RESEARCH

Dynamics of RSV hospitalization rates in ≤ 2-year-old children between 2020–2023 in Europe

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Abstract

With the newly approved RSV preventive strategies enabling universal protection of infants, it is crucial to gain a comprehensive understanding of RSV hospitalization incidence, prior to the introduction of these strategies in order to facilitate an assessment of their impact. Children ≤ 2 years hospitalized with laboratory-confirmed RSV infection between 2020–2023 in France, Germany, Spain, Italy, and United Kingdom were included and compared with the 2018–2019 season. The population-based incidence was calculated as number of RSV hospitalizations divided by market share-adjusted number of children in the catchment area. Across participating countries, we observed a decrease in RSV hospitalization incidence during the 2020–2021 season due to the COVID-19 pandemic, dropping to 5.9/1000 child-years (95%CI 5.4–6.3) compared with 11.3/1000 child-years (95%CI 10.6–11.9) in 2018–2019. This decline was followed by a rebound in incidence, with rates reaching 13.8/1000 child-years (95%CI 13.0–14.5) in 2021–2022 and 18.8/1000 child-years (95%CI 18.0–19.7) in 2022–2023. Distinct patterns of RSV resurgence were observed across countries. During the 2020–2021 season, there was an increase in PICU admissions (29.5% vs 20.0% pre-pandemic, $p < 0.001$), despite a lower total number of RSV admissions (610 vs 1,238) compared to the 2018–2019 season.

Conclusions: The population-based incidence of RSV hospitalization in children ≤ 2 years is substantial. Considerable variation in incidence was observed between 2020 and 2023, with an initial decline during the COVID-19 pandemic followed by a rebound in the subsequent seasons. Our study underscores the importance of RSV surveillance and flexibility in RSV preventive strategies.

What is Known:
• *RSV is a major cause of hospitalization in young children under 5 years of age worldwide.*
• *RSV seasonality was disrupted during the COVID-19 pandemic.*

What is New:
• *Distinct patterns of RSV resurgence were observed across five European countries during the COVID-19 pandemic, with an initial decline in incidence of RSV associated hospitalizations in children ≤ 2 years, followed by a rebound in the subsequent seasons, reaching 18.8 per 1,000 child-years (95% CI: 18.0 - 19.7) in 2022-2023.*

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Introduction

Respiratory syncytial virus (RSV) is a major cause of hospitalization and mortality in young children worldwide. It is estimated that approximately 3.6 million RSV-associated acute lower respiratory infection (LRTI) hospital admissions and about 100,000 RSV-attributable deaths in children less than 5 years of age occur globally, with more than 95% of

these deaths occurring in developing countries [1]. While premature infants and children with comorbidities such as hemodynamically significant congenital heart disease, bronchopulmonary dysplasia, and Down syndrome are at higher risk of RSV hospitalization, the majority of hospitalizations occur in healthy, full-term born infants [2, 3].

Until recently, palivizumab (SYNAGIS™), a short-acting monoclonal antibody was the only preventive option against RSV, indicated for the prevention of RSV among children at increased risk for severe LRTI [4]. However, the European Medicines Agency (EMA) and the U.S. Food and Drug Administration (FDA) have recently approved both a long-acting monoclonal antibody and a maternal RSV vaccination for infant RSV prevention. The long-acting monoclonal antibody BEYFORTUS™ (AstraZeneca AB, Södertälje, Sweden) is indicated for the prevention of RSV LRTI in infants entering their first season, and for children up to 24 months at high risk for severe RSV disease. The maternal RSV vaccine ABRYSVO™ (Pfizer, Inc., NY, USA) is indicated for the prevention of RSV-associated LRTI in infants from birth to six months [5, 6]. Another long-acting monoclonal antibody by Merck & Co., Inc., Rahway, NJ, USA, is in late stage development [7].

It is important to understand the burden of RSV-associated disease in young infants and children prior to implementing an immunization strategy. A recent multi-country birth cohort study in Europe estimated the incidence of RSV-associated hospitalizations in healthy full-term infants during their first year of life to be 1.8% [2]. Other single-center or single-country studies in Europe have reported rates of RSV-associated hospitalizations ranging from 0.9% to 5.6% for infants less than one year old [8–14]. However, comparing data among countries is challenging due to the lack of standardized outcome reporting and limited availability of population-based incidence rates for direct comparison.

