Real-world impact of nirsevimab immunisation against respiratory disease on emergency department attendances and admissions among infants: a multinational retrospective analysis

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Summary

Background Nirsevimab, a novel monoclonal antibody with a long half-life, has received European Union approval to prevent lower respiratory tract infections (LRTIs) caused by respiratory syncytial virus (RSV) during the first season of exposure. It was implemented in Catalonia (Spain) in the 2023–2024 season. Our main objective was to analyse the impact of the nirsevimab on LRTIs presenting to the Emergency Department (ED) in Catalonia (Spain) by comparing presentations to those at five sites in the United Kingdom (UK) and Rome (Italy).

Methods In this multi-national retrospective analysis of emergency department attendances and admissions, we retrospectively collected information for all diagnoses, respiratory diagnoses excluding bronchiolitis, and bronchiolitis, for different age groups from 68 hospitals in Catalonia (Spain), one hospital in Rome (Italy), and four hospitals in the UK (Bristol, Leicester, Glasgow, and Edinburgh), from May 1st, 2018, to April 30th 2024. Applying a generalised linear model (GLM) in Poisson regression, we obtained the risk ratio (RR) and 95% confidence intervals (CI) of bronchiolitis in 2023–2024 season compared to the mean of all previous seasons. We analysed data in annual bins, from May 1st to April 30th, excluding 2020–21 as a COVID year, for a total of 5 years of data.

Findings Data was available for 1,574,392 ED attendances (96,028 for bronchiolitis) and 255,689 hospital admissions (27,691 for bronchiolitis). In the 2023–2024 season, in Catalonia there was a reduction in the RR for bronchiolitis hospital admissions in the youngest infants aged <6 months (0.52, 95% CI: 0.48–0.55). There was also a reduction in Catalonia in the RR for hospital attendances for bronchiolitis in nirsevimab eligible age groups (0–11 months), with a RR of 0.56 (95% CI: 0.54–0.58) for infants <6 m and 0.93 (95% CI: 0.89–0.97) for infants 6–11 m. None of the other sites or age groups showed a significant reduction in the RR for attendances or admissions for the 2023–2024 season compared to previous years.

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Interpretation Nirsevimab had a clear impact in reducing attendances and admissions for infants with bronchiolitis aged <6 months in Catalonia. However, the impact on older infants was less clear.

Funding None.

Keywords: Nirsevimab; Bronchiolitis; Lower respiratory tract infections; Children

Research in context

Evidence before this study

We searched PubMed to identify relevant literature from February 23, 2017 (the publication of the Phase I trial for nirsevimab/MEDI8897) until January 29, 2025, using the key words "nirsevimab" and "RSV bronchiolitis". Out of 36 publications, we identified 16 original studies evaluating the effects of nirsevimab on reducing hospitalisations for RSV bronchiolitis, mostly in randomised controlled trials (including the first trial that led to the licence of the medication), and three real-world effectiveness studies. Most studies were published in Spain and France, and one from Northern Italy. However, no multi-national studies evaluated the wider impact of nirsevimab on acute emergency care attendances and hospitalisations, compared to countries that had not introduced this intervention, in the context of preceding bronchiolitis seasons.

Added value of this study

This is the first multinational study to analyse the real-world impact of the nirsevimab in the 2023–2024 season on lower-respiratory tract infection (LRTI) Emergency Department (ED) attendances and hospitalisations in a country that introduced this intervention (Catalonia, Spain), compared to EDs at five sites in two other European countries where nirsevimab had not been introduced.

Implications of all the available evidence

Nirsevimab had a clear impact in attendances and admissions for infants with bronchiolitis aged <6 months in Catalonia. However, the impact on older infants of age 6–11 and 12–23 months was less clear. As such, new, large, coordinated, multi-country, real-world evidence studies and cost-effectiveness analyses are required to optimise the use of new important interventions developed to reduce RSV burden. In addition, we note year-to-year variability in ED attendances and admissions for bronchiolitis, regardless of centre and including in the same country, which may mask or exaggerate the true impact of any intervention.

Introduction

Respiratory syncytial virus (RSV) is the main cause of lower respiratory tract infections (LRTIs) in children under one year of age, mostly associated with the diagnoses of bronchiolitis and pneumonia.[1–3] After more than fifty years of research in developing strategies for the prevention of these infections, on October 31, 2022, nirsevimab (Beyfortus®), a novel monoclonal antibody with a long half-life, received European Union approval as a preventive measure for LRTIs caused by RSV during the first season of the exposure to this virus.[4] Spain[5] was one of the first countries worldwide, alongside France,[6] Luxembourg[7] and the United States (US),[8] to systematically recommend and use nirsevimab in newborns and infants less than 6 months of age to reduce morbidity and mortality due to RSV in the 2023–24 season.[4] The implementation of this measure has had a significant impact on the epidemiology of RSV-associated disease in children under one year of age and has shown a good safety profile, with no new risks other than those previously identified in clinical trials,[9] as shown in a retrospective cohort study, conducted in Catalonia (Spain).[10] This study[10] analysed the incidence of visits to the emergency department (ED) for bronchiolitis, and hospital or paediatric intensive care unit (PICU) admission due to bronchiolitis or RSV infection. The authors concluded that a dose of nirsevimab was effective in reducing visits to the ED for all-cause bronchiolitis by 55.4% (95% CI: 48.4–61.5%), as well as reducing the risk of hospital admission for RSV bronchiolitis by 87.6% (95% CI: 82.1–91.4%) and need for PICU care for RSV bronchiolitis by 90.1% (95% CI: 76.3–95.9%).[10]

