

Virus Respiratorio Sinciziale nell'infanzia: la strada verso la prevenzione universale

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L'esperienza sul campo delle nuove strategie di prevenzione (Galizia)





L'ESPERIENZA SUL CAMPO DELLE NUOVE STRATEGIE DI PREVENZIONE (GALIZIA)

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A topographic map of the Iberian Peninsula, showing Spain and Portugal. The region of Galicia in northwestern Spain is highlighted with a red border. Major cities like Madrid, Barcelona, and Lisbon are labeled. The map also shows neighboring countries like France, Andorra, and Gibraltar.

1.- INTRODUCTION

Galicia

- 2.7 million inhabitants
- 14.500 births (2022)
- Migration uncommon




Health system

- SERGAS - Healthcare provider
- 98% public health coverage
- 7 healthcare areas
- 14 hospitals
- Centralized electronic health records

INMUNIZATION SCHEDULE

April 2024

VACINACIÓN	IDADE																	
	PRENATAL	0 MESES	2 MESES	4 MESES	6 MESES	11 MESES	12 MESES	18 MESES	3 ANOS	6 ANOS	12 ANOS	14 ANOS	15-18 ANOS	19-64 ANOS	65 ANOS	80 ANOS		
VIRUS RESPIRATORIO SINCIETIAL (VRS)		AcVRS (de 0 a 5 meses) (1)																
ROTAIVIRUS			RV (2)	RV (2)														
DIPTERIA-TÉTANO E TOSE FERINA	dTpa		DTPa	DTPa		DTPa				DTPa		Td	Td	Td	Td			
POLIOMIELITE			VPI	VPI		VPI				VPI								
HAEMOPHILUS INFLUENZAE B			HB	HB		HB												
HEPATITE B			HB (3)	HB		HB				HB								
ENFERMIDADE MENINGOCÓCICA			MenB	MenB MenACWY (4)				MenB MenACWY				MenACWY	MenACWY					
SARAMPELO-RUBÉOLA E PAROTIDITE								TV		TV		TV	TV					
VARICELA								VVZ	VVZ		VVZ	VVZ	VVZ					
VIRUS DO PAPILOMA HUMANO											VPI	VPI						
ENFERMIDADE PNEUMOCÓCICA			VNC	VNC	VNC	VNC											VNC	
HERPES ZÓSTER																	HZ (5)	HZ (5)
GRIFE	Gripe									Gripe (6 meses a 59 meses)							Gripe (60 anos en diante)	

 ADMINISTRACIÓN SISTEMÁTICA
  ADMINISTRACIÓN EN PERSOAS SUSCEPTIBLES OU NON VACINADAS CON ANTERIORIDADE
  VACINA COMBINADA

(1) Vacinación durante a tempada de VRS (ver instrución específica). (2) En nados a partir do 1 de agosto de 2025. (3) Vacínase con pauta 0, 2, 4 e 11 meses (4 doses) os fillos de nai portadora ou con cribado descoñecido de hepatite B durante o embarazo. (4) En nados a partir do 1 de xuño de 2023. (5) En nados a partir do 1 de xaneiro de 1958. (6) En nados a partir do 1 de xaneiro de 1943.

Vacuna/antígeno: TRIPLE VÍRICA

Dosis: Dosis 2

	2017	2018	2019	2020	2021	2022
	Cobertura %	Cobertura %	Cobertura %	Cobertura %	Cobertura %	Cobertura %
GALICIA	96,24 %	93,13 %	93,82 %	94,00 %	93,96 %	94,54 %

Vacuna/antígeno: HEXAVALENTE-HiB

Dosis: Recuerdo 1

	2017	2018	2019	2020	2021	2022
	Cobertura %	Cobertura %	Cobertura %	Cobertura %	Cobertura %	Cobertura %
GALICIA	96,55 %	95,87 %	96,42 %	95,41 %	95,10 %	93,98 %

Vacuna/antígeno: NEUMOCOCO CONJUGADA

Dosis: Recuerdo 1

	2017	2018	2019	2020	2021	2022
	Cobertura %	Cobertura %	Cobertura %	Cobertura %	Cobertura %	Cobertura %
GALICIA	93,34 %	95,55 %	96,02 %	95,28 %	97,16 %	93,83 %

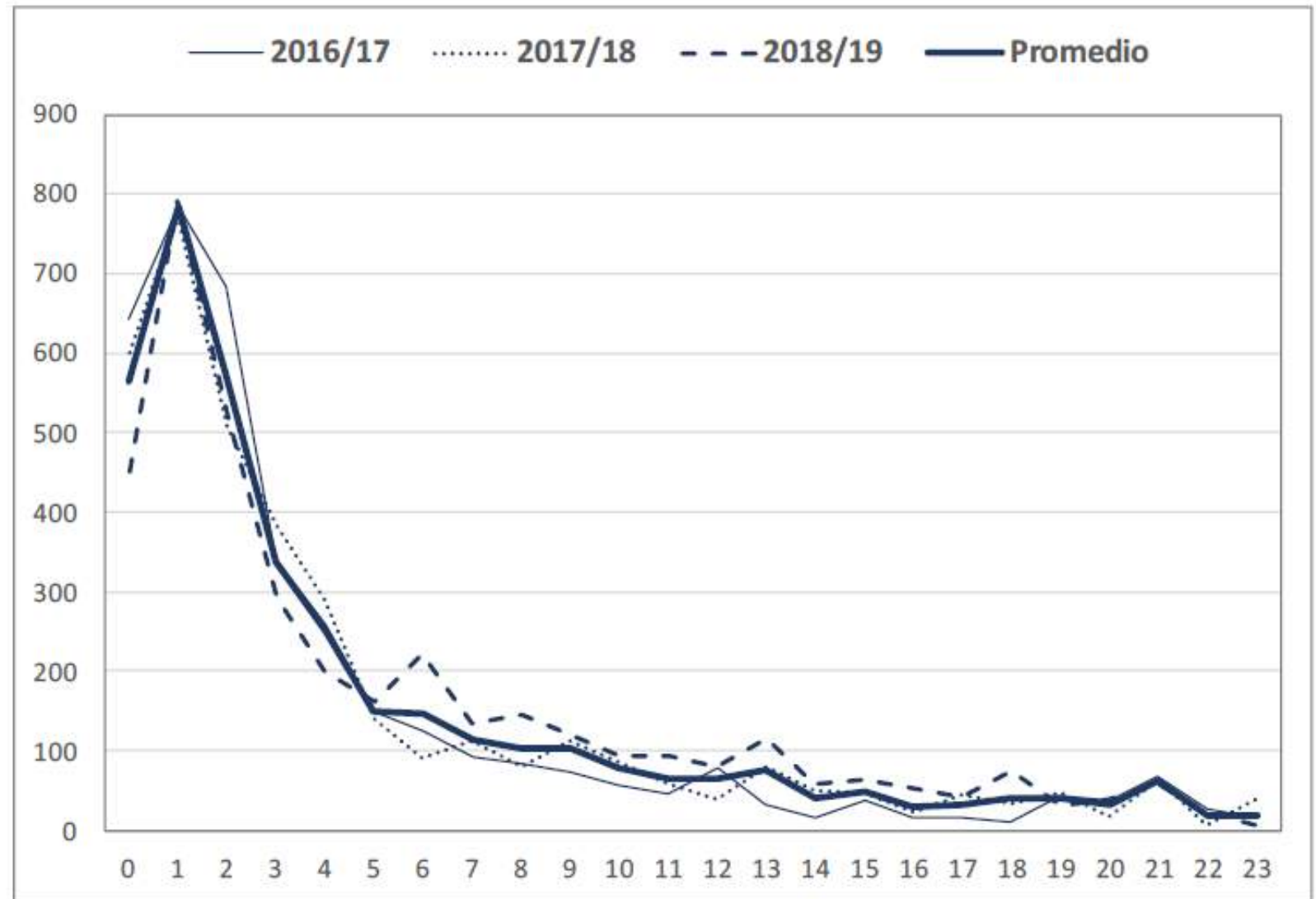
**PEDIATRIC
VACCINATION
COVERAGE >90%**





2.- RSV IN GALICIA

RSV-associated acute hospitalizations incidence rate by age (months) during 3 seasons and average in Galicia