The COVID-19 pandemic, which started in early 2020, greatly disrupted RSV seasonality worldwide [15, 16]; after a prolonged period of no RSV activity during the 2020–2021 winter, RSV rebounded with different patterns across the globe. Even within Europe, there were significant variations among countries [17] that were likely influenced by the COVID-19 prevention measures implemented by each country [18]. Population-based incidence for RSV hospitalization during the most recent RSV seasons, including the COVID-19 period, is understudied. The aim of the 'Burden of RSV Infection in young Children in European countries' (BRICE) Study Group was to provide population-based incidence estimates of RSV hospitalization in children aged ≤ 2 years in five European countries between 2020–2023.

Methods

Study design

The BRICE study is a prospective multicenter, multicountry cohort study that included children ≤ 2 years (≤ 24 months) old hospitalized with laboratory-confirmed RSV infection. A total of 10 study sites participated in this study across 5 European countries: Spain (Hospital Clínico Universitario de Santiago, Santiago de Compostela and Hospital La Paz, Madrid), France (Hopital Intercommunal de Créteil, Créteil and Centre Hospitalier Universitaire de Caen Côte de Nacre, Caen), Italy (Pediatric Hospital Meyer, Florence and Bambino Gesù Hospital, Rome), Germany (University Hospital Würzburg, Children's Hospital and University Hospital Schleswig Holstein—Campus Lübeck, Lübeck) and England (King's College Hospital, London and St George's University Hospital NHS Foundation Trust, London).

From October 1, 2020, to May 31, 2023, we prospectively identified children who were hospitalized with laboratory-confirmed RSV infection. To account for the disruption caused by the COVID-19 pandemic, the study team also retrospectively identified RSV cases at study hospitals during September 1, 2018, to April 30, 2019. RSV testing was standard of care for children ≤ 2 years who were admitted with respiratory symptoms at all study hospitals throughout the entire study period.

Outcomes

The primary outcome was the population-based annual incidence rate of laboratory-confirmed RSV hospitalization in children ≤ 2 years. The numerator represented the number of RSV hospitalizations among all children ≤ 24 months at study hospitals, during four RSV seasons: September 1, 2018, to April 30, 2019 (2018–2019, pre-pandemic season), October 1, 2020, to September 30, 2021 (2020–2021), October 1, 2021, to September 30, 2022 (2021–2022), and October 1, 2022, to May 31, 2023 (2022–2023). The denominator represented the annual total number of children ≤ 24 months living in the catchment area of the study hospitals (September 1, 2018, to August 31, 2019 (2018–2019, pre-pandemic season), October 1, 2020, to September 30, 2021 (2020–2021), October 1, 2021, to September 30, 2022 (2021–2022), and October 1, 2022, to September 30, 2023 (2022–2023)). Numbers were derived from publicly available sources for each calendar year. If there were multiple hospitals located within the same catchment area, numbers were adjusted to account for the market share of each study hospital.

Statistical analysis

In the calculation of annual incidence rates, certain months with low RSV activity, based on publicly available RSV surveillance data of participating countries (May 1, 2019, to August 31, 2019, and June 1, 2023, to September 30, 2023), were considered to have zero occurrences. Incidence rates and exact 95% confidence intervals were estimated using the *pois.exact function* from the epitools package in R.

Additionally, we describe the distribution of RSV-associated hospitalization by season, patient demographics (age and gender), and clinical characteristics (underlying medical conditions, pediatric intensive care unit (PICU) admission, and length of stay). For categorical variables, percentages were reported, and chi-square tests were used to compare proportions. Mean (standard deviation, SD) values were reported for length of stay. Pooled SDs were calculated as the square root of the weighted average of squared SDs available for each month per site and for each of the age groups (0–2, 3–5, 6–12 and 13–24 months) and with the corresponding number of hospitalized children minus one as the weight (as individual patient data was not available).

