Effectiveness and impact of universal prophylaxis with nirsevimab in infants against hospitalisation for respiratory syncytial virus in Galicia, Spain: initial results of a population-based longitudinal study

Sonia Ares-Gómez, Narmeen Mallah*, María-Isolina Santiago-Pérez*, Jacobo Pardo-Seco*, Olaia Pérez-Martínez, María-Teresa Otero-Barrós, Nuria Suárez-Gaiche, Rolf Kramer, Jing Jin, Leticia Platero-Alonso, Rosa-María Alvárez-Gil, Olga-María Ces-Ozores, Victoria Nartallo-Penas, Susana Mirás-Carballal, Marta Piñeiro-Sotelo, Alberto Malvar-Pintos, Juan-Manuel González-Pérez, Carmen Rodríguez-Tenreiro-Sánchez, Irene Rivero-Calle, Antonio Salas, Carmen Durán-Parrondo, Federico Martinón-Torres,* on behalf of the NIRSE-GAL study group*

Summary

Background Galicia (Spain) was one of the first regions worldwide to incorporate nirsevimab for universal respiratory syncytial virus (RSV) prophylaxis in infants into its immunisation programme. The NIRSE-GAL longitudinal population-based study aimed to assess nirsevimab effectiveness in preventing hospitalisations (ie, admittance to hospital).

Methods The 2023–24 immunisation campaign with nirsevimab in Galicia began on Sept 25, 2023, and concluded on March 31, 2024. The campaign targeted three groups: infants born during the campaign (seasonal group), infants younger than 6 months at the start of the campaign (catch-up group), and infants aged 6–24 months with high-risk factors at the start of the campaign (high-risk group). Infants in the seasonal group were offered immunisation on the first day of life before discharge from hospital. Infants in the catch-up and high-risk groups received electronic appointments to attend a public hospital or health-care centre for nirsevimab administration. For this interim analysis, we used data collected from Sept 25 to Dec 31, 2023, from children born up to Dec 15, 2023. Data were retrieved from public health registries. Nirsevimab effectiveness in preventing RSV-associated lower respiratory tract infection (LRTI) hospitalisations; severe RSV-related LRTI requiring intensive care unit admission, mechanical ventilation, or oxygen support; all-cause LRTI hospitalisations; and all-cause hospitalisations was estimated using adjusted Poisson regression models. Data from five past RSV seasons (2016–17, 2017–18, 2018–19, 2019–20, and 2022–23), excluding the COVID-19 pandemic period, were used to estimate the number of RSV-related LRTI hospitalisations averted along with its IQR. The number needed to immunise to avoid one case in the 2023–24 season was then estimated from the averted cases. Nirsevimab safety was routinely monitored. The NIRSE-GAL study protocol was registered on ClinicalTrials.gov (NCT06180993), and follow-up of participants is ongoing.

Findings 9408 (91·7%) of 10 259 eligible infants in the seasonal and catch-up groups received nirsevimab, including 6220 (89·9%) of 6919 in the seasonal group and 3188 (95·4%) of 3340 in the catch-up group. 360 in the high-risk group were offered nirsevimab, 348 (97%) of whom received it. Only infants in the seasonal and catch-up groups were included in analyses to estimate nirsevimab effectiveness and impact because there were too few events in the high-risk group. In the catch-up and seasonal groups combined, 30 (0·3%) of 9408 infants who received nirsevimab and 16 (1·9%) of 851 who did not receive nirsevimab were hospitalised for RSV-related LRTI, corresponding to an effectiveness of 82·0% (95% CI 65·6–90·2). Effectiveness was 86·9% (69·1–94·2) against severe RSV-related LRTI requiring oxygen support, 69·2% (55·9–78·0) against all-cause LRTI hospitalisations, and 66·2% (56·0–73·7) against all-cause hospitalisations. Nirsevimab effectiveness against other endpoints of severe RSV-related LRTI could not be estimated because of too few events. RSV-related LRTI hospitalisations were reduced by 89·8% (IQR 87·5–90·3), and the number needed to immunise to avoid one RSV-related LRTI hospitalisation was 25 (IQR 24–32). No severe adverse events related to nirsevimab were registered.

Interpretation Nirsevimab substantially reduced infant hospitalisations for RSV-associated LRTI, severe RSV-associated LRTI requiring oxygen, and all-cause LRTI when given in real-world conditions. These findings offer policy makers and health authorities robust, real-world, population-based evidence to guide the development of strategies for RSV prevention.

Funding Sanofi and AstraZeneca.

Copyright © 2024 Elsevier Ltd. All rights reserved, including those for text and data mining, AI training, and similar technologies.

Lancet Infect Dis 2024

Published Online
April 30, 2024
https://doi.org/10.1016/S1473-3099(24)00215-9

See Online/Comment
https://doi.org/10.1016/S1473-3099(24)00261-5

*Contributed equally

For the Spanish translation of the abstract see Online for appendix 1

Genetics, Vaccines, and Pediatric Infectious Diseases Research Group (GENVIP), Instituto de Investigación Sanitaria de Santiago de Compostela (IDIS), Santiago de Compostela, Spain (S Ares-Gómez PhD, N Mallah PhD, J Pardo-Seco PhD, C Rodríguez-Tenreiro-Sánchez PhD, I Rivero-Calle MD, Prof F Martinón-Torres PhD); **WHO Collaborating Centre for Vaccine Safety, Santiago de Compostela, Spain** (S Ares-Gómez, N Mallah, J Pardo-Seco, C Rodríguez-Tenreiro-Sánchez, I Rivero-Calle, Prof F Martinón-Torres); **Centro de Investigación Biomédica en Red de Enfermedades Respiratorias** (S Ares-Gómez, J Pardo-Seco, C Rodríguez-Tenreiro-Sánchez, I Rivero-Calle, Prof A Salas PhD, Prof F Martinón-Torres) **and Centro de Investigación Biomédica en Red de Epidemiología y Salud Pública** (N Mallah), **Instituto de Salud Carlos III, Madrid, Spain; Department of Preventive Medicine, University of Santiago de Compostela (USC), Santiago de Compostela, Spain** (N Mallah); **Department of Epidemiology** (M-I Santiago-Pérez BS, O Pérez-Martínez MD,

M-T Otero-Barrós MD, N Suárez-Gaiche MD, M Piñeiro-Sotelo RPH, A Malvar-Pintos MD) **and Department of Communicable Diseases** (R-M Alvárez-Gil MD, O-M Ces-Ozores RPH, V Nartallo-Penas PhD, S Mirás-Carballal RPH), **Dirección Xeral de Saúde Pública, Consellería de Sanidade, Xunta de Galicia, Galicia, Spain; Genética de Poblaciones en Biomedicina (GenPoB) Research Group, Instituto de Investigación Sanitaria (IDIS), Hospital Clínico Universitario de Santiago (SERGAS), Galicia, Spain** (J Pardo-Seco, Prof A Salas)**; Sanofi Vaccines, Lyon, France** (R Kramer PhD, J Jin PhD, L Platero-Alonso PhD)**; Subdirección de Sistemas y Tecnologías de la Información, Consellería de Sanidade, Xunta de Galicia, Galicia, Spain** (J-M González-Pérez BS)**; Translational Pediatrics and Infectious Diseases, Hospital Clínico Universitario de Santiago (SERGAS), Santiago de Compostela, Spain** (I Rivero-Calle, Prof F Martinón-Torres)**; Unidade de Xenética, Instituto de Ciencias Forenses, Facultade de Medicina, Universidade de Santiago de Compostela (USC), Galicia, Spain** (Prof A Salas)**; Dirección Xeral de Saúde Pública, Consellería de Sanidade, Xunta de Galicia, Galicia, Spain** (C Durán-Parrondo PhD)

Correspondence to: Prof Federico Martinón-Torres, Translational Pediatrics and Infectious Diseases, Hospital Clínico Universitario de Santiago (SERGAS), Santiago de Compostela 15706, Spain **federico.martinon.torres@sergas.es**