Age category	Year	RSV hospitalization (N)	Population size	RSV-hospitalization rate per 100,000 children
> 6 months	2016	64	18708	342.1
	2017	42	18945	221.69
	2018	40	18387	217.55
	2019	91	16567	549.28
	2022	76	14479	524.9
< 6 months	2016	711	18708	3800.51
	2017	436	18945	2301.4
	2018	370	18387	2012.29
	2019	601	16567	3627.69
	2022	522	14479	3605.22

RSV hospitalization numbers extracted from Configuration Management Data Base (conjunto mínimo básico de datos, CMBD) with the ICD-10-ES codes J21.0, J20.5, J12.1 and B97.4 included in the first 3 diagnostic positions.



TABLE 2 Incidence rate ratio (IRR) of primary care emergency (PCE) visits and hospital emergencies (HE) along with their 95% confidence intervals (CI) in RSV hospitalized children compared to those not hospitalized children.

Follow-up time (days)	Outcome	Hospitalized (N = 3313)		Not Hospitalized (N = 3313)		IRR (95% CI)
		Mean (SD)	% (N)	Mean (SD)	% (N)	
-30 to -1	PCE	0.2 (0.5)	14.9% (495)	0.0 (0.2)	3.2% (105)	4.89 (4.03–5.99)
	HE	0.9 (1)	58.4% (1936)	0.1 (0.4)	9.9% (328)	6.52 (5.88–7.25)
0 to 89	PCE	0.1 (0.5)	9.9% (327)	0.1 (0.3)	5.6% (185)	1.54 (1.31–1.82)
	HE	0.5 (0.9)	30.4% (1006)	0.2 (0.5)	12.5% (413)	2.39 (2.17–2.63)
90 to 364	PCE	0.7 (1.5)	30.7% (1017)	0.4 (1.0)	22.8% (755)	1.29 (1.21–1.39)
	HE	1.6 (2.2)	58.4% (1934)	0.8 (1.4)	35.9% (1190)	1.69 (1.61–1.77)
365 to 729	PCE	0.8 (1.6)	31.8% (1055)	0.5 (1.2)	22.6% (749)	1.25 (1.17–1.33)
	HE	1.4 (2.3)	49.5% (1641)	0.7 (1.6)	30.9% (1023)	1.45 (1.38–1.52)
≥730	PCE	1.7 (3.2)	41.1% (1362)	1.2 (2.6)	32.9% (1090)	1.13 (1.08–1.17)
	HE	2.1 (3.4)	50.6% (1676)	1.3 (2.6)	36.1% (1197)	1.24 (1.20–1.29)

Note: N: total number of children who attended at least once to primary care or hospital emergency. %, percentage of children who attended at least once to primary care or hospital emergency.

Abbreviation: SD, standard deviation.

Percentage of positive results in the RSV surveillance system that occur during waves defined by a threshold of 10%, 5%, and 3%.



Weeks with epidemic wave during different seasons defined by a threshold of 10%, 5%, and 3%.

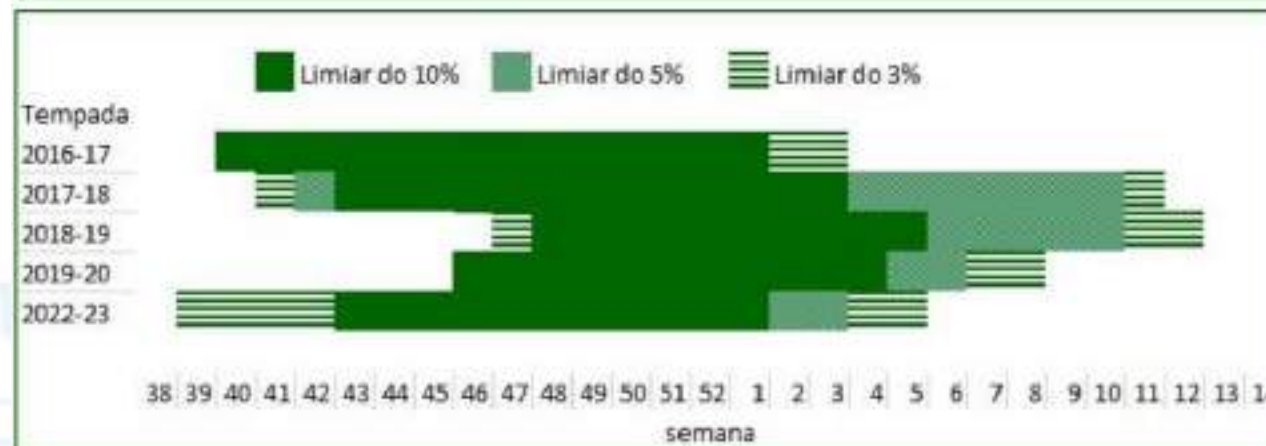


Table 3. Outcomes through 150 Days after the Injection.*

Outcome	Nirsevimab (N = 686) no. (%)	Placebo (N = 342)	Efficacy (95% CI)†	Cases Averted per 1000 Infants Treated (95% CI)‡	Number Needed to Treat (95% CI)§
Medically attended RSV-associated lower respiratory tract infection on any test result¶	17 (2.5)	37 (10.8)	77.0 (59.8 to 86.8)	83.4 (62.0 to 105.0)	12 (10 to 17)
Medically attended RSV-associated lower respiratory tract infection on central test result¶	15 (2.2)	33 (9.6)	77.2 (58.7 to 87.5)	74.7 (53.0 to 95.0)	14 (11 to 19)
Medically attended lower respiratory tract infection of any cause¶	60 (8.7)	62 (18.1)	51.5 (32.6 to 65.2)	93.6 (63.0 to 124.0)	11 (9 to 16)
Hospitalization for any respiratory illness due to RSV on any test result	9 (1.3)	11 (3.2)	59.0 (2.1 to 82.9)	19.0 (5.5 to 32.0)	53 (32 to 182)
Hospitalization for any respiratory illness due to RSV on central test result	7 (1.0)	9 (2.6)	61.1 (-3.7 to 85.4)	16.1 (4.5 to 28.0)	62 (36 to 223)
Hospitalization for any respiratory illness of any cause	16 (2.3)	14 (4.1)	42.8 (-15.8 to 71.7)	17.7 (2.0 to 33.0)	57 (31 to 500)

	Placebo group (n=786)	Nirsevimab group (n=1564)	Relative risk reduction (95% CI)	p value
Medically attended RSV LRTI*	51 (6%)	19 (1%)	79.5% (65.9–87.7)	<0.0001
Hospital admission for medically attended RSV LRTI†	21 (3%)	9 (1%)	77.3% (50.3–89.7)	0.0002
Very severe RSV LRTI‡	18 (2%)	5 (<1%)	86.0% (62.5–94.8)	<0.0001
Medically attended LRTI of any cause‡§	149 (19%)	191 (12%)	35.4% (21.5–46.9)	<0.0001
Hospital admission for respiratory illness of any cause‡§	51 (6%)	57 (4%)	43.8% (18.8–61.1)	0.0022

Relative risk reduction (95% CI) and p values were estimated on the basis of Poisson regression with robust variance across all case definitions. LRTI=lower respiratory tract infection. RSV=respiratory syncytial virus. *The model included study code, treatment group, and stratification factors (age at randomisation and hemisphere) as covariates obtained from PROC MIANALYZE after missing data imputation. †The model included study and treatment group as covariates for pooled studies obtained from PROC MIANALYZE after missing data imputation. ‡The model included treatment as a factor. §Included are all medically attended LRTIs according to the investigator’s judgement, regardless of whether they met the clinical criteria for the definition of medically attended LRTI (appendix p 4).

