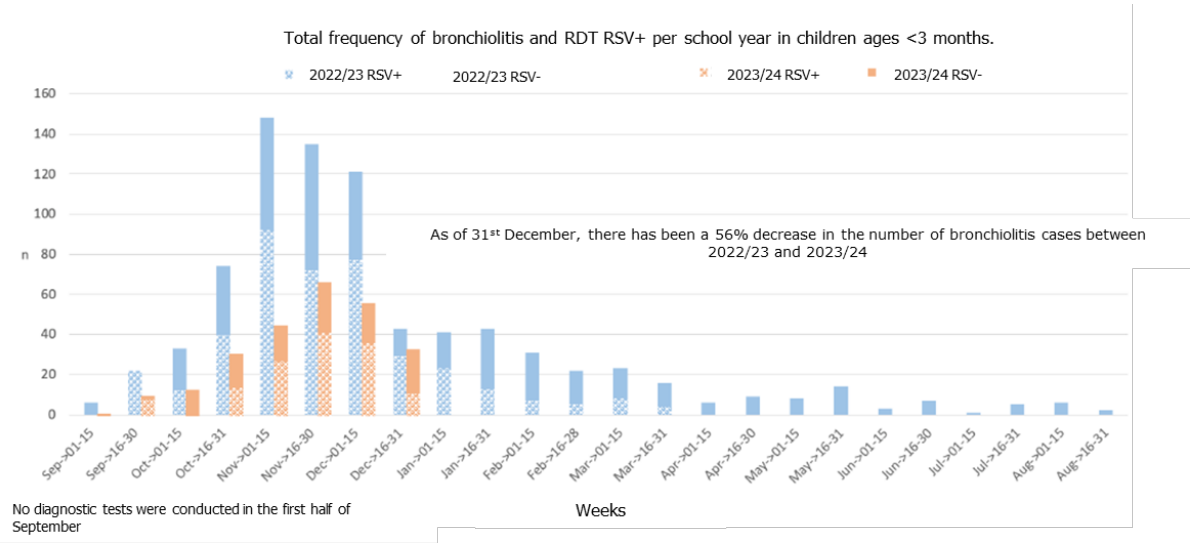

Figure 16. As of 31st December, there has been a 56% decrease in the number of bronchiolitis cases between 2022/23 and 2023/24 (last updated 2nd Jan 2024) [Infovac-France; 2024].

Liite 1. Yhteenveto nirsevimabia koskevista tosielämän tiedoista

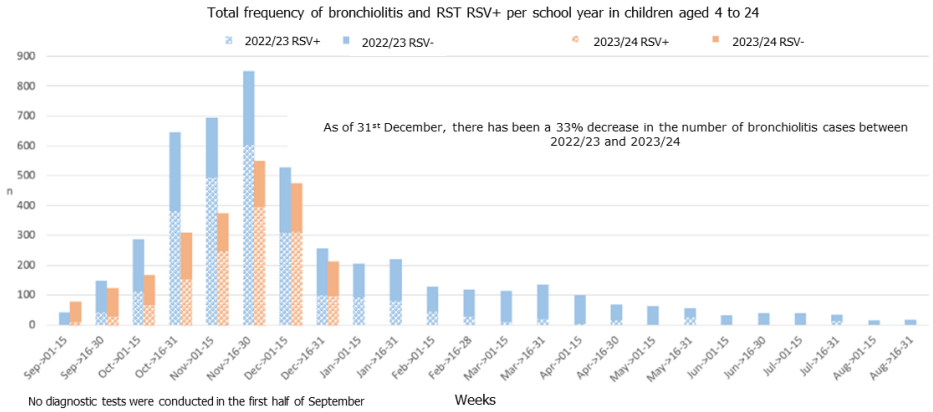

Figure 17: As of 31st December, there has been a 33% decrease in the number of bronchiolitis cases between 2022/23 and 2023/24 (last updated on 2nd Jan 2024) [Infovac-France; 2024].