Research in context

Evidence before this study

Nirsevimab, a long-acting monoclonal antibody against respiratory syncytial virus (RSV), has been approved in Europe (Oct 31, 2022), the UK (Nov 9, 2022), Canada (April 19, 2023), and the USA (July 17, 2023), thus constituting the first immunisation product available for universal RSV prophylaxis in infants. The phase 3 clinical trial (MELODY study) assessed nirsevimab efficacy in infants born at a gestational age of at least 35 weeks through to 150 days after nirsevimab administration. It reported 76·8% (95% CI 49·4–89·4) efficacy against hospitalisation (ie, admittance to hospital) for RSV-associated lower respiratory tract infections (LRTIs), and 76·4% (62·3–85·2) against medically attended RSV-associated LRTIs. Another clinical trial in preterm infants concluded that, compared with placebo, nirsevimab lowers the incidence of medically attended RSV-associated LRTI by 70·1% (95% CI 52·3–81·2), and that of hospitalisation for RSV-associated LRTI by 78·4% (51·9–90·3). The HARMONIE trial, a multicountry, pragmatic clinical trial in 8058 healthy infants, approximating real-world conditions, found 83% efficacy for nirsevimab against RSV-related LRTI hospitalisations, and 76% efficacy against very severe RSV-related LRTI in infants born at a gestational age of at least 29 weeks and entering their first RSV season, compared with no intervention. Given nirsevimab's novelty, findings from real-world studies on nirsevimab's effectiveness are still scarce. We searched PubMed using the terms (RSV AND effectiveness AND nirsevimab) on Feb 16, 2024, with no date or language restrictions. We also applied the snowball process to locate additional relevant publications by reviewing the reference lists of relevant studies. Only two relevant studies were available so far. The first study involved nine hospitals in Spain and reported a pooled nirsevimab effectiveness against RSV-related LRTI hospitalisations of 84·4% (95% CI 76·8–90·0) using a screening design, and 70·2% (38·3–88·5) using a test-negative design. The other study, from Luxembourg, compared the 2023–24 RSV season after nirsevimab implementation with the previous RSV season, and observed reductions of 38% and 69% in the number of RSV-related LRTI hospitalisations in children younger than 5 years and infants younger than 6 months, respectively. HARMONIE reported treatment-related adverse events in 2·1% of patients receiving nirsevimab, whereas the Luxembourg study reported no adverse events associated with nirsevimab immunisation. One of the first jurisdictions in the world to implement nirsevimab in its immunisation programme was Galicia, a region in northwest Spain with over 2·7 million inhabitants. NIRSE-GAL is a population-based longitudinal study initiated in collaboration with the Galician Directorate of Public Health of the Xunta de Galicia to assess nirsevimab effectiveness for a 36-month follow-up period. For this interim analysis, we used data collected from Sept 25 to Dec 31, 2023.

Added value of this study

Data on nirsevimab effectiveness from real-world studies are still emerging. We undertook a population-based study on the effectiveness of nirsevimab using real-world data. We estimated that the effectiveness of nirsevimab in seasonally born infants, and in those infants who were younger than 6 months at the start of the immunisation campaign, was 82·0% (95% CI 65·6–90·2) against RSV-related LRTI hospitalisations, 86·9% (69·1–94·2) against severe RSV-related LRTI requiring oxygen, 69·2% (55·9–78·0) against all-cause LRTI hospitalisations, and 66·2% (56·0–73·7) against all-cause hospitalisations. The estimated number needed to immunise to prevent one RSV-related LRTI hospitalisation was 25 (IQR 24–32). No serious adverse events were detected. Our study provides real-world evidence to inform deliberations for RSV prevention programmes.

Implications of all the available evidence

This early assessment of the effectiveness of nirsevimab implementation using population-based real-world data indicates that nirsevimab contributes to an important reduction in RSV-related LRTI hospitalisations, severe RSV-related LRTI requiring oxygen, all-cause LRTI hospitalisations, and all-cause hospitalisations. These results are aligned with the corresponding efficacy data reported for the phase 3 trial of nirsevimab (MELODY study), as well as a recent pragmatic clinical trial (HARMONIE trial). Our findings are also consistent with the recent report from Spain regarding nirsevimab effectiveness against RSV-related LRTI hospitalisations. They are also in line with the conclusion of the Luxembourg study, which showed a lower number of RSV-related LRTI hospitalisations among nirsevimab recipients compared with non-recipients, although the authors of this study did not report a measure of effect. Even though our findings need to be replicated in other settings, and with longer follow-up periods, they should be helpful for the many countries considering the adoption of universal RSV prophylaxis in infants, providing policy makers and health authorities with real-world population-based evidence for formulating effective and efficient RSV immunisation prevention strategies.

Introduction

The respiratory syncytial virus (RSV) generates a substantial disease burden worldwide, especially in infants, including those who are otherwise healthy.[1] In the EU, between 2006 and 2018, nearly 250 000 annual hospitalisations (ie, admittance to hospital) were associated with RSV infections in children younger than 5 years, with 75% of the hospitalisations occurring in infants younger than 1 year.[2,3] In Spain, two out of every 100 children younger than 2 years are hospitalised for RSV, averaging a 6-day stay, and resulting in an estimated annual cost of approximately €50 million to the National Health System.[4,5] More than 90% of RSV-related episodes occur in children without any comorbidity, and more

than a quarter of the total direct health-care expenditure is unrelated to hospitalisation.[2,6] Nirsevimab (Beyfortus, AstraZeneca [Södertälje, Sweden], and Sanofi [Gentilly, France]), a long-acting monoclonal antibody against RSV, was approved by the European Medicines Agency in October, 2022.[7] Nirsevimab was then authorised by the UK (Nov 9, 2022),[8] Canada (April 19, 2023),[9] and the USA (July 17, 2023).[10] In March, 2023, Galicia, a region in northwest Spain with approximately 2·7 million inhabitants and 14 495 annual births as of 2022,[11] became one of the first places in the world to introduce nirsevimab into its immunisation calendar as a prophylactic measure against RSV.[12,13]

The NIRSE-GAL study[14] is a population-based, 3-year longitudinal study initiated under a collaborative framework with the Galician Directorate of Public Health of the Xunta de Galicia (Galician Government). NIRSE-GAL aims to evaluate the effectiveness of nirsevimab against RSV-related lower respiratory tract infection (LRTI) hospitalisations, severe RSV-related LRTI, all-cause LRTI hospitalisations, and all-cause hospitalisations. The study also intends to estimate the number of averted cases and the number needed to immunise to avoid one RSV-related LRTI hospitalisation. As secondary objectives, NIRSE-GAL aims to monitor nirsevimab safety in Galicia and to determine the short-term and mid-term effects of nirsevimab on morbidity (eg, wheezing and asthma) and health-care use (eg, primary care and emergency care visits, and drug prescription) for RSV. Here, we report the outcomes of nirsevimab use up to 3 months after its practical implementation.

Methods

Study design and participants

Health care in Galicia (SERGAS) is structured in seven areas with a total of 14 public hospital complexes with paediatric and maternity services and 9818 hospital beds (data for 2022).[11] SERGAS uses a centralised digital health-care information system including different registries with a common personal identification number assigned at birth.

The immunisation campaign began in Galicia on Sept 25, 2023, and ended on March 31, 2024. The campaign closure date was decided based on the expected RSV season end according to data from the previous 12 seasons, excluding those during the COVID-19 pandemic (ie, 2020–21 and 2021–22). The campaign targeted three groups at risk of RSV infection who were classified according to their birth date and risk conditions: infants born during the immunisation campaign (seasonal group), infants who were younger than 6 months at the start of the campaign (ie, infants born between April 1 and Sept 24, 2023; catch-up group), and infants aged 6–24 months (ie, born between Oct 1, 2021, and March 31, 2023) with high-risk conditions at the start of the campaign (high-risk group; appendix 2 pp 1–2, 7). A full list of high-risk conditions is provided in appendix 2 (p 7). Infants in the seasonal group were offered immunisation on the first day of life before being discharged. Infants in the catch-up and high-risk groups received electronic appointments to be immunised in their reference hospitals. For the present work, the eligible population for nirsevimab administration comprised all infants born from April 1 to Dec 15, 2023, who were residing in Galicia. The follow-up start date was set as follows: the immunisation date for all immunised infants; Sept 25, 2023, for infants in the catch-up group and the high-risk group who were not immunised; and birth for infants in the seasonal group who were not immunised. Infants were followed up until outcome occurrence, death, or the end of the observation period (Dec 31, 2023), whichever occurred first.