Table 2: Efficacy of nirsevimab weight-band dose on different case definitions of medically attended LRTI to 150 days post-dose (intention-to-treat population)



Table 1: Adverse reactions

MedDRA SOC	MedDRA Preferred Term	Frequency
Skin and subcutaneous tissue disorders	Rash ^a	Uncommon
General disorders and administration site conditions	Injection site reaction ^b	Uncommon
	Pyrexia	Uncommon

^a Rash was defined by the following grouped preferred terms: rash, rash maculo-papular, rash macular.

^b Injection site reaction was defined by the following grouped preferred terms: injection site reaction, injection site pain, injection site induration, injection site oedema, injection site swelling.

3.- RSV INMUNIZATION CAMPAIGN

Season 2023/2024

I

Seasonal

Born from September 25, 2023 to March 31, 2024. They will receive a dose after birth.

II

Catch-up

Born between 1 April and 24 September 2023. They will receive a dose at the beginning of the season.

III

High-risk

Born, with risk factors, between 1 October 2021 and 31 March 2023. See the full list in **Table 1**.



Seasonal

All infants born during RSV season, i.e. from 25th September 2023 to 31 March 2025, will receive 1 dose of nirsevimab in the hospital, in the first 24 hours of life, unless medically contraindicated.



Catch-up

Immunization of all infants under 6 months at the start of the RSV season will receive 1 dose of nirsevimab in their reference hospitals following a flexible electronic personal citation, within 3 weeks of the start of the RSV prophylaxis campaign.



High risk

Any infant with any of the conditions listed below and under 24 months of age at the start of the RSV campaign, will be cited in the first week of the campaign to receive nirsevimab in their reference hospital.

- Patients with congenital heart diseases featuring significant hemodynamic impact.
- Severe immunosuppression
- Bronchopulmonary dysplasia
- Congenital metabolic disorders
- Neuromuscular diseases
- Severe pulmonary diseases
- Genetic syndromes with significant respiratory issues
- Down syndrome
- Cystic fibrosis
- Infants on palliative care
- * Premature infants under 35 weeks (including gestational age <29 weeks), a single dose before reaching 12 months of age.

The screenshot shows a YouTube video player for a webinar. The video frame features a baby in a meditative pose against a green background with the text "RESPIRA TRANQUILO" and "Immuniza ao teu fillo/a fronte ao VRS (Virus Respiratorio sincitial)". The video player includes a search bar at the top, a play button, and a progress bar. Below the video, there is a "WEBINAR" section with a "Suscribirse" button and a view count of 642. To the right, a playlist titled "RESPIRA TRANQUILO" lists several related videos with their respective durations.

Video Title	Duration
RESPIRA TRANQUILO	4:53
WEBINAR	7:41
POR QUE DEBO IMMUNIZAR AO MEU FILLO FRONTE AO...	1:51
COMO SE VAI A REALIZAR A IMMUNIZACION FRONTE AO...	2:14
QUE IMPORTANCIA TEN O VRS	2:27
EN QUE CONSISTE A IMMUNIZACION FRONTE AO...	2:19
CALES SON AS INDICACIONES DE IMMUNIZACION FRONTE...	3:04
PÓDESE UTILIZAR EN PACIENTES PREMATUROS E...	1:36
É SEGURA A PROFILAXE FRONTE AO VRS	1:17

Campaña de inmunización fronte ao virus respiratorio sincitial. Videos informativos. Dirección Xeral de Saúde Pública. Available from: https://www.youtube.com/watch?v=F8uFLIqKOS8&list=PLhArxgNG-_GcrkaDw8V9M0EKFYOY3EReD&index=1



Para quen é a inmunización pasiva?

- **Neonatos nados en tempada** (25 de setembro de 2023 ao 31 de marzo de 2024). Recibirán a inmunización no hospital tras o nacemento.
- **Menos/as nados antes da tempada** (desde o 1 de abril de 2023). Serán citados ao comezo desta para inmunizarse canto antes.
- **Prematuros e lactantes con alto risco de enfermidade grave por VRS.** Serán citados ao comezo da campaña.

Como se administra?

A administración será no músculo da zona anterolateral da coxa, como o resto das vacinas.



PROGRAMA GALEGO DE VACINACIÓN



<https://www.torga.gal/saude-publica/PGV>



Anticorpo fronte ao virus respiratorio sincitial (VRS)

PREVIR A ENFERMIDADE GRAVE E A HOSPITALIZACIÓN



Que é o virus respiratorio sincitial (VRS)?

É un virus estacional frecuente e moi contagioso que infecta case todos os lactantes nos dous primeiros anos de vida.

É unha das principais causas de bronquiolite e pneumonía en lactantes e nenos/as pequenos.

Ademais é a principal causa de hospitalización durante o primeiro ano de vida.

Cal é o período de circulación do VRS?

Adoita circular desde o outono ata a primavera (outubro a marzo).

Como se transmite?

A través das secrecións orais ou nasais:

- De persoa a persoa ao tocir ou esbirrar.
- Tamén por contacto con superficies contaminadas.

Que síntomas presenta?

Os síntomas leves son moi similares aos dun resfriado (conestión, tose, diminución do apetito...).

Non obstante, os síntomas poden progresar e requirir atención sanitaria.

Existe un tratamento específico?

No actualidade non existe un tratamento concreto para o VRS.

O tratamento vai dirixido a aliviar os síntomas, por este motivo é fundamental a prevención.

En que consiste a prevención do VRS?

Medidas hixiénicas

- Lavado de mans.
- Lavado frecuente de roupa, roupa de cama, superficies, etc.

- Reducir visitas, bicos e abrazos aos lactantes.

Inmunización pasiva

A Dirección Xeral de Saúde Pública introduce no Calendario de Inmunización ao longo de toda a vida un anticorpo (Insevimal) que consegue protexer o lactante de forma efectiva desde a súa administración.

Ao tratarse dun anticorpo, a protección é inmediata, xa que non depende do sistema inmunitario do neonato (como sucede coas vacinas).



Study

Evaluation of the effectiveness and impact of Nirsevimab in Galicia

The purpose of NIRSE-GAL is to evaluate the impact of the inclusion of nirsevimab in the Galician immunisation schedule on the prevention of Respiratory Syncytial Respiratory Syncytial Virus (RSV) infections in children.

[View report](#)



[Download report](#)



4.- RSV SURVEILLANCE & NIRSE-GAL STUDY



Objectives of the study

The primary objective of the study is to evaluate the effectiveness of nirsevimab on hospitalization for Respiratory Sincitial Virus (RSV) related to lower respiratory track infections (LRTI) during the RSV season (which starts on October 1st and ends on March 1st) in 3 groups of children: Infants born during RSV season, infants younger than 6 months at the start of RSV season and high-risk children younger than 24 months at the start of RSV season.