ENVIE study[1, 2] is a multicenter prospective observational (case-control) study in 6 hospitals in France including 690 infants <12 months hospitalized for bronchiolitis with RSV between 15 Oct and 10 Dec 2023 where 345 controls were children hospitalized in the same hospitals for non-RSV-related diseases.

- 83.0% (95% CI 73.4-89.2) against hospitalization for bronchiolitis associated with RSV
- 69.6% (95% CI 42.9-83.8) against bronchiolitis associated with RSV requiring intensive care
- 67.2% (95% CI 38.6-82.5) against bronchiolitis associated with RSV requiring respiratory assistance

1. Effectiveness of Nirsevimab in Children Hospitalised With RSV Bronchiolitis (ENVIE). ClinicalTrials.gov ID NCT06030505. Study Details | Effectiveness of Nirsevimab in Children Hospitalised With RSV Bronchiolitis | ClinicalTrials.gov
2. Recommandation vaccinale contre les infections à VRS chez les femmes enceintes (has-sante.fr)

Publication on data from **Saint-Etienne University Hospital** in France show that older children than previous years were hospitalized.

- Estimated nirsevimab administration rate of 76.5% (572 immunization for 748 births) in newborns
- 84.5% of the 705 patients with acute bronchiolitis in emergency departments had not vaccinated their child (preliminary unconsolidated data), indicating a majority were unprotected.

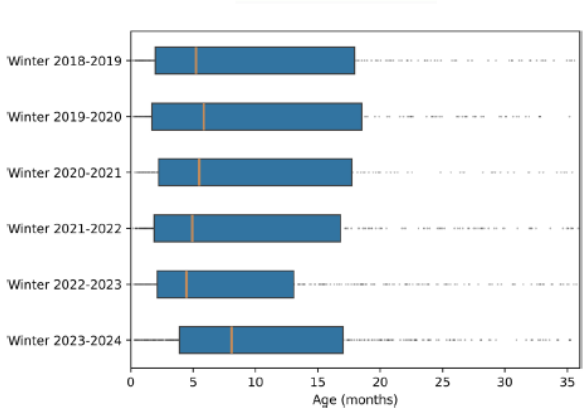

FIGURE 1 Box & Whisker plot of age distribution of cases of respiratory syncytial virus infections presenting at the University Hospital of Saint-Etienne during the winter season by epidemic year. The orange line is the median.

Cantais A et al. J Med Virol. 2024;96:e29483. https://doi.org/10.1002/jmv.29483

1.7. USA (CDC, Centers for Disease Control and Prevention)

RSV is the leading cause of hospitalisation among U.S. infants. In August 2023, the CDC recommended nirsevimab, to protect infants aged <8 months against RSV-associated lower respiratory tract infection in their first RSV season. The below analysis provides the first estimate from the U.S. for post-introduction nirsevimab effectiveness among U.S. infants during their first RSV season.

Among 1,036 eligible infants, 699 infants at four sites met inclusion criteria, including 407 (58%) case-patients and 292 (42%) control patients [Moline, H.L. et al.; 2024]. The reasons 337 infants were excluded from this analysis, included enrolment at a site with fewer than five infants who had received nirsevimab (296 from 3 US Sites), receipt of nirsevimab <7 days before symptom onset (20), missing or inconclusive RSV test result (20), maternal receipt of RSV vaccine during pregnancy (22), and receipt of palivizumab (10); reasons for exclusion are not mutually exclusive [Moline, H.L. et al.; 2024]. Receipt of nirsevimab was more frequent amongst infants with high-risk medical conditions than those without these conditions (46% versus 6%, p<0.001) [Moline, H.L. et al.; 2024]. Time since receipt of nirsevimab to Acute Respiratory Infection (ARI) symptom onset ranged from 7 to 127 days with a median of 45 days (IQR = 19–76 days) (Figure) [Moline, H.L. et al.; 2024]. Overall, six (1%) case-patients and 53 (18%) control patients received nirsevimab; among all included infants, receipt of nirsevimab ranged from 4% to 12% by site. Nirsevimab effectiveness was 90% (95% CI = 75–96) against RSV-associated hospitalisation [Moline, H.L. et al.; 2024].