For more on the **NIRSE-GAL study** see https://www.nirsegal.es/en

For prospective data collection in the NIRSE-GAL study, a specific public health surveillance programme for RSV was implemented. Seven SERGAS information system registries were queried to carry out this study: the Galician registry health-care card; the vaccine registry; hospital admissions; microbiology laboratory test results; the newborn metabolic disorders screening test registry; the Healthy Child regional programme in Galicia, which encompasses two pre-scheduled visits in the first 15 days of life; and the Minimum Basic Data Set hospital registry. The Spanish Minimum Basic Data Set includes data on hospitalisation episodes, diagnoses, and procedures performed during hospitalisation, all coded using International Classification of Diseases (ICD)-10 codes. Data on the following sociodemographic characteristics were collected: sex; age (in months) on Dec 31, 2023; enrolment group (catch-up, seasonal, and high-risk); weight at birth (in grams); gestational age (in weeks); Healthy Child programme visits as a proxy for the use of public health resources (yes or no); and residential area (north Galicia *vs* south Galicia). Data extraction and curation were performed by Galician Health Information Systems experts following predefined procedures (appendix 2 p 3).

Adverse events related to nirsevimab administration were routinely monitored in all patients through the Galician pharmacovigilance system.[15,16] In addition, active surveillance of any potential adverse event or hospitalisation in the first 3 weeks since nirsevimab administration was conducted in the preterm population (ie, those with a gestional age less than 37 weeks).

The NIRSE-GAL study protocol was approved by the regional independent reference ethics committee of Galicia (CEIC 2023–377). The study was developed in compliance with the International Council for Harmonization Guidelines for Good Clinical Practice and the principles of the Declaration of Helsinki. Data were obtained through the electronic registries of the Galician surveillance system by personnel independent of data analysis and were anonymised before analysis. Patients were immunised as part of the public health system immunisation schedule, offered to all eligible

See **Online** for appendix 2

infants, and no informed consent is required either for immunisation purposes or for study purposes, as reassured by the ethics committee.

Endpoints and definitions

The primary endpoint was hospital admission for RSV-related LRTI. Secondary endpoints were: severe RSV-related LRTI requiring neonatal or paediatric intensive care unit admission; severe RSV-related LRTI requiring mechanical ventilation; severe RSV-related LRTI requiring oxygen support; all-cause LRTI hospitalisations; and all-cause hospitalisations.

All cases were identified from hospital and microbiological registries (appendix 2 pp 3–4). Only the first hospitalisation episode after the follow-up start date was considered. Nosocomial RSV infections were excluded from the analysis. All hospitalisations with a positive RSV result during the hospitalisation or within 10 days before admission were reviewed by public health specialists who classified them as an RSV-related LRTI and as non-severe or severe (requiring intensive care unit admission, mechanical ventilation, or oxygen support) according to the patient's records. All-cause LRTI hospitalisations were defined as any LRTI hospitalisation with an RSV test (positive or negative). All-cause hospitalisation included any hospitalisation occurring after the start date of follow-up. A second evaluation of doubtful cases was undertaken by an expert advisory committee. Disagreements were resolved by discussion between the public health specialists who performed the initial review and the expert advisory committee. If a consensus was not achieved, the expert advisory committee evaluation prevailed. Details on how the assessment of these hospitalisations was done are available in appendix 2 (p 4).

Historical data

Retrospective data on RSV-related hospitalisations in the RSV seasons spanning the period 2016–23 were collected from the Minimum Basic Data Set hospital registry to ensure enough observations from infants unexposed to nirsevimab. 2016 was selected as the start year because it corresponded to the time that the Minimum Basic Data Set registry completely transitioned from the ICD-9 to the ICD-10 system in Galicia. Data on RSV seasons occurring during the COVID-19 pandemic (2020–22) were not included in the analysis, to account for changes in RSV epidemiology during the pandemic.[17] Hospitalisations for RSV were considered if any of the following ICD-10 codes were present in the discharge diagnosis: J21.0 (acute bronchiolitis due to respiratory syncytial virus), J20.5 (acute bronchitis due to respiratory syncytial virus), J12.1 (respiratory syncytial virus pneumonia), or B97.4 (respiratory syncytial virus as the cause of diseases classified elsewhere). If any of these codes were present in the first two diagnostic positions, the hospitalisation was considered as related to RSV.

Statistical analysis

Statistical differences in demographics between infants who did and did not receive nirsevimab during the immunisation programme in Galicia were evaluated using a Student's *t*-test and Wilcoxon rank-sum test for continuous variables and the χ^2 test for categorical variables. Furthermore, missing data were reported and were excluded for statistical comparisons.

In the statistical analyses to estimate nirsevimab effectiveness, each individual contributed person-time data. Any hospitalisation with an LRTI and positive RSV test that occurred after immunisation was considered a case for the main analysis (ie, the intention-to-treat analysis). In a sensitivity analysis, we considered the public health specialist's and expert advisory committee's assessment of the event's relation to RSV infection and fulfillment of breakthrough case definition criteria. The expert advisory committee's decision prevailed in cases of doubt (appendix 2 p 5). Only RSV-related LRTI hospitalisations were included. Breakthrough cases should fulfil the following criteria: the patient had received nirsevimab at least 7 days before admission for RSV-related LRTI; the patient did not present clinical symptoms described by the US Centers for Disease Control and Prevention as compatible with RSV infection[18] or an RSV-positive result in the 7 days after nirsevimab administration; and the patient did not have an RSV-positive test result in the 15 days before immunisation and 30 days before admission. Participants who were immunised but did not meet these criteria were classified as having not received nirsevimab in the sensitivity analysis (appendix 2 p 5).

Poisson regression with robust variance and Cox proportional hazards models were used for estimating nirsevimab effectiveness. Incidence rate ratios (from Poisson regression) and hazard ratios (from Cox proportional hazards) are presented with 95% CIs. The models were adjusted for enrolment group (seasonal or catch-up) as a proxy of age and sex for their biological plausibility, as well as for the residential area as a proxy of socioeconomic level. The potential confounding effects of prematurity (ie, a gestational age less than 37 weeks) and Healthy Child programme visits as a proxy of public health-care service use were tested in a univariate analysis against the outcome and added to the multivariable model if a p value of less than 0·20 was shown. These covariables were retained in the final model only if the originally estimated incidence rate ratio or hazard ratio for outcome occurrence changed by at least 10%.[19] The effectiveness of nirsevimab against RSV hospitalisation was estimated as (1−point estimate)×100, and its 95% CI was obtained from the Poisson or Cox models. Only participants who had complete data on the variables included in the final models and non-zero follow-up time were included.

The impact of nirsevimab administration on RSV-related LRTI hospitalisation was assessed using the