Secondary objectives include:

- I To evaluate nirsevimab coverage.
- II To estimate the effectiveness of nirsevimab in Reducing the risk of:
 1. Very severe RSV-related LRTI defined by requiring neonatal and/or pediatric ICU admission.
 2. Very severe RSV-related LRTI defined by label of severity.
 3. All cause LRTI hospitalization
 4. All cause hospitalization
- III To evaluate the impact of nirsevimab on primary care/healthcare consumption.
- IV To assess longitudinally the impact of nirsevimab on (recurrent) wheezing and asthma.
- V To study the above mentioned primary and secondary endpoints in the 2nd and 3rd year after nirsevimab administration.

Vaccination coverage

Immunized in campaign: infants born after September 25 (up to 31-03-2024)

92,4%

with a total of **6,890** immunized infants

Catch-up vaccinated: infants born between April 1 and September 24 (up to 31-03-2024)

84.8%

with a total of **6,237** immunized infants

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

Evolution of the RSV epidemic wave

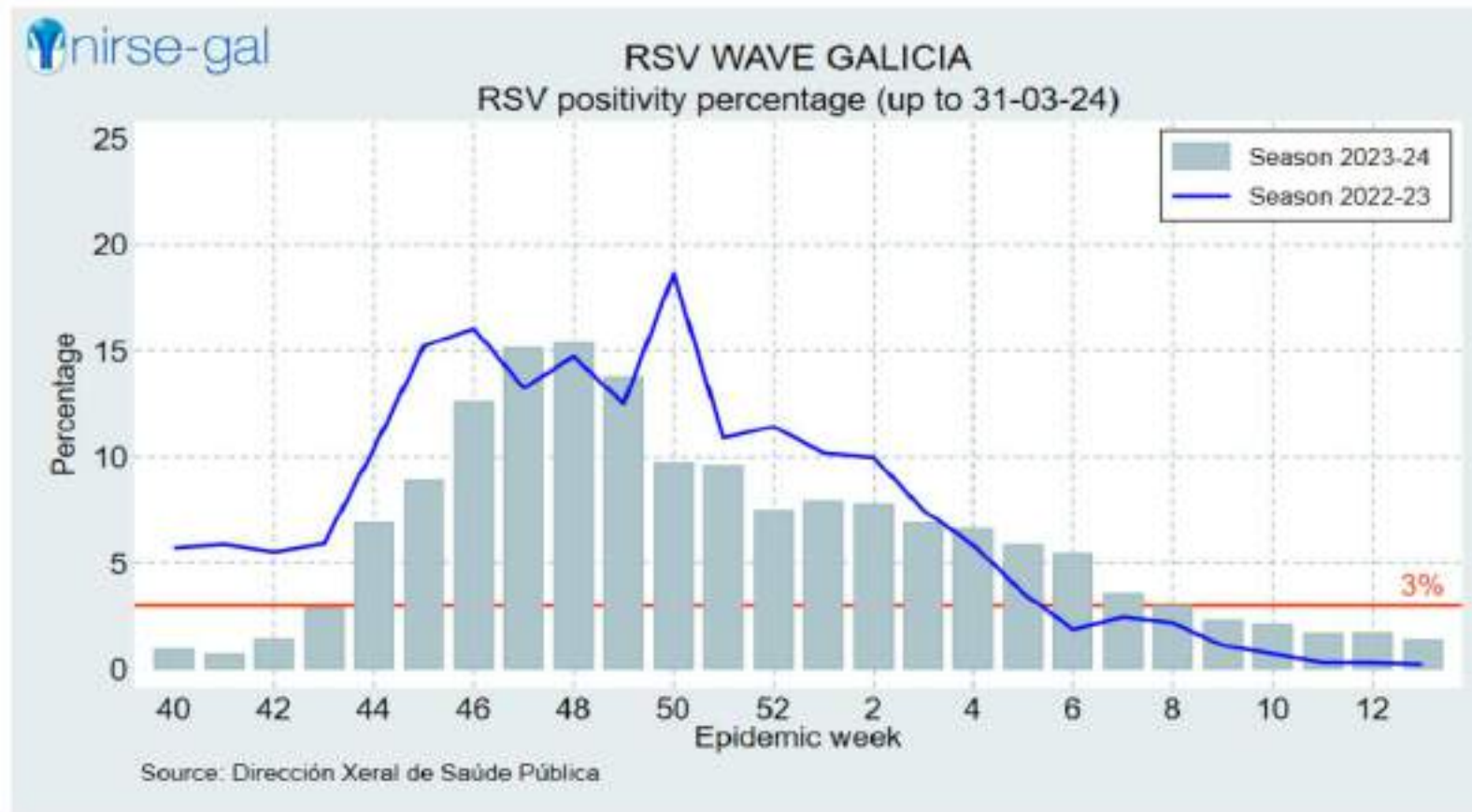
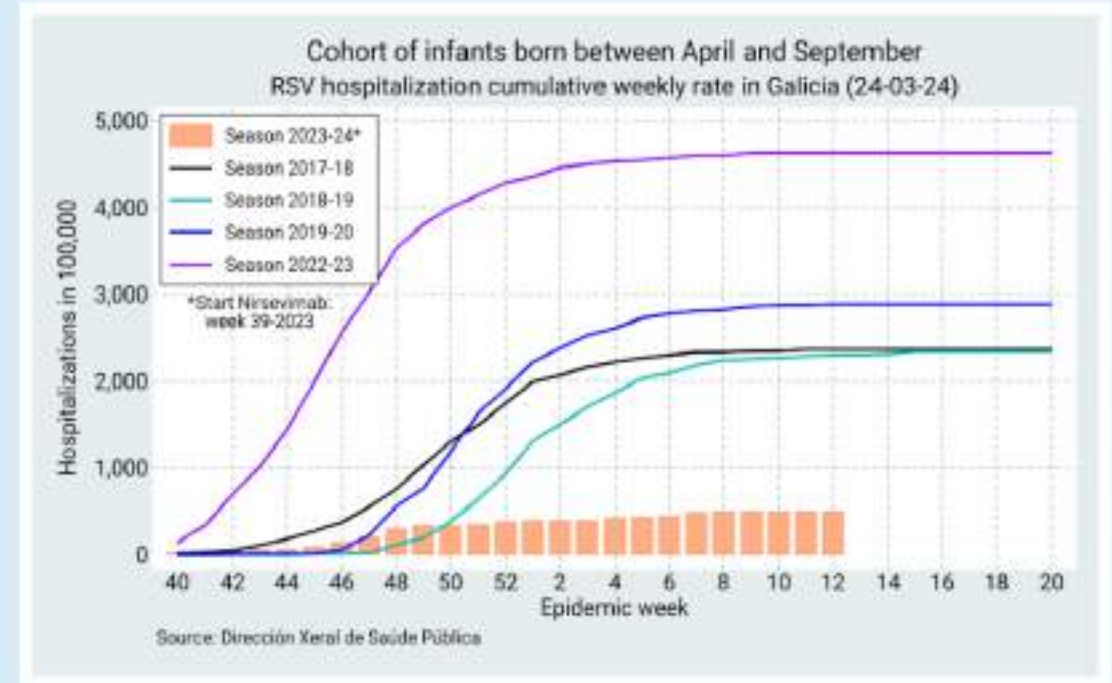
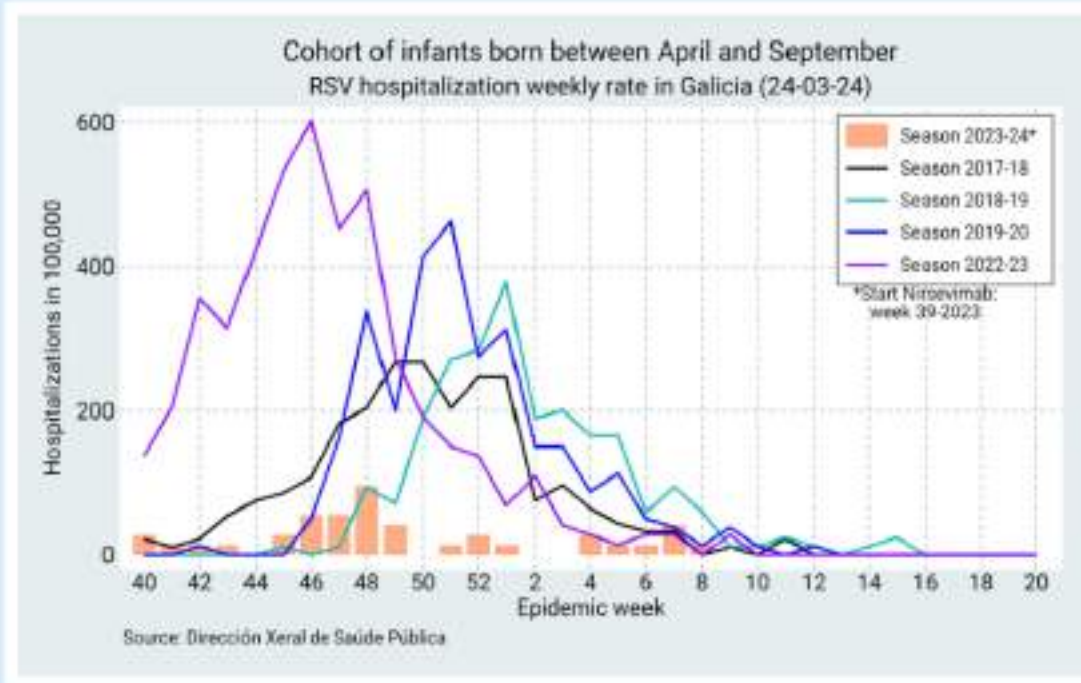