The study was conducted in accordance with the Declaration of Helsinki. Ethical approval was obtained from all study sites prior to the initiation of the research; Ethikkommission der Universität zu Lübeck (no. 20–345) and Ethik-Kommission der Universität Würzburg (no. 1/20_z) in Germany, Comité de Ética de la Investigación de Santiago y Lugo (no. 2020/452) and Comité de Ética de la Investigación Hospital Universitario La Paz (no. 22/2020) in Spain; Comitato Etico Regione Toscana—Pediatrico c/o Azienda Ospedaliero Universitaria Meyer (no. 247/2020) and Comitato Etico Ospedale Pediatrico Bambino Gesù IRCCS (no. 2275/2020) in Italy; London—Brighton & Sussex Research Ethics Committee (no. 21/LO/0578) in England; Comité de protection des personnes Sud Ouest et Outre Mer IV Cabanis Haut – Centre Cabanis Haut (no. 20.10.09.60811/CPP2020-11-094b) in France. Since only anonymized/aggregated data were collected, no informed consent was obtained for this part of the BRICE study.

Results

Distribution of RSV hospitalizations by patient characteristics

A total of 5,169 RSV hospitalizations were included in the study. Overall, the age distribution of RSV- hospitalizations remained the same across the seasons; over 50% of hospitalizations occurred in infants < 3 months (Table 1). However, there were notable differences within specific countries. In Italy, there was an increase in the proportion of hospitalizations in infants 6–12 months during the 2020–2021 RSV season (31%, 4/13) compared with the pre-pandemic season (10%, 22/227) although numbers during the 2020–2021 season were low. Similarly, in the United Kingdom, the proportion of children 13–24 months hospitalized with RSV significantly increased during the 2020–2021, 2021–2022, and 2022–2023 RSV seasons compared with the pre-pandemic season (40% (43/107), 36% (77/217) and 27% (55/201) respectively), compared with 15% (27/176) in the pre-pandemic season ($p < 0.05$) (Fig. 1, Supplementary Table 1). However, the increase was less pronounced in the latest season. More than 80% of children hospitalized with RSV had no underlying medical condition. The proportion varied between seasons, but the differences were not statistically significant (Table 1).

The proportion of children admitted to the PICU was significantly higher in 2020–2021 with 29.5% (180/610), compared with the other seasons, with 20.0% (248/1238) in 2018–2019, 19.8% (279/1410) in 2021–2022, and 22.3% (427/1911) in 2022–2023 ($p < 0.05$, Table 1). This increase was primarily driven by a higher proportion of infants 0–2 months being admitted to the PICU during 2020–2021 (43.2%, 134/312, Table 1).

The proportion of PICU admissions varied considerably between countries. Spain had a significantly higher percentage of PICU admissions during 2020–2021 (35.5%, 50/141) compared with the pre-pandemic season (21.2%, 87/402 $p < 0.05$, Supplementary Table 2) despite fewer hospital and PICU admissions in that season. In the 2022–2023 season, the proportion decreased to pre-pandemic level. In the United Kingdom, the proportion of PICU admissions was lower in the 2021–2022 season (25.3%, 55/217) compared with the pre-pandemic season (36.4%, 64/176, $p < 0.05$).

Overall, the length of stay was similar across seasons. The mean (SD) number of days ranged from 5.5 (3.7) in 2020–2021 to 5.8 (6.0) in 2022–2023 (Table 1), which was comparable with the pre-pandemic season (mean number of days: 5.7 (4.2)).

Annual incidence rates of RSV hospitalizations

Prior to the COVID-19 pandemic, the overall population-based annual incidence rate across the five countries in children 0–24 months was 11.3/1000 child-years (95%CI 10.6–11.9) (Table 1). During the 2020–2021 season, the annual incidence rate declined to 5.9/1000 child-years (95%CI 5.4–6.3) but rebounded in the 2021–2022 season to 13.8/1000 child-years (95%CI 13.0–14.5). In the 2022–2023 season, the annual incidence rate was even higher at 18.8/1000 child-years (95%CI 18.0–19.7). This pattern was observed across all age groups (Table 2).