The approach to RSV prevention is dynamic, and there is a need to both establish the impact of current interventions (nirsevimab[4]) and generate baseline data prior to the introduction of new ones (maternal RSV vaccination[11]). We therefore designed a retrospective observational study to analyse ED attendances and admissions to hospital from the ED due to bronchiolitis in centres that had implemented different approaches toward RSV immunisations, relative to total respiratory diagnoses and all-causes diagnoses for a study period between the seasons 2018–19 and 2023–24. The participating sites were from Spain (Catalonia, where nirsevimab was widely introduced), compared with the

United Kingdom (UK) (Leicester, Bristol, Edinburgh, and Glasgow), Italy (Rome), where neither nirsevimab nor maternal RSV vaccination was introduced during the study period.

Our main objective was to examine the impact of the nirsevimab campaign in reducing the number of infants presenting with LRTIs to the ED in Catalonia (Spain) (intervention group) in comparison with sites where this measure was not implemented: the UK and Italy. The data generated by this study will also serve as a baseline to understand the ongoing impact of nirsevimab in its second season of use, and the impact of the first season of maternal RSV vaccination. Secondly, we aimed to provide information on the seasonal and centre-by-centre variability of bronchiolitis ED attendances and hospitalisations, to understand potential limitations to the assessment of the comparative impact of novel RSV interventions across Europe.

Methods

We collected data from the EDs of all the centres in Catalonia (Spain), Gemelli University Hospital in Rome (Italy), the Bristol Royal Hospital for Children in Bristol (UK), the Leicester Royal Infirmary in Leicester (UK), the Royal Hospital for Children, Glasgow (UK) and the Royal Hospital for Children and Young People, Edinburgh (UK). Study centres were selected to compare hospital outcomes in Catalonia, a region where nirsevimab was widely implemented with sites in two countries that at the time of the study had not yet implemented any population level RSV prevention measures (the UK and Italy).

For each site, for seasons May 1st, 2018, to April 30th, 2019, until May 1st, 2023, to April 30th, 2024, we gathered total ED attendances and total admissions from the ED for all diagnoses, respiratory diagnoses (RD) excluding bronchiolitis, and bronchiolitis diagnoses for children <6 months, 6–11 months, and 12–23 months. The codes used for these diagnoses (ICD-10 for Catalonia and Rome (Italy); Emergency Care Data Set (ECDS) and SNOMED CT for the UK sites) are provided in Supplementary Table S1. SNOMED CT is a structured clinical vocabulary for use in electronic health records. The coding procedures are mostly comparable, particularly for this study when we focused the case-research on well-defined conditions (bronchiolitis and respiratory diagnoses).

Catalonia recommended nirsevimab for all infants born from October 1st, 2023, onwards as part of the infant immunisation program; it was made available free of charge for all eligible infants. The recommendations include immunisation for all infants born before the epidemic season, between April and September, at primary care centres (PCCs) during October, as well as for all newborns born during the epidemic season, between October and March, in public and private hospitals within the first days of life and before hospital discharge. Additionally, nirsevimab was made available throughout the entire epidemic season at PCCs to ensure accessibility for newborns who were not immunised in hospital settings. Nirsevimab dosing was as per the European Medicines Agency recommendations: 50 mg for those <5 kg and 100 mg for those ≥5 kg.[12]

In Catalonia, data from hospital admissions were obtained from the Minimum Basic Data Set (CMBD) and hospital ED visits from the CMBD-UR for the 68 hospitals in Catalonia. The CMBD includes information on hospital discharges from all hospitals in Catalonia, encompassing both public and private hospitals. In the UK, data was obtained from the local Emergency Department Information System associated with that hospital. In Italy, data were obtained from the electronic system of the hospital, coding all attendances and admissions to the hospital. For all sites ethical permissions allowed for the use of aggregate patient data only, and we were therefore unable to report on attendance/admissions using sex, socio-economic status, or race/ethnicity as descriptive variables.

We calculated the percentage of bronchiolitis among all diagnoses, and among RDs and visualised these data by site and age group. To assess the differences between the 2023 and 2024 season and previous years, we calculated the mean of total ED attendances, RD-related ED attendances and bronchiolitis-related ED attendances, as well as admissions from ED, for 2018–2019, 2019–2020, 2021–2022 and 2022–2023. We analysed data in annual bins, from May 2018 to April 2024, excluding 2020–21 as a COVID year, for a total of 5 years of data. We excluded the 2020–2021 season from our calculations, as we anticipated that low case rates related to lockdown measures introduced in response to the COVID-19 pandemic could skew average ED attendances/admissions for the preceding and subsequent seasons.

The population at risk in the region of Catalonia was the entire population of children under the age of two years of age for each study season, as healthcare is universal and free at point of the point of delivery. The population at risk for each UK hospital is harder to estimate[13] but was assumed to remain constant over the study period to allow inter-year comparability. The study site in Rome is one of four major paediatric hospitals in Rome, again without a clearly defined patient population, but again the population at risk was assumed to remain comparable over the study period.