Figure 4. Total population positivity percentage (RSV) in Galicia, in seasons 2022-23 and 2023-24 up to 31-03-2024.

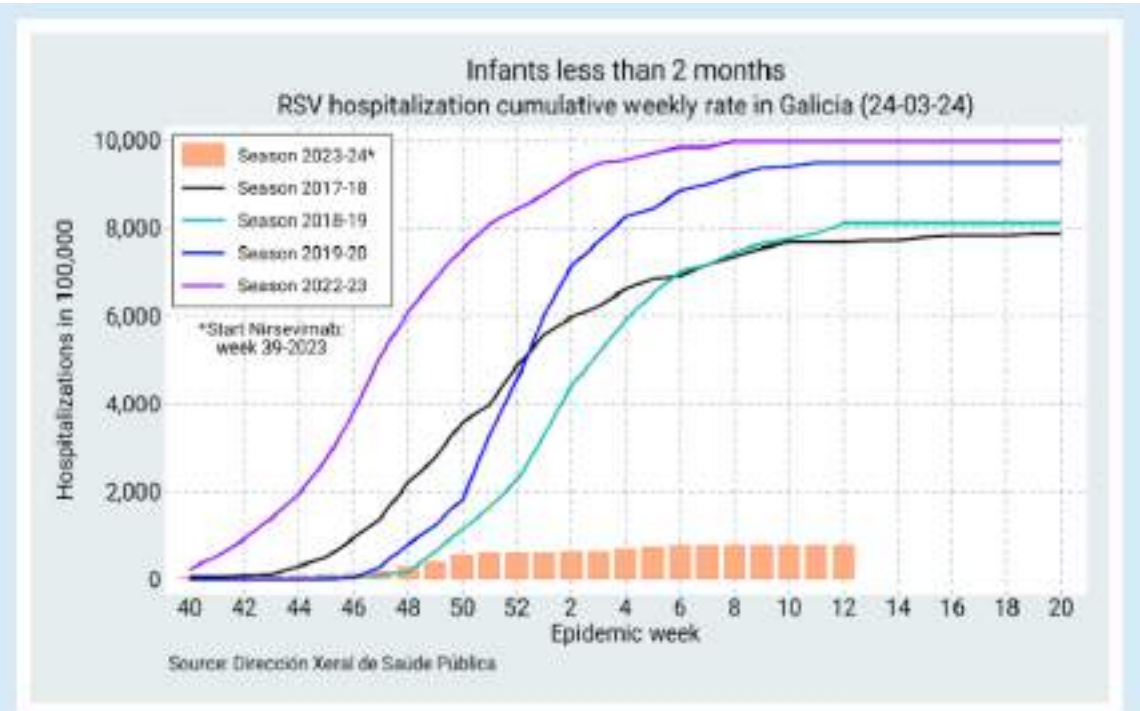
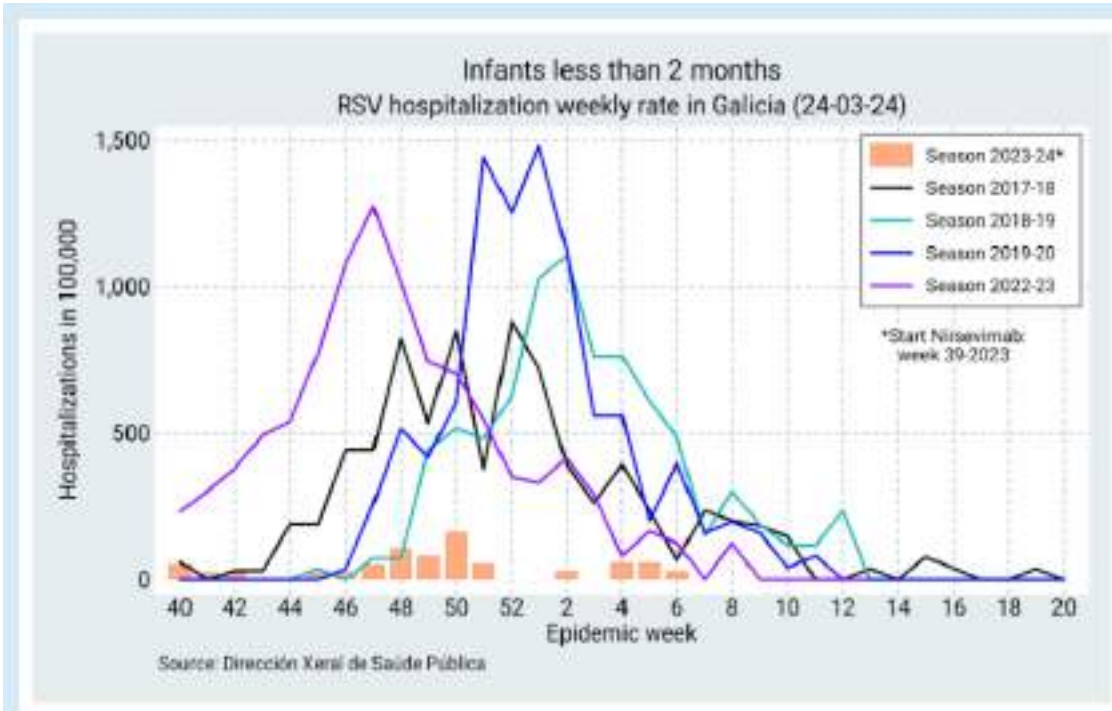
Cohort of infants born between April – September (Catch-up)



Weekly RSV hospitalization rate in Galicia, by season, up to 31-03-2024. Cohort of infants born between April and September.