In this multisite analysis of 699 infants hospitalised with ARI during their first RSV season, receipt of nirsevimab was 90% effective against RSV-associated hospitalisation at a median of 45 days from receipt of nirsevimab to ARI symptom onset [Moline, H.L. et al.; 2024]. This early effectiveness estimate supports existing recommendations for the prevention of severe RSV disease in infants in their first RSV season [Moline, H.L. et al.; 2024].

The strengths of this first estimate of U.S. post-introduction nirsevimab effectiveness include enrolment of infants using a standardised ARI definition, systematic RSV testing, and receipt of nirsevimab verification with state immunisation information systems or medical records for all infants [Moline, H.L. et al.; 2024]. In this analysis, the median interval from receipt of nirsevimab was 45 days, whereas the median duration of the U.S. RSV season before the COVID-19 pandemic was 189 days [Hamid S. et al.; 2023]. In clinical trials, nirsevimab remained highly efficacious against RSV-associated lower respiratory tract infection in infants through 150 days after receipt of nirsevimab, consistent with an extended half-life of 63–73 days [Hammitt L.L. et al.; 2022].

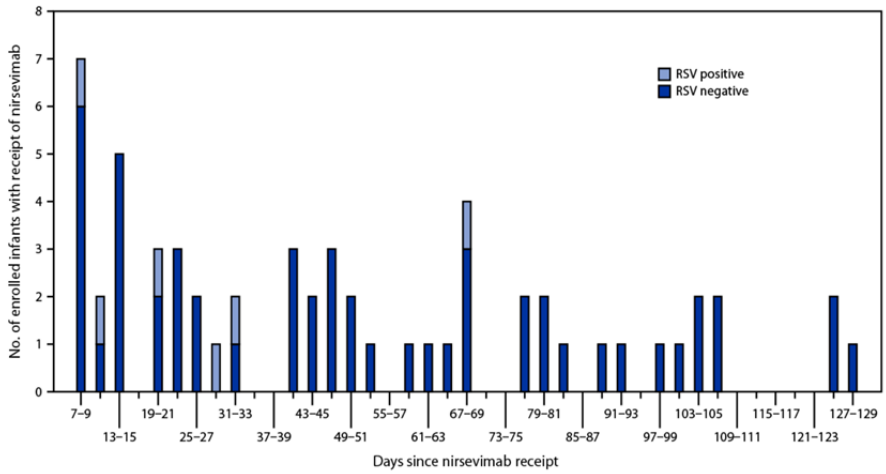

Figure 18: time from receipt of nirsevimab* to symptom onset among infants born during or entering their first respiratory syncytial virus season who were hospitalized with acute respiratory illness, by respiratory syncytial virus test result — New Vaccine Surveillance Network, October 2023–February 2024. *Days 0–6 are not included because infants with receipt of nirsevimab within 7 days of symptom onset were excluded from this analysis. [Moline, H.L. et al;2024]

Liite 1. Yhteenveto nirsevimabia koskevista tosielämän tiedoista

Table 1. Real World Evidence and Resources From Other Countries

Country/Region	Link	Comment
Madeira, Portugal	Look up (madeira.gov.pt)	
United States	RSVVaxView | CDC	Weekly Respiratory Syncytial Virus (RSV) Vaccination Dashboard
United States	Nirsevimab Receipt and Intent for Infants, United States | CDC	Nirsevimab Receipt and Intent for Infants, United States
United States	https://www.aap.org/en/patient-care/respiratory-syncytial-virus-rsv-prevention/nirsevimab-implementation-resources/	Implementation ressources
United States	https://www.aap.org/en/patient-care/respiratory-syncytial-virus-rsv-prevention/nirsevimab-implementation-resources/	Nirsevimab FAQ
United States	https://www.aap.org/en/patient-care/respiratory-syncytial-virus-rsv-prevention/respiratory-season-webinar-series/	Webinar series

Liite 1. Yhteenveto nirsevimabia koskevista tosielämän tiedoista