With these datasets we then calculated a generalised linear model (GLM) in Poisson regression form per place and age group, obtaining the risk ratio (RR) and 95% confidence intervals (CI) of bronchiolitis. Comparisons were made between 2023 and 2024 and each previous season individually (see Supplementary Materials), as well as against all previous seasons together but 2020–2021 labelling them as "pre-nirse"

and setting it as reference level. Since the findings were consistent across these comparisons, we present results using the latter approach in the main paper, and more detailed comparisons in the Supplementary Materials. We added as offset term the natural logarithm of total admissions for comparability. This model can be expressed as:

$$\ln(\mathrm{E}[bronchiolitis]) = \beta_0 + \beta_1 \cdot season + \ln(all\ diagnoses) \quad \text{EQ (1)}$$

where: E[*bronchiolitis*]: expected number of bronchiolitis diagnoses; β_0: Intercept; β_1: Coefficient related to the difference for season respect to the baseline, in this case, the average between seasons.

With the exponential of β_1 in EQ (1), the RR (95% CI) can be calculated. There were some seasons in which for a certain age group there were no bronchiolitis diagnoses. Results for those cases are marked as "-".

As a sensitivity analysis, we employed the synthetic control method[14–16] to estimate the incidence of bronchiolitis in Catalonia for infants under 6 months. This approach leveraged the incidence of bronchiolitis, total diagnoses, and RVI from other study sites as predictors, separately modelling attendances at the ED and admissions from the ED. We computed incidence as cases per 100,000 population, using as reference population the local population of each city/Health Board, and regional data in the case of Catalonia (see Supplementary Methods and Supplementary Table S2). Given the substantial variability in incidence across sites, we standardised the data by normalising each incidence measure relative to its mean value. The detailed results of this analysis are provided in Supplementary Figures S1 and S2.

Python v.3.9.20[17] and R v. 4.4.2[18] were used for data analyses and visualisation. Scripts used for these analyses and visualisation are available at https://github.com/BIOCOM-SC/cloud-of-codes/tree/main/Aida_Perramon-Malavez/TLRHEUROPE-D-25-00124.

Ethic approval

This retrospective observational study involving human participants followed the ethical standards of the institutional and national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Ethical approval was obtained for aggregate data from Catalonia (Vall d'Hebron Research Institute (EOM(AG)006/2024 (6232)) and Fundació IDIAP-Jordi Gol (25/041-EOm) with the approval dates on March 15, 2024 and March 6, 2025) and Rome (Italy; [Comitato Etico Fondazione Policlinico Universitario A. Gemelli IRCCS ID 3497, Prot 0049226/20, 02/10/2020]). In the UK sites data collection was registered under the umbrella of a service evaluation project; under Health Research Authority guidance these projects are exempt from formal ethical approval. Consent was not required at any site for these aggregated, population level datasets.

Role of the funding source

There was no funding source for this study.

Results

Data was available for 1,574,392 attendances to Emergency Departments, 217,351 non-bronchiolitis respiratory attendances, and 96,028 bronchiolitis attendances. Data was available for 255,689 admissions to hospital from Emergency Departments, 22,980 non-bronchiolitis respiratory admissions, and 27,691 bronchiolitis admissions; Table 1 provides a breakdown of patient numbers by age, diagnosis, and study site. Comparing ED attendances and hospital admissions over time for infants of less than 6 months of age for sites from the three countries where data was available for (Spain, United Kingdom, and Italy) [Fig. 1], we found year to year variability for both all cause ED attendances/hospital admissions, and RD attendances/admissions. In this age group bronchiolitis was both the most common RD for ED attendances and for hospital admissions; however, the proportion of attendances that were coded as bronchiolitis varied by site. For admissions at all sites bronchiolitis was the predominant respiratory cause of admissions for this age group. However, respiratory diagnoses represented only a subset of all attendances to ED and admissions to ED [Fig. 1].

A significant reduction in respiratory and bronchiolitis attendances and admissions in the <6-month age group was seen at all sites for the 2020–2021 season, as documented previously.[19] Subsequently, the 2023–2024 season showed a reduction in all diagnoses in Catalonia for all cause respiratory ED attendances and respiratory hospital admissions, a reduction that was not found at any other sites in the study. This reduction in attendances and admissions was driven by a reduction in bronchiolitis diagnoses.

Season to season variability for all age groups is compared in Supplementary Tables S3 and S4, and consistently hereby we provide season variability with respect to the seasons previous to 2023–2024 except 2020–2021 in Fig. 2, with further data in Table 2 and Table 3, which provide the RR for attendances to EDs and admissions from EDs with a primary diagnosis of bronchiolitis respectively. Risk ratios were calculated for each age group with a GLM in Poisson regression, comparing data on bronchiolitis from the 2023–2024 season with the other seasons (Supplementary Material, taking 2023–2024 as reference) and the remainder of seasons included in the study categorised as "pre-nirse", excluding 2020–2021, weighting by all diagnoses. For the latter analysis, the RR for the 2023–2024 season compared to previous seasons is significantly lower in Catalonia for ED attendances eligible age groups that