Cumulative weekly RSV hospitalization rate in Galicia, by season, up to 31-03-2024. Cohort of infants born between April and September

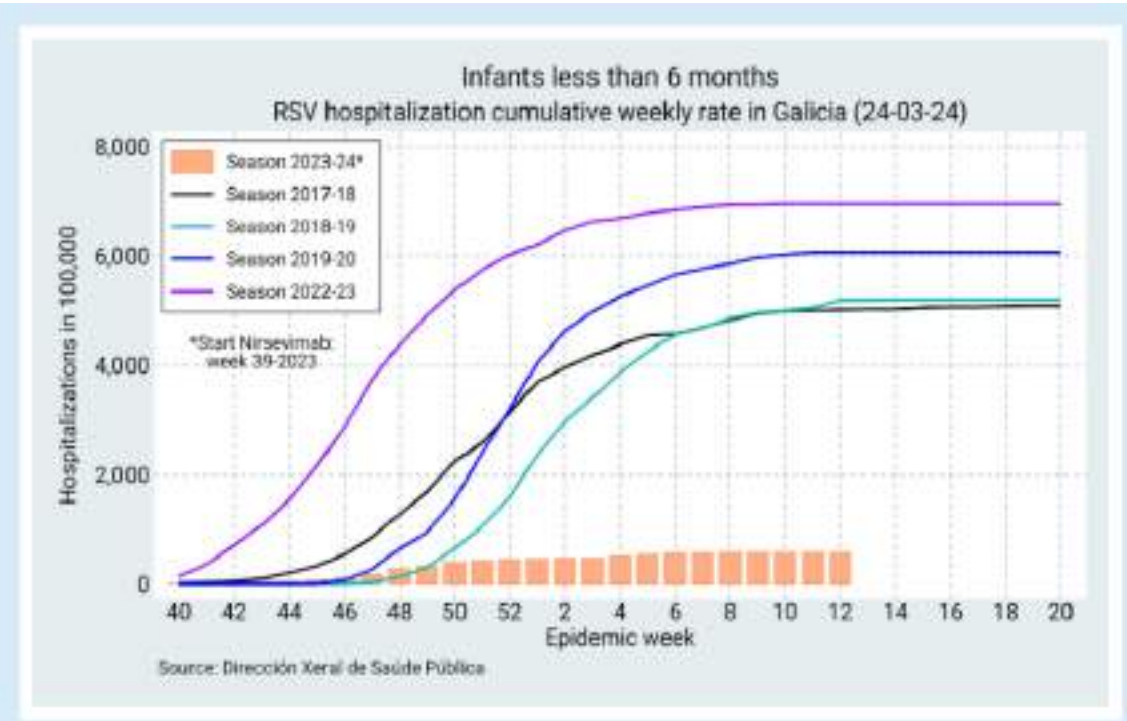
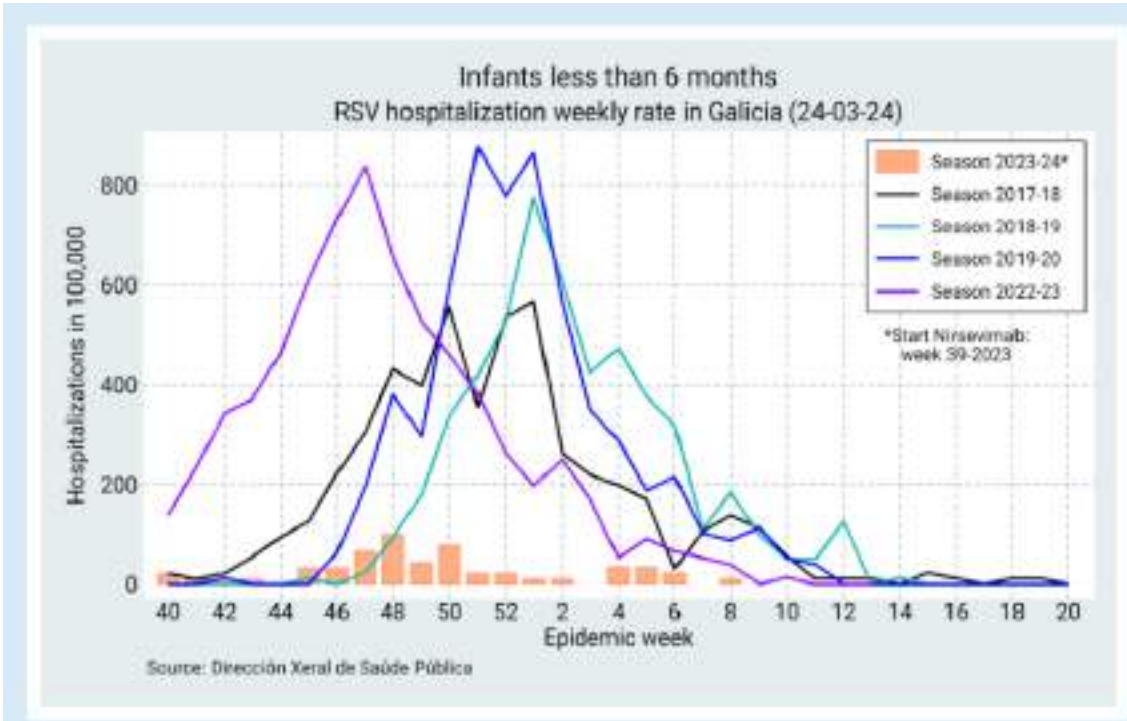
Infants under 2 months of age



Weekly RSV hospitalization rate in Galicia, by season, up to 31-03-2024. Infants less than 2 months

Cumulative weekly RSV hospitalization rate in Galicia, by season, up to 31-03-2024. Infants less than 2 months.