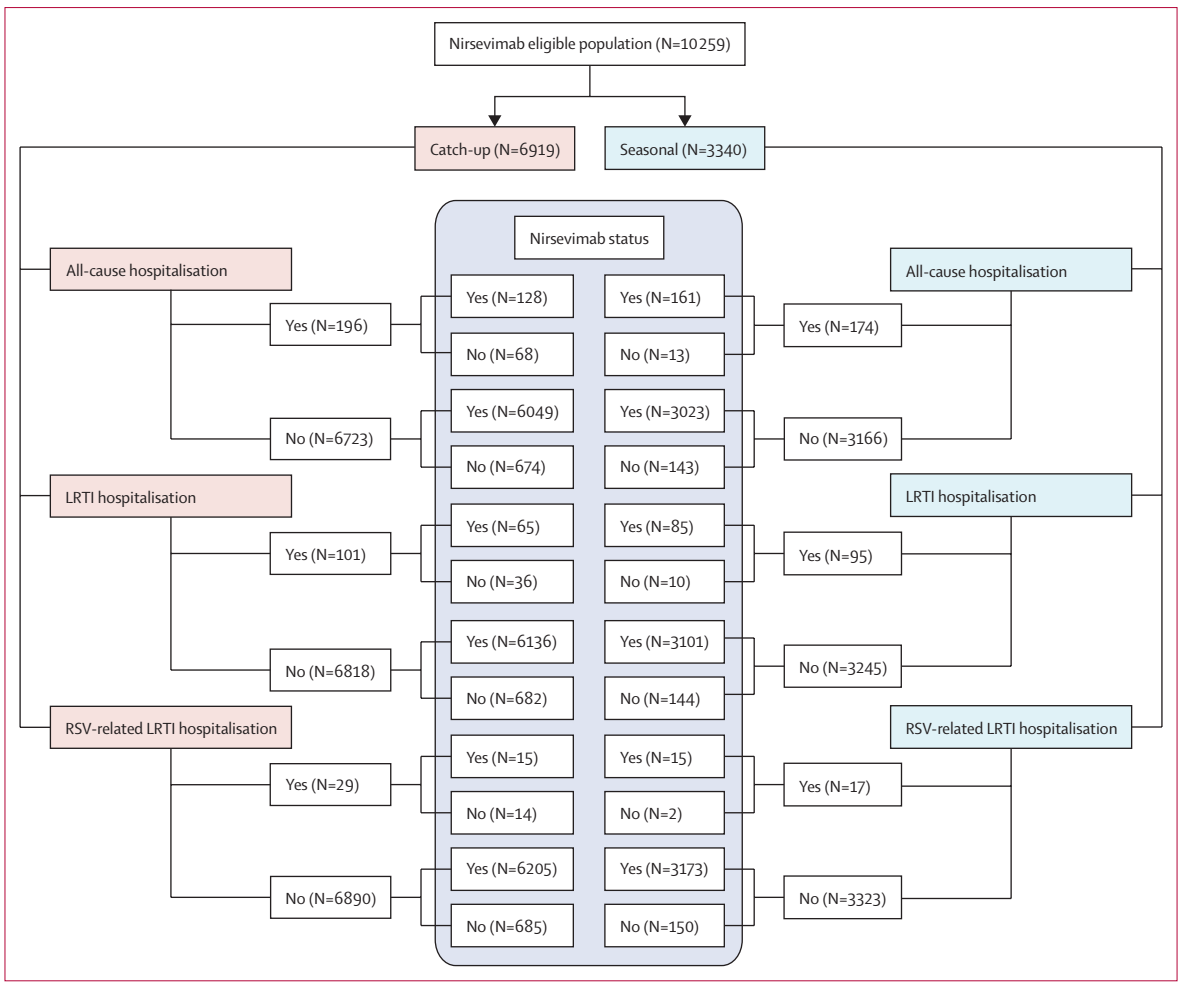

Figure 1: **Flow chart of NIRSE-GAL infants eligible for the immunisation campaign along with their exposure and outcome classifications**
Infants in the seasonal group were born during the immunisation campaign. Infants in the catch-up group were born between April 1 and Sept 24, 2023. A similar flow chart for the high-risk group, who were infants aged 6–24 months with high-risk conditions at the start of the campaign, is available in the appendix (p 13). LRTI=lower respiratory tract infection. RSV=respiratory syncytial virus.

catch-up and seasonal groups combined and separately using a Poisson model comparing RSV hospitalisation rate in the 2023–24 RSV season to rates in the historical seasons (appendix 2 p 6). The difference in cumulative incidence rates between those receiving nirsevimab and those not receiving nirsevimab was estimated through linear regression models adjusted for the epidemic week.

To estimate the number of averted cases, defined as the estimated number of RSV-related LRTI hospitalisations averted as a direct effect of the nirsevimab immunisation campaign, cumulative hospitalisation rates from epidemiological week 40 were calculated up to week 52 in both children passing their first and children passing their second RSV seasons, along with the ratio between them, for each of the five historical seasons. To estimate what would be the expected number of RSV-related LRTI hospitalisations in the 2023–24 season without a nirsevimab intervention, we used the hospitalisation rate in the 2023–24 RSV season for children in their second RSV season, assuming that the ratio between these two rates (ie, children in their first RSV season *vs* children in their second RSV season) was the one observed in each of the previous seasons. The number of averted cases was then estimated by subtracting the number of observed hospitalisations in nirsevimab-eligible infants in the 2023–24 RSV season from the number expected. The number of averted cases and the number needed to immunise (computed as the inverse of the adverted number of cases per one case) to avoid one case in the 2023–24 season are presented as median (IQR). The same analysis was repeated but excluding the 2022–23 RSV season because of its unusually high hospitalisation rates compared with the four seasons before the COVID-19 pandemic.

All planned analyses as per the study protocol for the mid-RSV season were undertaken and reported. No deviations took place. Stata (version 17.0) was used for the data curation, and R (version 4.3.1) was used for statistical

	Overall (N=10 259)	Nirsevimab recipients (n=9408)	Nirsevimab non-recipients (n=851)	p value
Age, months				
Mean (SD)	4·22 (2·44)	4·14 (2·44)	5·05 (2·29)	<0·001*
Median (Q1–Q3)	4·00 (2·00–6·00)	4·00 (2·00–6·00)	5·00 (3·00–7·00)	<0·001†
Age categories, months	..	..	..	<0·001‡
≤3	4279 (41·7%)	4064 (43·2%)	215 (25·3%)	..
>3 to 6	3677 (35·8%)	3311 (35·2%)	366 (43·0%)	..
>6	2303 (22·4%)	2033 (21·6%)	270 (31·7%)	..
Sex	..	..	..	0·245‡
Female	5060 (49·3%)	4657 (49·5%)	403 (47·4%)	..
Male	5199 (50·7%)	4751 (50·5%)	448 (52·6%)	..
Enrolment group	..	..	..	<0·001‡
Catch-up§	6919 (67·4%)	6220 (66·1%)	699 (82·1%)	..
Seasonal¶	3340 (32·6%)	3188 (33·9%)	152 (17·9%)	..
Weight at birth, grams				
Mean (SD)	3230 (520)	3220 (519)	3270 (530)	0·015*
Median (Q1–Q3)	3260 (2940– 3560)	3250 (2940–3560)	3290 (3000–3590)	0·016†
Data missing (%)	309 (3·0%)	216 (2·3%)	93 (10·9%)	..
Gestational age at birth, weeks				
Mean (SD)	39·0 (1·74)	39·0 (1·75)	39·1 (1·68)	0·270*
Median (Q1–Q3)	39·0 (38·0– 40·0)	39·0 (38·0–40·0)	39·0 (38·0–40·0)	0·623†
Data missing (%)	323 (3·1%)	227 (2·4%)	96 (11·3%)	..
Preterm	..	..	..	0·154‡
No (≥37 weeks)	9280 (90·5%)	8565 (91·0%)	715 (84·0%)	..
Yes (<37 weeks)	656 (6·4%)	616 (6·5%)	40 (4·7%)	..
Data missing	323 (3·1%)	227 (2·4%)	96 (11·3%)	..
Healthy Child programme visits	..	..	..	<0·001‡
≥1	9527 (92·9%)	8810 (93·6%)	717 (84·3%)	..
0	732 (7·1%)	598 (6·4%)	134 (15·7%)	..
Residential area	..	..	..	0·207‡
North	5954 (58·0%)	5478 (58·2%)	476 (55·9%)	..
South	4305 (42·0%)	3930 (41·8%)	375 (44·1%)	..

Data are n (%) unless otherwise stated. *p value from Student's *t*-test. †p value from Wilcoxon rank sum test. ‡p value from χ^2 test. §Birth dates between April 1 and Sept 24, 2023. ¶Birth dates between Sept 25 and Dec 15, 2023.

Table 1: **Demographic characteristics of infants born between April 1 and Dec 15, 2023, who were eligible for immunisation with nirsevimab**

analysis and visualisation. Statistics and survival packages[20,21] were used for the Poisson and Cox models, respectively.

Role of the funding source

The funders of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The funders provided support during the planning of the statistical analysis and reviewed the statistical section of the Methods.

Results

By Dec 15, 2023, 10 259 infants eligible for nirsevimab were included in the catch-up and seasonal groups (6919 [67·4%] in the catch-up group and 3340 [32·6%] in the seasonal group; figure 1). Of them, 9408 (91·7%) received nirsevimab (6220 [89·9%] of the catch-up group and 3188 [95·4%] of the seasonal group). Additionally, 360 children at high risk were offered immunisation, 348 (97·0%) of whom received nirsevimab (appendix 2 pp 9, 13). 5800 (83·8%) of the infants in the catch-up cohort, 347 (96·4%) of those in the high-risk cohort, and 1104 (92·6%) of those in the seasonal cohort were immunised before the start of the RSV season (ie, by Oct 20, 2023, according to RSV surveillance). The weekly immunisation coverage stratified by seasonal and catch-up cohorts is presented in appendix 2 (p 12).

Most of the non-receipt of immunisation was due to infants' non-attendance at scheduled appointments or an inability to contact the parents to book an appointment for immunisation through their registered contact information in SERGAS. Few families refused to immunise their infants (204 [2·0%] of 10 259). Immunisation refusal was not meaningfully different between the seasonal (63 [1·9%] of 3340) and catch-up (141 [2·0%] of 6919) groups.