Region	2018–2019			2019–2020			2020–2021			2021–2022			2022–2023			2023–2024		
	<6 m	6–11 m	12–23 m	<6 m	6–11 m	12–23 m	<6 m	6–11 m	12–23 m	<6 m	6–11 m	12–23 m	<6 m	6–11 m	12–23 m	<6 m	6–11 m	12–23 m
Catalonia																		
Attendances to ED																		
All diagnoses	56,668	59,562	114,458	46,438	44,728	84,575	37,132	37,509	79,794	51,141	51,396	99,461	55,721	55,185	98,344	45,120	48,639	89,140
Respiratory diagnoses (w/o Bronchiolitis)	5580	9026	16,911	3779	5925	11,681	1984	3490	8374	4209	6292	12,438	5084	7043	13,046	4033	6302	12,281
Bronchiolitis	6263	2747	1048	5612	2403	948	2142	1408	1005	5102	2387	1307	7023	3167	1575	3109	2438	1258
Admissions from ED																		
All diagnoses	21,558	4046	7540	20,771	3088	5503	18,862	2596	5257	20,751	3185	6190	22,396	4124	7239	14,890	2747	5503
Respiratory diagnoses (w/o Bronchiolitis)	476	748	1368	367	459	976	140	188	674	385	451	1183	527	703	1435	349	522	1191
Bronchiolitis	2204	443	209	1883	402	225	716	275	243	1621	442	334	2441	614	372	881	456	281
Bristol																		
Attendances to ED																		
All diagnoses	4965	3782	7104	4763	3786	6491	3312	2013	3677	4965	3731	7202	4992	3867	6670	5148	3842	6301
Respiratory diagnoses (w/o Bronchiolitis)	556	1037	2707	517	1100	2632	169	331	749	501	1095	3109	506	1115	2679	571	1038	2378
Bronchiolitis	1090	606	181	1065	643	102	116	98	31	1111	671	163	1453	754	249	1318	713	251
Admissions from ED																		
All diagnoses	972	383	686	995	406	654	634	208	384	907	359	602	962	366	575	991	363	576
Respiratory diagnoses (w/o Bronchiolitis)	37	54	273	46	58	301	19	7	81	40	48	247	43	45	182	51	44	220
Bronchiolitis	312	124	51	313	168	26	23	32	11	234	133	32	322	149	64	321	154	55
Leicester																		
Attendances to ED																		
All diagnoses	5175	3999	7375	6068	4249	7267	4154	2373	3998	5942	4230	8082	6201	4237	6776	6217	4012	6739
Respiratory diagnoses (w/o Bronchiolitis)	715	1258	2751	724	1376	2756	296	637	1013	698	1365	3255	705	1242	2470	650	1102	2208
Bronchiolitis	997	578	116	1030	571	75	172	157	34	998	665	181	1402	716	150	1308	670	155
Admissions from ED																		
All diagnoses	1539	630	1288	1757	581	1247	970	184	347	1075	269	675	1089	363	489	1258	347	532
Respiratory diagnoses (w/o Bronchiolitis)	94	184	744	106	143	710	21	31	145	33	48	368	30	55	235	57	48	229
Bronchiolitis	416	174	36	381	163	18	26	24	6	201	93	26	311	148	17	315	124	35
Rome																		
Attendances to ED																		
All diagnoses	1412	1087	2260	1226	960	1893	722	388	734	1001	755	1548	1292	922	1767	1262	986	1685
Respiratory diagnoses (w/o Bronchiolitis)	154	186	443	140	199	309	26	17	52	102	96	204	108	134	293	157	143	249
Bronchiolitis	149	62	21	113	49	12	5	5	3	134	56	31	219	68	23	173	91	17
Admissions from ED																		
All diagnoses	388	75	140	328	66	106	283	52	75	289	65	111	337	57	110	343	75	111
Respiratory diagnoses (not including Bronchiolitis)	6	6	23	5	6	9	2	1	2	6	4	7	6	2	17	3	5	9
Bronchiolitis	50	11	4	37	10	6	2	2	0	47	14	10	74	9	6	57	18	6

(Table 1 continues on next page)

Region	2018–2019			2019–2020			2020–2021			2021–2022			2022–2023			2023–2024		
	<6 m	6–11 m	12–23 m	<6 m	6–11 m	12–23 m	<6 m	6–11 m	12–23 m	<6 m	6–11 m	12–23 m	<6 m	6–11 m	12–23 m	<6 m	6–11 m	12–23 m
(Continued from previous page)																		
Glasgow																		
Attendances to ED																		
All diagnoses	6803	5243	10104	7027	5511	9819	4144	2683	5392	6635	4980	9838	7462	6064	10310	7657	5394	9622
Respiratory diagnoses (w/o Bronchiolitis)	493	801	1838	509	768	1695	98	230	419	407	567	1624	452	742	1502	437	614	1396
Bronchiolitis	1012	797	476	999	806	461	66	113	66	837	648	506	1216	993	389	1041	796	423
Admissions from ED																		
All diagnoses	2599	1074	2003	3093	1290	2367	2119	693	1103	2767	993	2089	3028	1320	2202	3079	1077	1943
Respiratory diagnoses (not including Bronchiolitis)	74	88	447	118	90	493	22	26	117	82	60	484	78	85	390	79	62	372
Bronchiolitis	342	216	164	422	272	196	20	53	34	285	178	161	414	283	126	365	206	133
Edinburgh																		
Attendances to ED																		
All diagnoses	5041	3881	7358	4860	3766	7001	3748	2125	4110	5014	3516	7348	5045	4067	7206	4842	3570	6590
Respiratory diagnoses (w/o Bronchiolitis)	387	671	1565	293	623	1639	124	260	498	296	646	1937	331	724	1831	313	576	1544
Bronchiolitis	1042	696	395	1052	693	350	262	92	69	1227	555	351	1417	788	347	1280	677	327
Admissions from ED																		
All diagnoses	1370	522	980	1428	508	957	931	219	402	1252	414	954	1523	544	1003	1517	484	922
Respiratory diagnoses (w/o Bronchiolitis)	97	73	298	48	47	319	27	17	81	40	57	391	49	59	405	42	66	359
Bronchiolitis	402	194	172	472	191	155	89	24	24	427	160	140	585	254	174	548	215	152