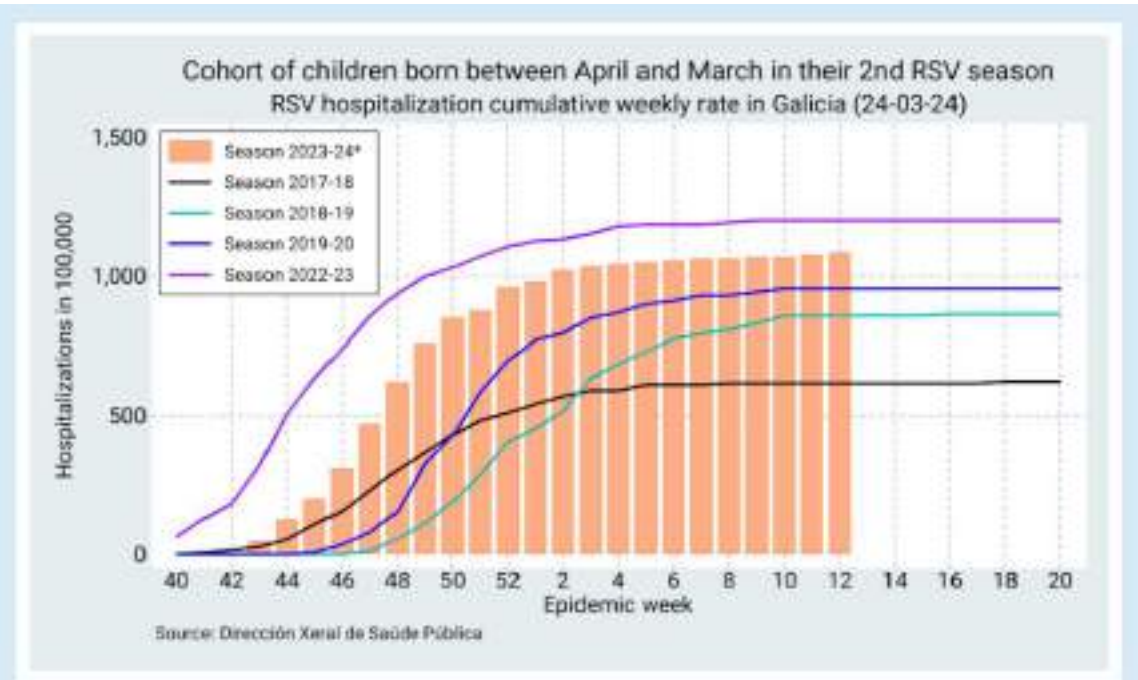
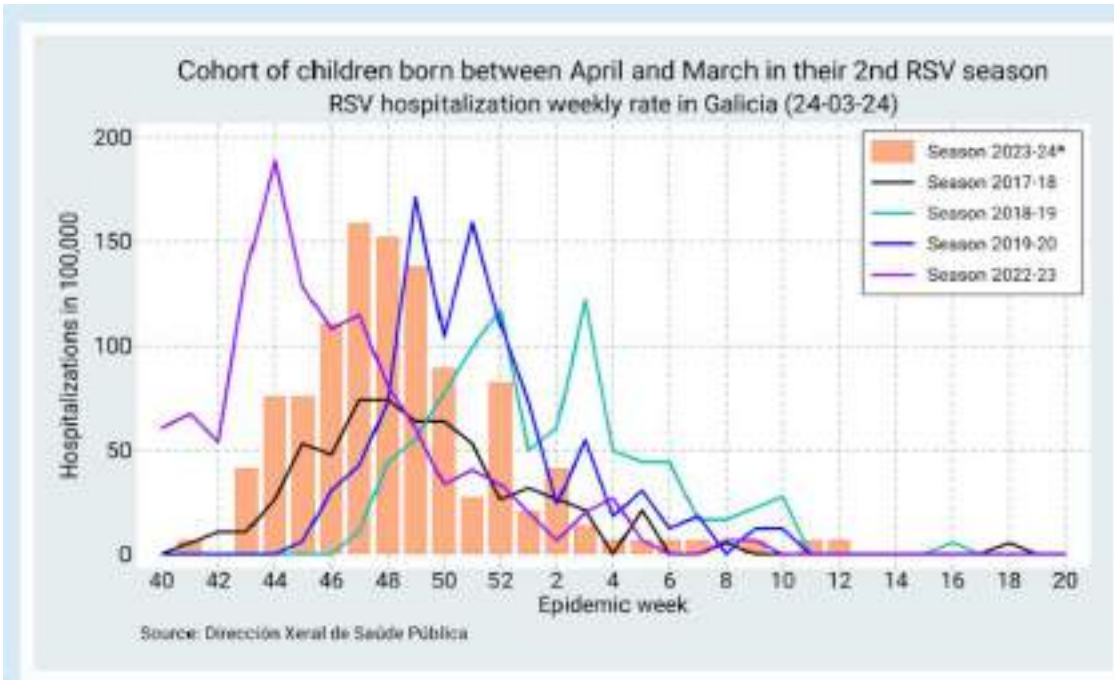
Infants under 6 months of age



Weekly RSV hospitalization rate in Galicia, by season, up to 31-03-2024. Infants less than 6 months.

Cumulative weekly RSV hospitalization rate in Galicia, by season, up to 31-03-2024. Infants less than 6 months.

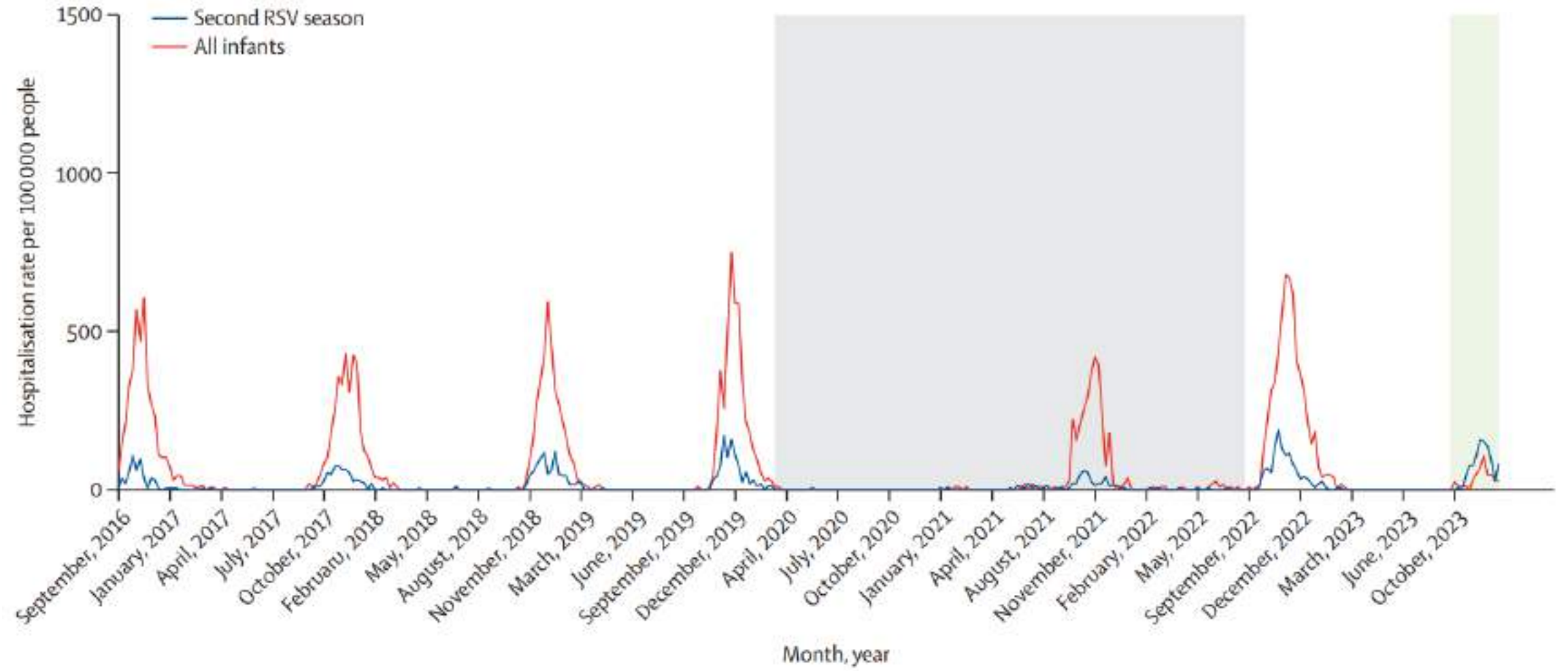
Infants born between April - March in their 2nd RSV season



Weekly RSV hospitalization rate in Galicia, by season, up to 31-03-2024. Cohort of infants born between April and March in their 2nd RSV season.

Cumulative weekly RSV hospitalization rate in Galicia, by season, up to 31-03-2024. Cohort of infants born between April and March in their 2nd RSV season.