Sex was almost equally distributed between the infants who did and did not receive nirsevimab (5199 [50·7%] of 10 259 were male and 5060 [49·3%] were female; table 1). The participants' age ranged between 0 months and 9 months, with a median of 4 months. The median gestational age at birth was 39 weeks (IQR 38–40). 656 (6·6%) of 9936 (the sum of the non-missing categories) infants were born preterm, 616 (93·9%) of whom received nirsevimab (table 1). 9527 (92·9%) of 10 259 infants had at least one visit as part of the Healthy Child regional programme, indicating a high use of public health services, including 8810 (93·6%) of 9408 nirsevimab recipients and 717 (84·3%) of 851 non-recipients. Although the difference in Healthy Child regional programme visits between nirsevimab recipients and non-recipients was significant in the χ^2 test (p<0·001), it did not fulfil the pre-specified criterion for inclusion in the multivariable model (change in incidence rate ratio or hazard ratio by ≥10%).

Descriptive characteristics of high-risk group nirsevimab recipients are shown in appendix 2 (p 9). The high-risk group was not included in the effectiveness analysis due to its small sample size (including only 12 infants who did not receive nirsevimab) and the low number of events in this group: 22 all-cause hospitalisations, nine all-cause LRTI hospitalisations, and three RSV-related LRTI hospitalisations (appendix 2 p 13).

For this mid-season analysis, participants were followed up for a median of 81 days (IQR 68–87). For the primary outcome of RSV-related LRTI hospitalisations, 46 events took place during the study period (table 2). 30 (65%) RSV-related LRTI hospitalisations occurred in nirsevimab recipients over 1877·71 person-years (incidence rate 15·9 per 1000 person-years, 95% CI 11·2–22·8). The other 16 events (35%) occurred in nirsevimab non-recipients

	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**

over 207·0 person-years (incidence rate 77·23, 95% CI 47·4–126·1). Nirsevimab effectiveness against RSV-related LRTI hospitalisation was 82·0% (95% CI 65·6–90·2) in the Poisson regression analysis (table 2). These findings were consistent with those estimated by Cox-regression models (effectiveness 82·4%, 95% CI 66·9–90·6; appendix 2 p 14).

Effectiveness against severe RSV-related LRTI requiring oxygen support was 86·9% (95% CI 69·1–94·2) in the Poisson regression analysis (table 2). Nirsevimab effectiveness against other secondary endpoints of severe RSV-related LRTI (requiring intensive care unit admission or mechanical ventilation) could not be determined due to insufficient numbers of events (table 2).

Nirsevimab also showed substantial protection against all-cause LRTI hospitalisations, with an effectiveness estimate of 69·2% (95% CI 55·9–78·0), and against all-cause hospitalisations, with an effectiveness estimate of 66·2% (56·0–73·7; table 2).

In the sensitivity analysis, five (17%) of 30 cases of RSV-related LRTI hospitalisation in nirsevimab recipients in the main analysis were re-classified by public health specialists or the expert advisory committee: one was considered a non-RSV-related hospitalisation, and four were considered non-breakthrough cases. In the non-nirsevimab group, one case of RSV-related LRTI hospitalisation was re-classified as a non-RSV-related hospitalisation (table 2). Nirsevimab effectiveness against RSV-related hospitalisation in the sensitivity analysis, as estimated by the Poisson regression model, was 87·5% (95% CI 76·6–93·2), and against severe RSV-related LRTI requiring oxygen support was 90·0% (76·6–95·7; table 2). Stratified analysis by study group (catch-up *vs* seasonal) is shown in appendix 2 (pp 10, 11).

The RSV positivity rate exceeded 3% in epidemiological week 44 of 2023, indicating the start of the RSV season. At week 52 of the 2023–24 RSV season, we observed a cumulative hospitalisation rate per 100 000 infants of 472 in 9408 infants who received nirsevimab, which was almost half the cumulative hospitalisation rate of children in their second RSV season (901 per 100 000 infants) who were not eligible for nirsevimab and lower than the median cumulative hospitalisation rate per 100 000 infants in the previous five RSV seasons (figure 2).

The cumulative hospitalisation rates for RSV-related LRTI in infants in the 2023–24 RSV season were significantly lower than those of the previous seasons (based on weekly hospitalisation rates) in the catch-up group (p=0·003), the seasonal group (p<0·0001), and the two enrolment groups combined (0·001; figure 2A–C). Children in their second RSV season who did not receive nirsevimab did not show a significantly different cumulative hospitalisation rate for RSV-related LRTI compared with those of the previous RSV seasons (p value 0·088; figure 2D).

As shown in figure 3 and confirmed by Poisson regression models, lower weekly RSV-related hospitalisation rates were observed in nirsevimab recipients in 2023–24 compared with non-nirsevimab recipients in previous seasons. This was observed for nirsevimab recipients who were enrolled in the catch-up group (incidence rate ratio 0·13, 95% CI 0·12–0·14) and seasonal group (0·085, 0·08–0·09), as well as when the two enrolment groups were analysed together (0·11, 0·10–0·12).

All-cause hospitalisation rates (not related to LRTIs) for the 2023–24 season and previous seasons (since the

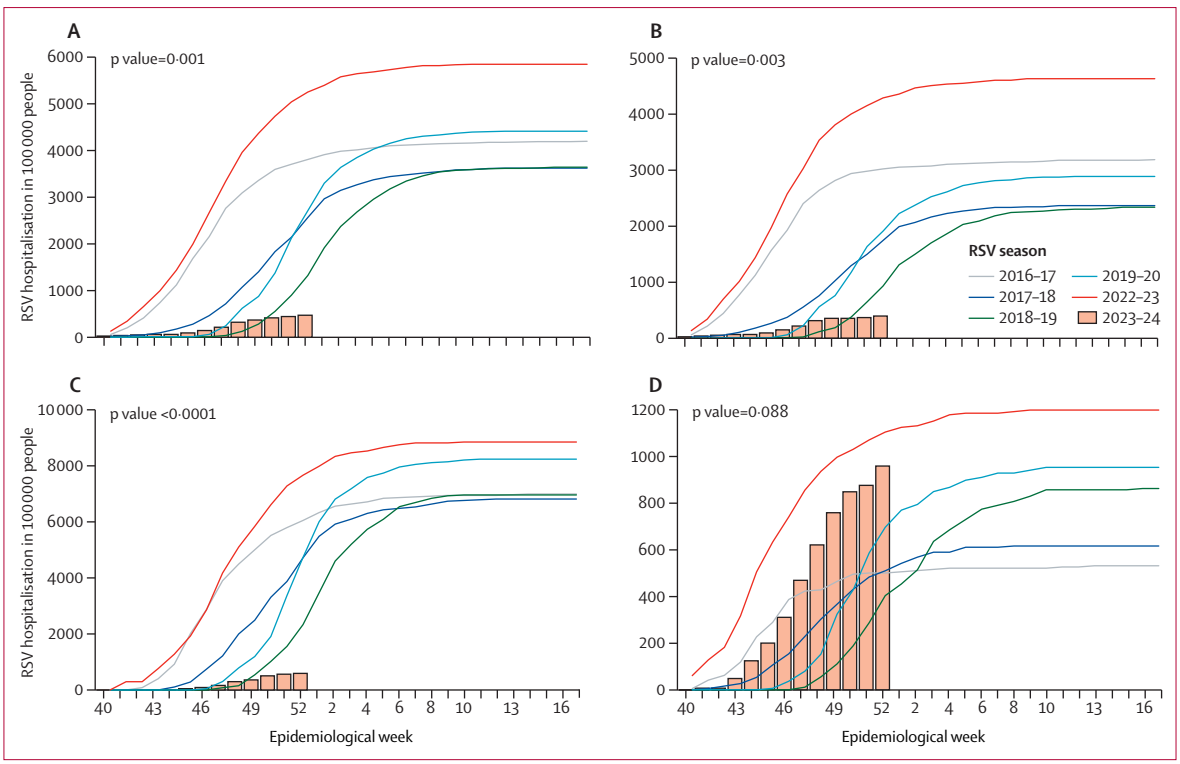

Figure 2: **Cumulative RSV hospitalisation rate (per 100 000) in Galicia, by RSV season, up to Dec 31, 2023 (week 52)**
(A) Catch-up and seasonal groups combined (ie, infants born between April 1 and Dec 15). (B) Catch-up group (ie, infants born between April 1 and Sept 24). (C) Seasonal group (ie, infants born between Sept 25 and Dec 15). (D) Comparison group (ie, infants born between April and March of the previous RSV season and so in their second RSV season—in 2023–24, this meant they were not eligible for nirsevimab). p values were obtained from linear regression model analysis of accumulated incidence rates comparing nirsevimab recipients with non-recipients and adjusting by the epidemic week. Note, y-axis scales differ between graphs. RSV=respiratory syncytial virus.