Attendances and admissions by age, study site and diagnosis for Catalonia, Bristol, Leicester, Rome, Glasgow and Edinburgh. From season 2018–2019 to season 2023–2024, age groups <6 months, 6–11 months, 12–23 months old.

Table 1: **Details of attendances and admissions.**

received nirsevimab (0.56 (95% CI: 0.54–0.58) for <6 m and 0.93 (95% CI: 0.89–0.97) for 6–11 m, blue and green, respectively), and for the youngest children looking at admissions (0.52 (95% CI: 0.48–0.55) for <6 m) (Fig. 2). This effect was not observed for children who were not a target population for nirsevimab (12–23 m, magenta). None of the other sites showed a significant reduction in the risk ratio for the 2023–2024 season relatively compared to previous years, since all other sites show RR greater than 1 or with CI crossing the threshold; interestingly a number of sites showed a significant increase in bronchiolitis ED attendances (Bristol and Leicester) and admissions (Leicester) for the 12–23 m age group in the 2023–2024 season. ED attendances and admissions for respiratory diagnoses for the 6–11 and 12–23 months old groups are reported in Supplementary Figures S3 and S4.

Discussion

In this study, we analysed the impact of nirsevimab implementation on the number of infants presenting with LRTIs to the ED in Catalonia (Spain), where nirsevimab was rolled out to infants up to the age of 11 months in late summer 2023, compared with four paediatric centres in the UK and one in Rome (Italy), where widespread RSV-prevention measures had not yet been introduced. Overall, we found a significant association between the introduction of nirsevimab for the 2023–2024 season and a reduction in ED respiratory attendances for infants aged 0–11 m, and admissions for those <6 months of age. This supports previous epidemiological data which found RSV to be the single main cause of bronchiolitis in this age group,[20] and the risk ratios (for ED presentations 0.56 (0.54–0.58) for infants <6 months, 0.93 (0.89–0.97) for infants 6–11 months; 0.52 (0.48–0.55) for hospital admissions for infants <6 months) when 2023–2024 is compared to previously seasons similarly suggests that around half of all cases in this cohort are likely to be caused by RSV. Additionally, the effect size seen is comparable to that observed in other studies examining the impact of nirsevimab on ED attendances and hospitalisations.[21] However, we also found a substantial year to year variability in attendances and admissions for bronchiolitis, regardless of centre, including in the same country (UK). This year-to-year variability in ED attendances and admissions highlights the likely difficulties in understanding the impact of any RSV intervention with a single season's data: year to year variability may mask or exaggerate the true impact of any intervention.

While the potential impact of nirsevimab on a patient level is clear and demonstrated by a number of trials and real-world evidence studies,[10,22–29] the impact on a population level, and therefore on a wider public health perspective, may be less clear. In fact, one of the debates about routine nirsevimab implementation is around its