Weekly hospitalisation rate: 2nd season vs immunization cohort



	Nirsevimab non-recipients			Nirsevimab recipients			Incidence rate ratio (95% CI)	Effectiveness, % (95% CI)*
	Events	Number analysed	Person-years	Events	Number analysed	Person-years		
RSV-related LRTI hospitalisation								
Intention-to-treat analysis†	16	851	207·03	30	9408	1877·71	0·18 (0·10–0·34)	82·0 (65·6–90·2)
Sensitivity analysis‡	19	855	207·55	25	9404	1877·64	0·13 (0·07–0·23)	87·5 (76·6–93·2)
Severe RSV-related LRTI with oxygen support								
Intention-to-treat analysis†	10	851	207·03	15	9408	1877·71	0·13 (0·06–0·31)	86·9 (69·1–94·2)
Sensitivity analysis‡	11	855	207·55	13	9404	1877·64	0·10 (0·04–0·23)	90·0 (76·6–95·7)
Severe RSV-related LRTI with intensive care unit admission	0	851	207·03	10	9408	1877·71	NA	NA
Severe RSV-related LRTI with non-invasive mechanical ventilation	0	851	207·03	7	9408	1877·71	NA	NA
Severe RSV-related LRTI with invasive mechanical ventilation	0	851	207·03	0	9408	1877·71	NA	NA
All-cause LRTI hospitalisation	43	826	206·80	150	9237	1861·84	0·31 (0·22–0·44)	69·2 (55·9–78·0)
All-cause hospitalisation§	77	817	205·81	289	9072	1840·74	0·34 (0·26–0·44)	66·2 (56·0–73·7)

LRTI=lower respiratory tract infection. NA=not applicable. RSV=respiratory syncytial virus. *Nirsevimab effectiveness was estimated from incidence rate ratios calculated using Poisson regression models, which were adjusted for enrolment group (catch-up and seasonal), sex, and health district area. Only patients with non-zero follow-up time were included. †For the main analysis (intention-to-treat analysis), any event that took place after immunisation with nirsevimab was considered a case; all analyses were done in this population unless otherwise indicated. ‡For the sensitivity analysis, after the reviewers' and expert advisory committee's assessment of the event's relation to RSV infection and considering the definition of breakthrough cases, patients immunised but not meeting these criteria were allocated to the non-nirsevimab group. §All-cause hospitalisations include non-LRTI hospitalisations.

Table 2: Nirsevimab effectiveness against NIRSE-GAL study endpoints estimated in infants for the first 3 months of the 2023–24 vaccination campaign using Poisson regression models

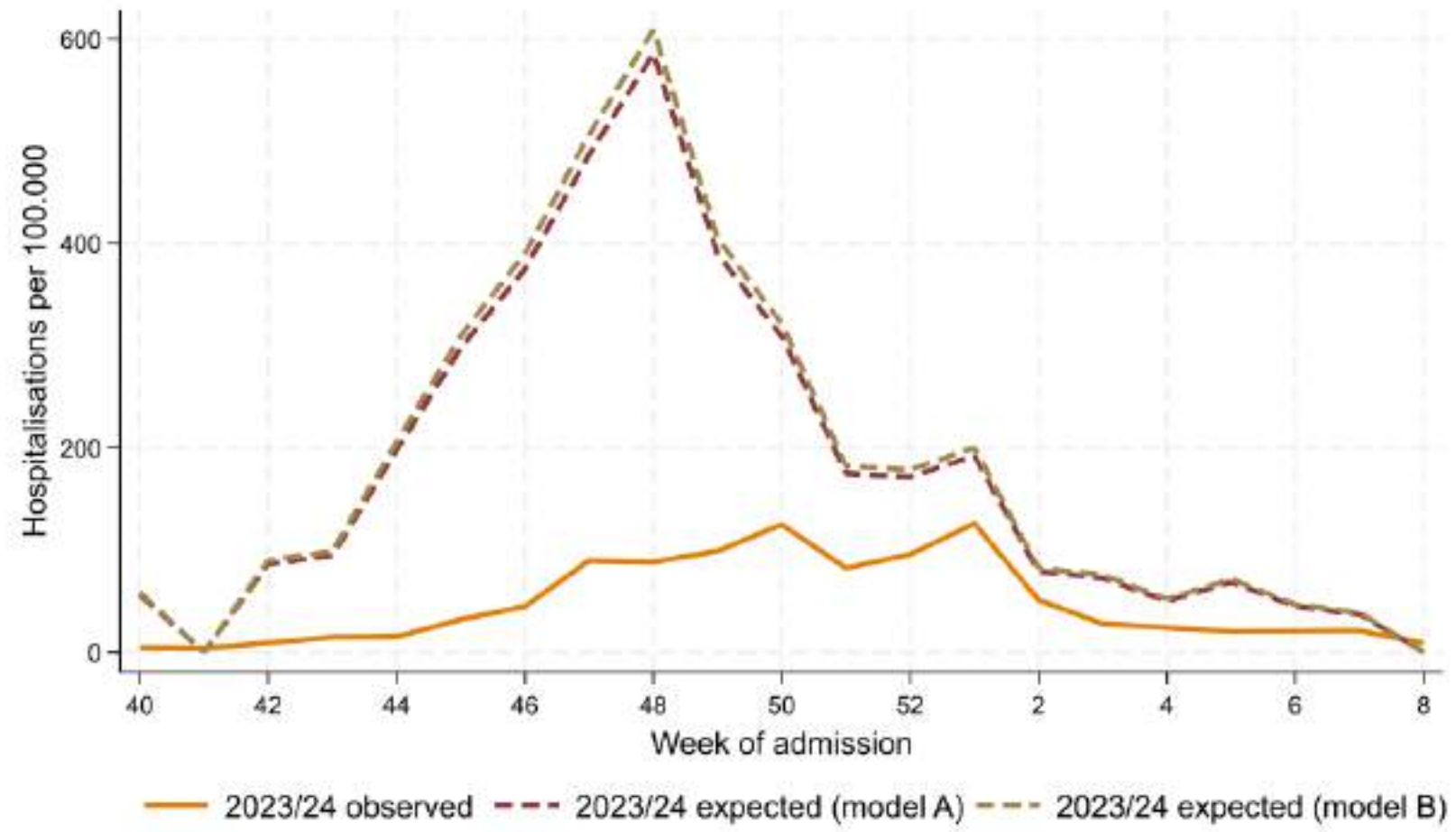


FIGURE 2 | Estimated number of observed respiratory syncytial virus (RSV) hospitalisations in <1-year-olds in Spain, weeks 40/2023-8/2024. Expected cases are obtained by applying to the observed cases from the equivalent weeks in 2022/23 a scaling factor (see Table 1) in 1- to 4-year-olds (2023/24 expected [Model A]) or 1- to 110-year-olds (2023/24 expected [Model B]). The RSV proxy hospitalisation rates each week are applied to the population size by age group and autonomous community; data are aggregated across autonomous communities for the number of weekly cases in Spain, referred to as observed.



Episode Coding	Immunization Group	Sex		Related to nirsevimab	
		Male	Female	YES	NO
Adverse reaction to vaccination (A87.01)	Catch-up	4	1	0	5
Adverse effect of correct dose medication (A85)	At birth	1	0	0	1
	Catch-up	3	3	0	6
	Risk	1	0	0	1
Medication intoxication/poisoning/overdose (A84)	At birth	0	1	0	1
	Catch-up	2	1	0	3
Total		11	6	0	17

Table 11. Episodes coded in primary care suspicious of possible adverse reactions among individuals immunized with nirsevimab in Galicia classified after the review of medical history, up to week 8 of the year 2024.

A close-up photograph of a baby's face being held by an adult. The baby has dark hair and is looking towards the camera with a slight smile. The adult's hand is visible, supporting the baby's head. The background is a solid, muted blue color. The text "GRAZIE PER L'ATTENZIONE" is overlaid in white, bold, uppercase letters across the center of the image.

GRAZIE PER L'ATTENZIONE