2017–18 season) are presented in appendix 2 (pp 15–17). The RSV seasons 2016–17, 2017–18, 2018–19, 2019–20, and 2022–23 had a median of 12 864 all-cause hospitalisations per 100 000 infants taking place in infants after their 3rd day of life, and a median of 4197 RSV-related LRTI hospitalisations per 100 000. In these years, between 23·5% and 34·5% of all-cause hospitalisations were for RSV-related LRTIs. For the 2023–24 season, we observed that 24·7% of all-cause hospitalisations in non-nirsevimab recipients were for RSV-related LRTI, whereas only 10·4% of all-cause hospitalisations were for RSV-related LRTI in nirsevimab recipients.

In the absence of the nirsevimab campaign, the median number of expected RSV-related LRTI hospitalisations in infants born between April 1 and Dec 15, 2023, was 453 (IQR 370–474; table 3). The immunisation campaign contributed to a median of 407 averted cases (IQR 324–428), equivalent to 39·66 (31·61–41·72) averted hospitalised cases per 1000 infants. The number needed to immunise to avoid one case of RSV-related LRTI hospitalisations was 25 (IQR 24–32; table 3). The estimated reduction in hospitalised cases relative to the expected number of cases is therefore 89·84% (IQR 87·58–90·30; table 3). Excluding the 2022–23 RSV season from the baseline calculations because of its unusually high hospitalisation rates, the median number of averted cases was 376 (IQR 309–495) and averted hospitalised cases per 1000 infants was 36·7 (30·18–48·27).

After the administration of 9408 administered doses (8565 in full-term infants and 616 doses in preterm infants; table 1), five adverse events were reported, three of them categorised as severe, and none of them considered to be related to nirsevimab.

Discussion

Shortly after the approval of the long-acting monoclonal antibody nirsevimab in 2023, Galicia, an autonomous region in northwest Spain, incorporated nirsevimab into its immunisation programme.[12] The NIRSE-GAL study, a prospective, population-based study, was launched to assess nirsevimab effectiveness,[14] and the results after 3 months of its implementation show a significant impact on the prevention of RSV-related LRTI hospitalisations, all-cause LRTI hospitalisations, and all-cause hospitalisations.

In the previous RSV seasons (2016–23), three to five infants out of every 100 infants in Galicia were hospitalised for RSV per year, urging the need for preventive measures. As of March, 2023, when Galicia approved the nirsevimab

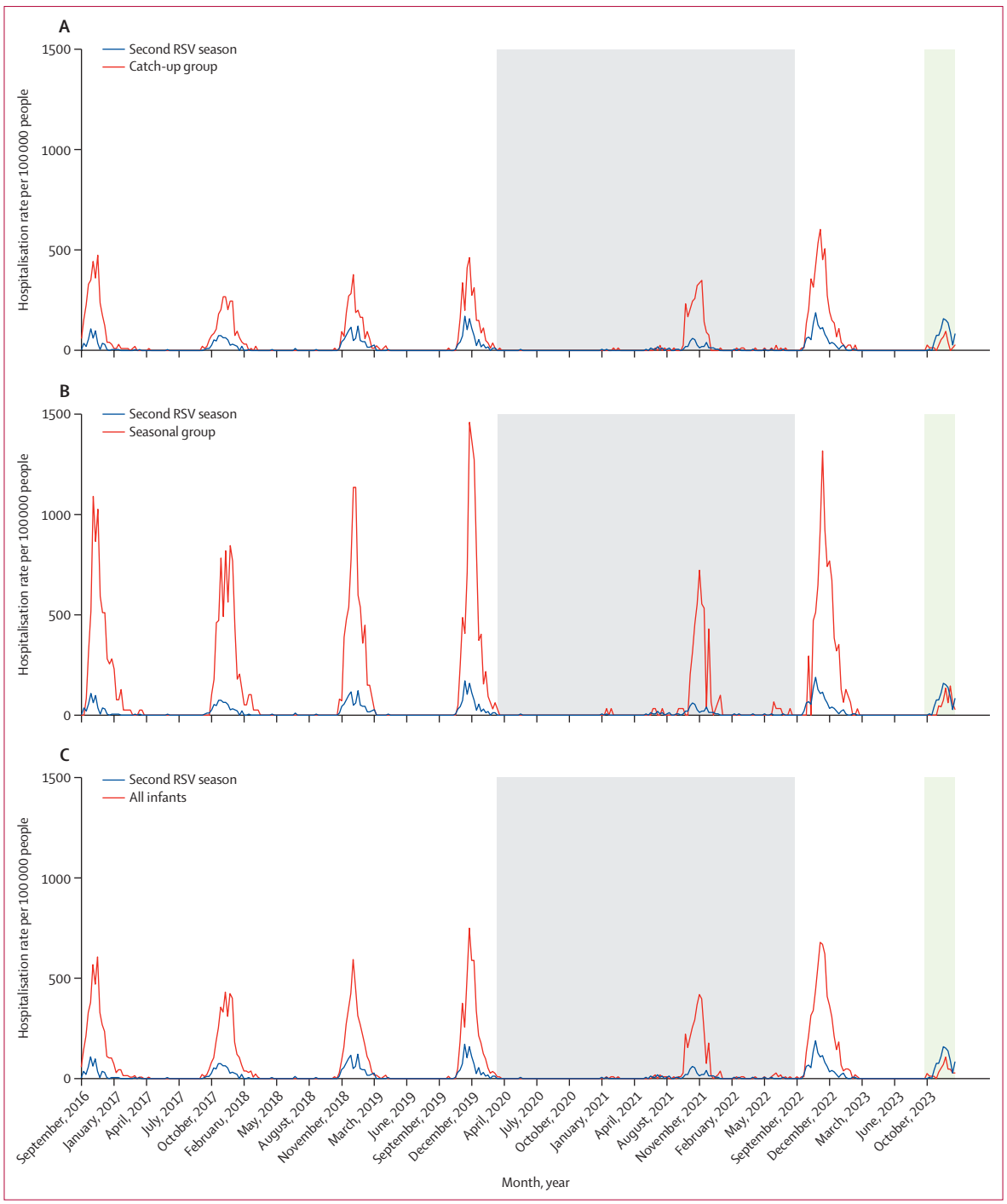

Figure 3: **Weekly hospitalisation rate of infants in Galicia for RSV (2016–23)**
The grey-shadowed area corresponds to RSV seasons affected by the COVID-19 pandemic (2020–22) that were excluded from the analysis. The green-shadowed area indicates the initiation of the universal prophylaxis campaign with nirsevimab in infants. Infants born between April and March of the previous RSV season (for the 2023–24 cohort, this meant they were ineligible for nirsevimab) are compared with infants who were eligible (2023–24 cohort) or would have been eligible (historical cohorts) for nirsevimab, divided into three study groups: (A) the catch-up group (ie, infants born between April 1 and Sept 24), (B) the seasonal group (ie, infants born between Sept 25 and Dec 15), and (C) all infants (ie, those born between April 1 and Dec 15). RSV=respiratory syncytial virus.

immunisation campaign, only this prophylactic measure had been licensed against RSV in infants. Given the novelty of nirsevimab and the scarce availability of extensive cost-effectiveness studies, Galician authorities adopted a pragmatic approach to nirsevimab introduction—a public health decision addressing

	RSV season					Median (IQR)	
	2016–17	2017–18	2018–19	2019–20	2022–23	Main analysis	Excluding 2022–23*
RSV-related LRTI hospitalisation rate per 100 000							
First RSV season†	3774·25	2533·84	1322·88	2692·70	5152·12	..	..
Second RSV season‡	469·56	494·05	392·61	672·17	1051·36	..	..
Ratio (first:second)	8·04	5·13	3·37	4·01	4·90	..	..
Estimates for the 2023–24 RSV season							
Expected rate per 100 000§	7241·18	4620·35	3035·45	3608·92	4414·71	4414·71 (3608·92–4620·35)	4414·64 (3465·55–5275·56)
Expected number of cases¶	743	474	311	370	453	453 (370–474)	422 (355–541)
Averted number of cases‖	697	428	265	324	407	407 (324–428)	376 (309–495)
Relative reduction (%)	93·81	90·30	85·23	87·58	89·84	89·84 (87·58–90·30)	88·94 (86·99–91·18)
Averted number of cases per 1000	69·93	41·72	25·87	31·61	39·66	39·66 (31·61–41·72)	36·66 (30·18–48·27)
Number needed to immunise	14	24	39	32	25	25 (24–32)	28 (22–24)

LRTI=lower respiratory tract infection. RSV=respiratory syncytial virus. *Median calculated excluding the 2022–23 RSV season because of its unusually high hospitalisation rates. †The first RSV season corresponds to infants who were experiencing the RSV season for the first time—for instance, for the 2016–17 RSV season, infants were born between April 1 and Dec 15, 2016. ‡The second RSV season corresponds to infants who were experiencing the RSV season for the second time—for instance, for the 2016–17 RSV season, children were born between April 1, 2015, and March 31, 2016. §The expected hospitalisation rate up to week 52 was calculated using the observed rate for infants in their second RSV season in the 2023–24 RSV season (901 per 100 000) and the ratio of hospitalisation rates between children in their first and second RSV seasons in the historical comparator RSV season; a median value and IQR across historical comparators was then obtained. ¶The expected number of cases was estimated by applying the expected rate to the 10 259 eligible infants observed in the 2023–24 RSV season. ||Averted cases were estimated by extracting the 46 hospitalisations observed in the 2023–24 RSV season from the number of expected cases.