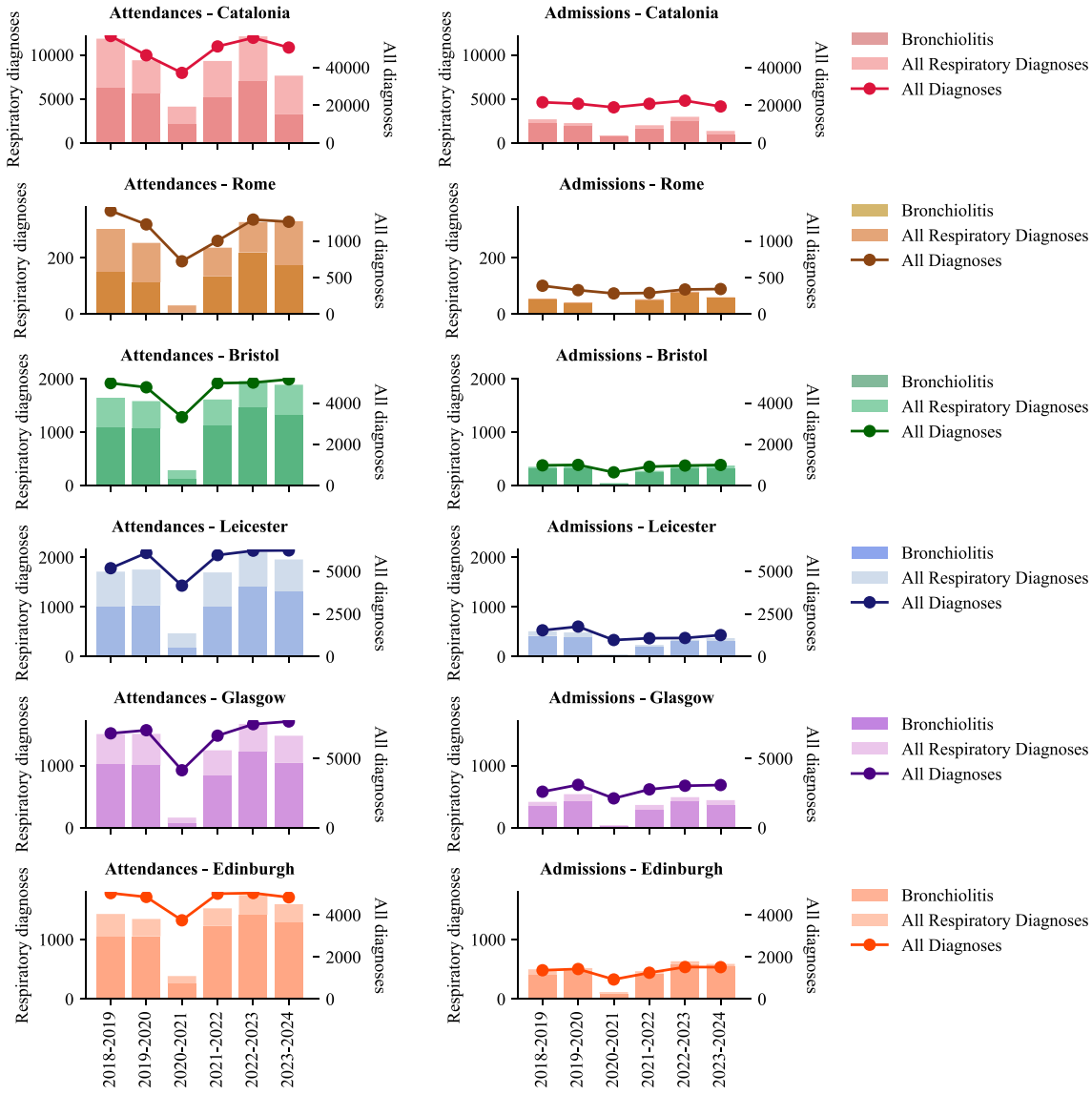

Fig. 1: **Emergency Department (ED) attendances and hospitalisations for infants <6 months of age at study sites**. The number of bronchiolitis (dark) and all respiratory diagnoses (light) cases attending each site's ED and admitted from the ED are shown on the right and left, respectively, with numbers shown on the left y-axis. The right y-axis shows the total number of ED attendances and admissions, respectively, at the study sites.

cost-effectiveness and long-term sustainability for national health systems. The data we present from Catalonia shows that in terms of overall case numbers, despite the introduction of nirsevimab, the total number of ED attendances and hospital admissions in those age <6 months in 2023–2024 was similar to those in 2021–2, and in fact higher than 2019–2020; respiratory diagnoses constitute only a proportion of attendances/hospitalisations.

As similar studies are not yet available, different countries are implementing different policies. Some settings, like Catalonia, have policies aimed at immunising all infants.[9] Others, like the UK,[11] have recently decided to implement maternal RSV vaccination, which was also found to be efficacious in clinical trials.[30] In Italy, nirsevimab was only implemented in the second half of October 2024[31] and given the low number of available doses, it is likely that only at-risk children and those younger than three months of age during a bronchiolitis season are currently eligible. Moreover, when considering the whole framework for RSV prevention, an expected positive and wider effect on a