Table 3: **Impact of nirsevimab on RSV-related LRTI hospitalisations in infants eligible for nirsevimab in the first 3 months of the 2023–24 RSV season based on historical data (excluding 2020–21 and 2021–22, the COVID-19 pandemic period)**

immediate health-care needs. This decision was based on an analysis of the disease burden and the anticipated cost savings, including reduced palivizumab consumption.[12,22] The pricing of nirsevimab in Galicia was established for 1 year, with a commitment to reassess pricing and cost-effectiveness based on the actual savings derived from reduced hospitalisations and medical interventions, measured through the ongoing NIRSE-GAL study. This innovative step by Galicia sets a precedent for evidence-based decision making in regional immunisation strategies, highlighting the importance of adapting health-care policies to the specific needs and challenges of the population.

Our findings show that nirsevimab was highly accepted in Galicia, as more than 90% of eligible infants for the NIRSE-GAL study were immunised within 3 months of the campaign launch. This high uptake was driven by a series of measures that Galicia used to ensure a rapid and effective campaign, including: a robust information and education campaign; hospital-based roll-out; an individualised and flexible electronic appointment system, including weekends, for all eligible infants in their reference hospital; and capturing of any eligible infant or child who missed the original immunisation appointment through the network of primary care paediatricians. The high coverage of nirsevimab aligns with data from all infant vaccines in Galicia, where coverage exceeds 90%.[23]

In our setting, nirsevimab reduced the risk of RSV-related LRTI hospitalisations by more than 80%. These findings align with those of the phase 3 clinical trial (MELODY) on nirsevimab efficacy in healthy late-preterm and term infants, which reported 76·8% efficacy against RSV-related LRTI hospitalisations.[24] Our findings also coincide with those of a pragmatic randomised controlled trial (HARMONIE), which estimated a nirsevimab efficacy of 83% against hospitalisations for RSV-associated LRTI.[25] Elsewhere in Spain, a study involving nine hospitals also estimated nirsevimab effectiveness against RSV-related LRTI hospitalisations, and reported effectiveness of 84% and 70%, depending on the study design (screening and test-negative design, respectively).[26] In Luxembourg, a substantial decrease in the number of RSV-related LRTI hospitalisations was observed in children younger than 5 years (38% reduction) and infants younger than 6 months (69%) after nirsevimab implementation, compared with the 2022–23 RSV season before nirsevimab.[27] Nevertheless, that study did not estimate the immunisation effectiveness of nirsevimab. Using the 2022–23 RSV season exclusively as a reference will likely overestimate the immunisation effectiveness of nirsevimab implementation as RSV showed intensified circulation in 2022.[28]

We also found that nirsevimab reduced the risk of severe RSV-related LRTI requiring oxygen support by 86·9%, a finding that was confirmed in the sensitivity analysis, even with a slightly higher magnitude (90·0%). No other real-world studies have measured nirsevimab effectiveness against this outcome. The HARMONIE pragmatic study, which resembled real-world settings, reported 76% efficacy for nirsevimab in preventing severe RSV-related LRTI.[25] The MELODY clinical trial also estimated a 78·6% efficacy against very severe medically attended RSV-related LRTI.[24]

To our knowledge, we have provided the first real-world estimates of the effectiveness of nirsevimab against all-cause LRTI hospitalisations and all-cause hospitalisations. We believe that these estimates represent substantial indicators of nirsevimab's potential wide-ranging impact from a public health perspective, particularly in settings for which the true burden of RSV might be underestimated. The extended benefits of RSV prevention could be partially attributed to RSV's role in co-infections or interactions with other pathogens, such as pneumococci, or by mitigating RSV's incremental effects on patients with pre-existing conditions.[29]

The strength of our study lies in its population-based prospective design. However, the present report only includes data from the first 3 months of the nirsevimab campaign in Galicia. The NIRSE-GAL study is ongoing, with a planned follow-up period of at least 36 months. The use of historical data from the past five RSV seasons, excluding the COVID-19 pandemic period, and not relying only on data from the 2022–23 RSV season, allowed us to account for changes in RSV circulation in the season after the pandemic.[17,28] The quality of the Galician health services' records helped diminish bias from exposure or endpoint ascertainment (appendix 2 p 3). Nonetheless, our present findings should be interpreted with caution as the 2023–24 RSV season had not concluded at the time of analysis. Evaluating the same endpoints once the RSV season has finished will be crucial. We did not have sufficient observations on severe RSV-related LRTI requiring intensive care unit admission or mechanical ventilation to estimate effectiveness against these endpoints. This is most likely due to the almost 100% immunisation coverage in the high-risk group and the high nirsevimab uptake in the catch-up and seasonal groups who are in healthier conditions. Further data from real-world settings would be beneficial to estimate nirsevimab effectiveness against severe RSV disease. Moreover, owing to sample size limitations, the number of averted RSV-related hospitalisations was calculated along with the IQR instead of a CI. Finally, we had missing data for at-birth variables (prematurity, weight at birth, and gestational age at birth) for almost 3% of the overall study population. Those variables did not fulfil the inclusion criteria for their retention in the final statistical models, hence the missing data are unlikely to have affected our findings.

Nirsevimab use in Galicia has shown a significant impact in the prevention of RSV-related hospitalisations, but also of all-cause LRTI hospitalisations and all-cause hospitalisations. Results are aligned with those reported in clinical trials so far. These experiences can illuminate the deliberations of other countries in shaping their programmatic approaches, providing policy makers with crucial information for formulating effective and efficient RSV immunisation prevention strategies.

Contributors

SA-G: data curation, formal analysis, methodology, visualisation of results, project administration, writing the original draft, and reviewing and editing subsequent drafts. NM: literature search, data interpretation, investigation, methodology, visualisation of results, writing the original draft, and reviewing and editing subsequent drafts. M-IS-P and JP-S: data curation, formal analysis, methodology, and reviewing and editing subsequent drafts. AM-P: data curation, formal analysis, methodology, visualisation of results, and reviewing and editing subsequent drafts. OP-M, M-TO-B, NS-G, MP-S, and J-MG-P: raw data collection, data curation, and reviewing and editing subsequent drafts. RK, JJ, and LP-A: methodology and reviewing and editing subsequent drafts. R-MA-G, O-MC-O, VN-P, SM-C, CR-T-S, and IR-C: provision of resources, project administration, and reviewing and editing subsequent drafts. AS: figures, investigation, and reviewing and editing subsequent drafts. CD-P: conceptualisation, project administration, resources, supervision, and reviewing and editing subsequent drafts. FM-T: conceptualisation, funding acquisition, investigation, methodology, project administration, resources, supervision, visualisation of results, writing the original draft, and reviewing and editing subsequent drafts. All authors reviewed the manuscript, approved its publication, and are responsible for its content.

Declaration of interests

FM-T reports having acted as principal investigator in randomised controlled trials for Ablynx, Abbott, Seqirus, Sanofi Pasteur, Cubist, Wyeth, Merck, Pfizer, Roche, Regeneron, Jansen, Medimmune, Novavax, Novartis, and GSK, with honoraria paid to his institution and relationships with GSK Vaccines, Pfizer, Sanofi Pasteur, Janssen Pharmaceuticals, MSD, and Seqirus that include consulting or advisory roles. RK, JJ, and LP-A are Sanofi employees and hold shares or stock options in the company. All other authors declare no competing interests.