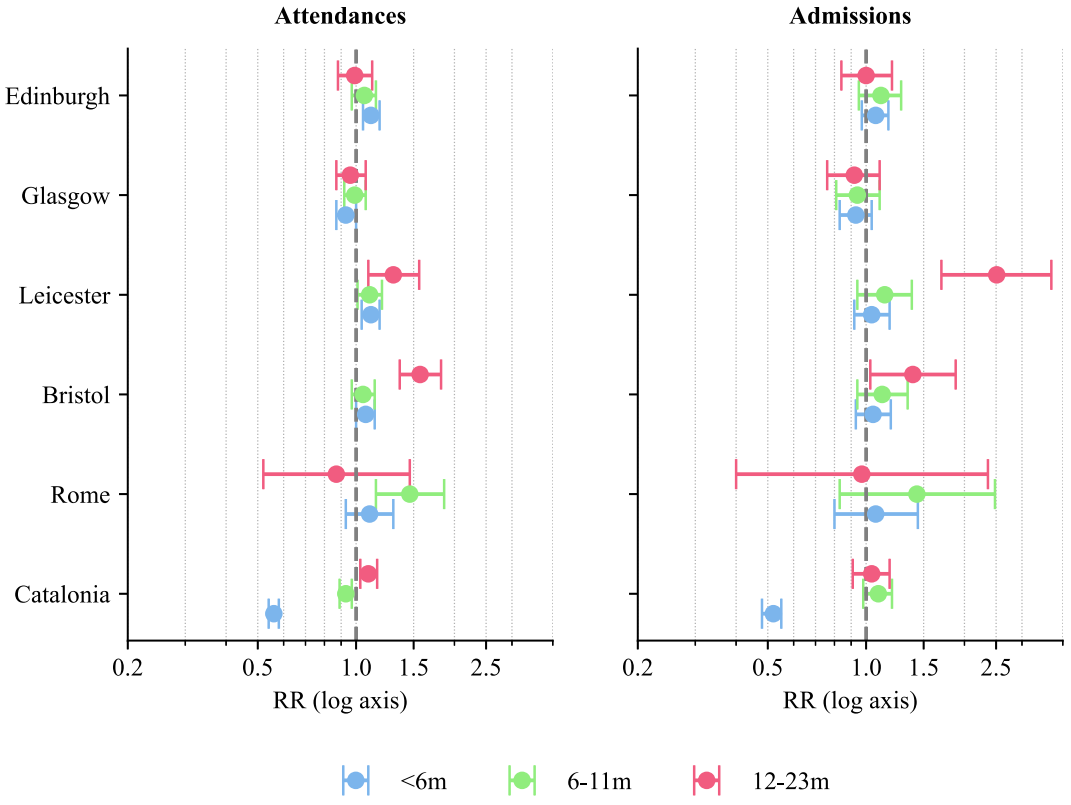

Fig. 2: **Risk ratios with confidence intervals (CI) 95% obtained with a Poisson regression for ED attendances and admissions with a primary diagnosis of bronchiolitis, by study site and by age group**. Case numbers in the 2023–2024 season are compared to the grouped "pre-nirse" 2018–2019, 2019–2020, 2021–2022 and 2022–2023 seasons. Confidence intervals which do not cross 1 have a p-value of less than 0.05.

population level would be to reduce the immense pressures on ED capacity and inpatient-PICU admissions during successive RSV seasons providing not only the direct benefit on reducing the costs associated to ED care and admissions, but also having an indirect effect on other patients by reducing ED overcrowding, waiting times and cognitive burden on staff.[32]

Our approach documented a lesser impact of nirsevimab in reducing ED visits and admissions associated with bronchiolitis in infants older than 6 months of age. This finding could have a number of explanations. Firstly, the larger benefit in younger infants could be related to a real larger biological effect of nirsevimab in infants immunised closer to the time of RSV infection and therefore providing a higher amount of neutralising antibody against RSV. Secondly, it is possible that in younger infants there is a double protective effect of having higher blood level of nirsevimab and residual maternal antibodies. However, it is also possible that the greater effect in younger infants can also be associated to differences in classification and coding, as debate exists on the ideal cut-off age for the diagnosis of bronchiolitis (six vs twelve vs twenty-four months), and it is possible that some patients older than six months may have been classified as wheezing, viral LRTI or pneumonia and not bronchiolitis. Also, it is possible that a larger proportion of young infants have been immunised in Catalonia, compared with older infants, therefore achieving a larger population effect. Moreover, the 6–11 months group includes attendance to ED and admissions of infants who are that age at the time of the outcome. Since the data is analysed for the entire season, the outcomes from the beginning of the RSV epidemic include a population that was not immunised (i.e. those who were 11 months-old in December were not part of the population eligible for nirsevimab immunisation).

An additional interesting finding is the variability of bronchiolitis and LRTI estimates, in particular the variability between the UK-based study sites. While we don't have a specific explanation for these findings, we can hypothesise that several factors are implicated in the epidemiology of bronchiolitis, from epidemiological ones (family members including school children, smoking, family income and overcrowding, climate), to single patient factors (gestational age, comorbidities), to

Location	Age group	RR (95% CI)	p-value
Catalonia	<6 m	**0.56 (0.54–0.58)**	**<0.0001***
	6–11 m	**0.93 (0.89–0.97)**	**0.0006***
	12–23 m	**1.09 (1.03–1.16)**	**0.0038***
Rome	<6 m	1.10 (0.93–1.30)	0.27
	6–11 m	**1.46 (1.15–1.86)**	**0.0021***
	12–23 m	0.87 (0.52–1.46)	0.59
Bristol	<6 m	1.07 (1.00–1.14)	0.034
	6–11 m	1.05 (0.97–1.14)	0.22
	12–23 m	**1.57 (1.36–1.82)**	**< 0.0001***
Leicester	<6 m	1.11 (1.04–1.18)	**0.0008***
	6–11 m	1.10 (1.01–1.20)	0.023
	12–23 m	**1.30 (1.09–1.56)**	**0.0041***
Glasgow	<6 m	0.93 (0.87–1.00)	0.051
	6–11 m	0.99 (0.92–1.07)	0.83
	12–23 m	0.96 (0.87–1.07)	0.47
Edinburgh	<6 m	**1.11 (1.05–1.18)**	**0.0006***
	6–11 m	1.06 (0.97–1.15)	0.19
	12–23 m	0.99 (0.88–1.12)	0.92

Risk ratios with confidence interval (CI) 95% obtained with a Poisson regression for attendances to the ED with a primary diagnosis of bronchiolitis in the 2023–2024 season compared to grouped "pre-nirse" 2018–2019, 2019–2020, 2021–2022 and 2022–2023 seasons, for study sites. p-values with * are those of less than 0.05 (95% significance). Bold is referred to statistically significant.

Table 2: **Risk ratios for bronchiolitis attendances to Emergency Departments (EDs), comparing grouped data from preceding seasons to 2023–2024.**

Location	Age group	RR (95% CI)	p-value
Catalonia	<6 m	**0.52 (0.48–0.55)**	**<0.0001***
	6–11 m	1.09 (0.98–1.20)	0.11
	12–23 m	1.04 (0.91–1.18)	0.56
Rome	<6 m	1.07 (0.80–1.44)	0.64
	6–11 m	1.43 (0.83–2.48)	0.19
	12–23 m	0.97 (0.40–2.36)	0.95
Bristol	<6 m	1.05 (0.93–1.19)	0.42
	6–11 m	1.12 (0.94–1.34)	0.22
	12–23 m	**1.39 (1.03–1.88)**	**0.037***
Leicester	<6 m	1.04 (0.92–1.18)	0.49
	6–11 m	1.14 (0.94–1.38)	0.19
	12–23 m	**2.51 (1.70–3.69)**	**<0.0001***
Glasgow	<6 m	0.93 (0.83–1.04)	0.22
	6–11 m	0.94 (0.81–1.10)	0.44
	12–23 m	0.92 (0.76–1.10)	0.36
Edinburgh	<6 m	1.07 (0.97–1.17)	0.18
	6–11 m	1.11 (0.95–1.28)	0.19
	12–23 m	1.00 (0.84–1.20)	0.99

Risk ratios with confidence interval (CI) 95% obtained with Poisson regression for admissions with a primary diagnosis of bronchiolitis from the ED for the 2023–2024 season compared to grouped "pre-nirse" 2018–2019, 2019–2020, 2021–2022 and 2022–2023 seasons, for study sites. p-values with * are those of less than 0.05 (95% significance). Bold is referred to statistically significant.

Table 3: **Risk ratios for bronchiolitis admissions from Emergency Departments (EDs), comparing grouped data from preceding seasons to 2023–2024.**

psychological ones (e.g. attitude of families to attend the ED for less severe cases, awareness of the disease), and local system organisation (e.g. availability of outpatient family paediatricians vs general practitioners, their availability during the whole day and week vs only day time excluding weekends). As such, bronchiolitis and LRTI epidemiology estimates may have significant variability even within the same countries, which may complicate attempts to understand the impact of RSV interventions at a national or international level.

Our study has some limitations. Firstly, it is a retrospective analysis. Secondly, the proportion of all attendances and admissions that were coded as bronchiolitis varied widely across UK/Spain/Italy. This could be due to coding differences or health system factors, and not real epidemiological differences. Therefore, nirsevimab could lead to apparently different effects after introduction depending on the setting and it may be intrinsically difficult to translate findings from our setting to another. In this regard, to better quantify the global local impact of nirsevimab or similar interventions, national health systems should work to optimise and homogenise clinical coding and electronic databases: a limitation of our analysis is the inability to directly match for all diagnoses ICD-10 to SNOMED codes (Supplementary Table S1). However, this is a key point to highlight for studies aiming to compare the impact of RSV interventions at a pan-European level. Thirdly, due to limited virology testing of ED attendances, we were unable to determine the relative contribution of RSV towards this burden in the seasons studied. However, an understanding that there is significant year-to-year variability in the burden of respiratory disease should highlight to policy makers that assessing the *impact* (rather than just the *effectiveness*) of a newly introduced intervention is likely to be challenging, if only a single season is examined. Future work should additionally aim to determine the relative burden of non-RSV respiratory viruses in the post-immunisation era. Fourthly, we were unable to report detailed sex, ethnicity, or socioeconomic status data for attendances/admissions, as we relied on anonymised aggregate data provided by study sites. However, we believe that these patient characteristics are likely to have remained broadly similar over the time period of the study and are unlikely to impact on our overall findings. Finally, we could not assess the RR based on the incidence rates between the sites of the study because the referral population for some of them was unavailable. However, we believe that the differences in the referral population between different years at the same location are not of clinical significance.

In conclusion, our study showed that nirsevimab had a clear impact in attendances and admissions for infants with bronchiolitis aged <6 months in Catalonia. However, the impact on older infants was less clear, making

it unrealistic to imagine a substantial change in the epidemiology of infants accessing EDs or inpatient wards, at least in the near future. New, large, coordinated, multi-country, real-world evidence studies and cost-effectiveness analyses are required to optimise the use of new important tools developed to reduce RSV burden.

Contributors

ASA, CP, DR, TCW, and DB conceptualised the study. APM, CP, TCW performed statistical analyses. RM, EC, SF, PL, RM, MMM, JM, DR, TCW, JV, ACC were responsible for data collection. All authors had access to all data and ASA, CP, verified the data. All authors read and approve the final version of the manuscript and had responsibility for the decision to submit for publication.

Data sharing statement

The dataset will be held for a minimum of 3 years and is available to be shared on reasonable request to the corresponding author, by providing a formal request supported by a hypothesis, research proposal that included a statistical plan and a local ethic committee approval. A data sharing agreement will be needed to be signed.

Declaration of interests

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Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.lanepe.2025.101334.

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