Data sharing

Anonymised data will be made available upon reasonable request to the corresponding author.

Acknowledgments

The NIRSE-GAL study (CEIC 2023–377) was funded by Sanofi and AstraZeneca through a research grant to the Healthcare Research Institute of Santiago, Spain. This work was also supported by the Framework Partnership Agreement between the Consellería de Sanidad de la Xunta de Galicia and GENVIP-IDIS-2021–2024 (SERGAS-IDIS March, 2021; Spain). In addition, it received support from: (1) Instituto de Salud Carlos III TRINEO PI22/00162, DIAVIR DTS19/00049, Resvi-Omics PI19/01039 (to AS), ReSVinext PI16/01569, Enterogen PI19/01090, OMI-COVI-VAC PI22/00406 (to FM-T), and co-financed FEDER; (2) GAIN IN607B 2020/08 and IN607A 2023/02 (to AS), GEN-COVID IN845D 2020/23 (to FM-T), and IIN607A2021/05 (to FM-T); (3) ACIS BI-BACVIR (PRIS-3, to AS) and CovidPhy (SA 304 C, to AS); and (4) Consorcio Centro de Investigación Biomédica en Red de Enfermedades Respiratorias (CB21/06/00103, to AS and FM-T). This study was also supported by grants from the Galician Supercomputing Center, the Spanish Ministry of Science and Innovation, the Galician Government, and the European Regional Development Fund, the European Seventh Framework Programme for Research and Technological Development (FP7) under the EUCLIDS project (grant agreement number 279185).

References

1 Wildenbeest JG, Billard M-N, Zuurbier RP, et al. The burden of respiratory syncytial virus in healthy term-born infants in Europe: a prospective birth cohort study. *Lancet Respir Med* 2023; **11:** 341–53.

2 Martinón-Torres F, Carmo M, Platero L, et al. Clinical and economic hospital burden of acute respiratory infection (BARI) due to respiratory syncytial virus in Spanish children, 2015–2018. *BMC Infect Dis* 2023; **23:** 385.

3 Del Riccio M, Spreeuwenberg P, Osei-Yeboah R, et al. Burden of respiratory syncytial virus in the European Union: estimation of RSV-associated hospitalizations in children under 5 years. *J Infect Dis* 2023; **228:** 1528–38.

4 Martinón-Torres F, Carmo M, Platero L, et al. Clinical and economic burden of respiratory syncytial virus in Spanish children: the BARI study. *BMC Infect Dis* 2022; **22:** 759.

5 Gea-Izquierdo E, Gil-Prieto R, Hernández-Barrera V, Gil-de-Miguel Á. Respiratory syncytial virus-associated hospitalization in children aged <2 years in Spain from 2018 to 2021. *Hum Vaccin Immunother* 2023; **19:** 2231818.

6 Mao Z, Li X, Dacosta-Urbieta A, et al. Economic burden and health-related quality-of-life among infants with respiratory syncytial virus infection: a multi-country prospective cohort study in Europe. *Vaccine* 2023; **41:** 2707–15.

7 European Medicines Agency. Beyfortus nirsevimab. 2022. https://www.ema.europa.eu/en/medicines/human/EPAR/beyfortus#ema-inpage-item-authorisation-details (accessed Feb 6, 2024).

8 UK Government Department of Health and Social Care. Independent report. Respiratory syncytial virus (RSV) immunisation programme for infants and older adults: JCVI full statement, 11 September 2023. 2023. https://www.gov.uk/government/publications/rsv-immunisation-programme-jcvi-advice-7-june-2023/respiratory-syncytial-virus-rsv-immunisation-programme-for-infants-and-older-adults-jcvi-full-statement-11-september-2023 (accessed Feb 6, 2024).

9 Government of Canada. Product information. 2024. https://health-products.canada.ca/dpd-bdpp/info?lang=eng&code=102594 (accessed Feb 6, 2024).

10 Food and Drug Administration. FDA approves new drug to prevent RSV in babies and toddlers. 2023. https://www.fda.gov/news-events/press-announcements/fda-approves-new-drug-prevent-rsv-babies-and-toddlers (accessed Feb 6, 2024).

11 Galician Statistical Institute. Population report. Feb 1, 2024. https://www.ige.gal/web/mostrar_seccion.jsp?idioma=gl&codigo=0201 (accessed Feb 6, 2024) (in Spanish).

12 Martinón-Torres F, Mirás-Carballal S, Durán-Parrondo C. Early lessons from the implementation of universal respiratory syncytial virus prophylaxis in infants with long-acting monoclonal antibodies, Galicia, Spain, September and October 2023. *Euro Surveill* 2023; **28:** 2300606.

13 Martinón-Torres F, Navarro-Alonso JA, Garcés-Sánchez M, Soriano-Arandes A. The path towards effective respiratory syncytial virus immunization policies: recommended actions. *Arch Bronconeumol* 2023; **59:** 581–88.

14 NIRSE-GAL. Evaluation of the effectiveness and impact of nirsevimab in Galicia. 2024. https://www.nirsegal.es/ (accessed Feb 6, 2024).

15 Galician Health Service (SERGAS). Follow-up report on immunization with nirsevimab in Galicia. 2024. https://www.sergas.es/Saude-publica/Documents/7512/Report_RSV_week9.pdf (accessed Feb 6, 2024).

16 Galician Health Service (SERGAS). Pharmacovigilance security. https://www.sergas.gal/Saude-publica/Seguridade-e-farmacovixilancia?idioma=es (accessed Feb 6, 2024) (in Spanish).

17 Olsen SJ, Winn AK, Budd AP, et al. Changes in influenza and other respiratory virus activity during the COVID-19 pandemic—United States, 2020–2021. *MMWR Morb Mortal Wkly Rep* 2021; **70:** 1013–19.

18 US Centers for Disease Control and Prevention. Respiratory syncytial virus infection (RSV), symptoms and care. 2023. https://www.cdc.gov/rsv/about/symptoms.html (accessed Feb 6, 2024).

19 Greenland S. Dose-response and trend analysis in epidemiology: alternatives to categorical analysis. *Epidemiology* 1995; **6:** 356–65.

20 Therneau TM. A package for survival analysis in R. 2020. https://CRAN.R-project.org/package=survival (accessed April 25, 2024).

21 R Core Team. The R project for statistical computing. 2013. http://www.R-project.org/ (accessed April 25, 2024).

22 Galician Health Service (SERGAS). Galician RSV immunoprophylaxis campaign. Sept 25, 2023. https://www.sergas.es/Saude-publica/INMUNIZACION-FRONTE-AO-VIRUS-RESPIRATORIO-SINCITIAL (accessed Feb 6, 2024; in Spanish).

23 Ministerio de Sanidad. Sistema de Información de Vacunaciones. https://pestadistico.inteligenciadegestion.sanidad.gob.es/publicoSNS/I/sivamin/informe-de-evolucion-de-coberturas-de-vacunacion-por-vacuna (accessed Feb 6, 2024).

24 Muller WJ, Madhi SA, Seoane Nuñez B, et al. Nirsevimab for prevention of RSV in term and late-preterm infants. *N Engl J Med* 2023; **388:** 1533–34.

25 Drysdale SB, Cathie K, Flamein F, et al. Nirsevimab for prevention of hospitalizations due to RSV in infants. *N Engl J Med* 2023; **389:** 2425–35.

26 López-Lacort M, Muñoz-Quiles C, Mira-Iglesias A, et al. 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. *Euro Surveill* 2024; **29:** 2400046.

27 Ernst C, Bejko D, Gaasch L, et al. Impact of nirsevimab prophylaxis on paediatric respiratory syncytial virus (RSV)-related hospitalisations during the initial 2023/24 season in Luxembourg. *Euro Surveill* 2024; **29**.

28 European Centre for Disease Prevention and Control. Intensified circulation of respiratory syncytial virus (RSV) and associated hospital burden in the EU/EEA. 2022. https://www.ecdc.europa.eu/en/publications-data/intensified-circulation-respiratory-syncytial-virus-rsv-and-associated-hospital (accessed Feb 6, 2024).

29 Ben-Shimol S, Ramilo O, Leber AL, et al. A hypothesis-generating prospective longitudinal study to assess the relative contribution of common respiratory viruses to severe lower respiratory infections in young children. *Pediatr Infect Dis J* 2023; **42:** 396–404.