Across all countries and seasons, the incidence rate was highest in the 0–6 months age group. In most seasons, France

Table 1 Distribution of RSV hospitalizations by patient characteristics and season

	2018 Sept – 2019 Aug[1]		2020 Oct – 2021 Sept		2021 Oct – 2022 Sept		2022 Oct – 2023 Sept[2]	
	N	%	N	%	N	%	N	%
Total number of RSV hospitalizations	1238		610		1410		1911	
Age group (months)								
0–2	635	51.3	312	51.1	743	52.7	1063	55.6
3–5	252	20.4	98	16.1	230	16.3	358	18.7
6–12	190	15.3	110	18.0	226	16.0	276	14.4
13–24	161	13	90	14.8	211	15.0	214	11.2
PICU admission	248	20.0	180	29.5	279	19.8	427	22.3
Age 0–2	175	27.6	134	43.0	181	24.4	296	27.9
Age 3–5	34	13.5	21	21.4	41	17.8	68	18.9
Age 6–12	26	13.7	14	12.7	25	11.1	33	11.9
Age 13–24	13	8.1	11	12.2	32	15.2	30	14.0
Gender								
Female	550	45.7[3]	278	45.6	609	45.8[3]	769	43.5[3]
Underlying medical conditions[4]								
No underlying medical Conditions	781	80.8	396	83.7	979	82.0	1133	80.9
Chronic lung disease	19	2.0	8	1.7	29	2.4	38	2.7
Congenital heart disease	42	4.3	17	3.6	40	3.4	63	4.5
Prematurity (GA < 36 weeks)	90	9.3	34	7.2	96	8.0	101	7.2
Immunodeficiency (e.g., Cancer, transplant, chemotherapy)	11	1.1	3	0.6	3	0.3	7	0.5
Down syndrome	7	0.7	3	0.6	7	0.6	13	0.9
Others (e.g., congenital abnormalities of airway, neuromuscular disease, neurologic problems, cystic fibrosis)	64	6.6	38	8.0	99	8.3	86	6.1
Unknown medical conditions[5]	272	22	137	22.5	216	15.3	511	26.7
LOS, days (mean, SD)[6]	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**
Total	*5.7*	*4.2*	*5.5*	*3.7*	*5.7*	*4.2*	*5.8*	*6.0*
Age 0–2	*6.3*	*4.1*	*6.3*	*4.1*	*6.0*	*3.9*	*6.0*	*6.3*
Age 3–5	*5.3*	*5.3*	*5.1*	*3.6*	*5.4*	*4.0*	*5.8*	*6.1*
Age 6–12	*4.9*	*3.1*	*4.5*	*2.6*	*5.3*	*4.3*	*5.4*	*3.6*
Age 13–24	*5.1*	*3.9*	*4.3*	*2.9*	*5.3*	*5.2*	*5.7*	*6.7*

[1]The data were collected between October 1, 2018, and April 30, 2019, assuming that no cases occurred outside this period

[2]The data were collected between 1 Sept 2022 and 31 May 2023, assuming that no cases occurred outside this period

[3]The proportion was calculated among those for whom gender information was available. It was 1204, 1329, and 1815 for the 2018–2019, 2020–2021, and 2022–2023 seasons, respectively

[4]The proportion was calculated among those for whom the presence of underlying medical conditions is known

[5]One site (3302) was not able to collect information on underlying medical conditions

[6]LOS of entire hospital stay (including HDU and/or PICU). Pooled standard deviations were calculated as the square root of the weighted average of squared standard deviations available for each month per site and for each of the age group (0–2, 3–5, 6–12 and 13–24 months) and with the corresponding number of hospitalized children minus one as the weight (as individual patient data was not available). The resulting pooled SDs do not account for any systematic variation between year, site and age groups in the mean LOS and may therefore underestimate the true standard deviations

Sept September, *Aug* August, *Oct* October, RSV Respiratory Syncytial Virus, *PICU* Paediatric Intensive Care Unit, *LOS* length of stay, *GA* Gestational Age, *SD* standard deviation

had the highest incidence rates in this age group (range 52.7 [95%Cl 46.0–60.1]—114.1 [95%CI 103.9–125.0] per 1000 child-years) and Germany the lowest (range 3.1 [95%Cl 1.9–4.8]—24.8 [95%CI 21.0–29.1] per 1000 child-years) (Fig. 2, Supplementary Table 1). In all countries except Spain, the incidence rate in infants 0–6 months in the 2022–2023 season was higher than in the pre-pandemic season.
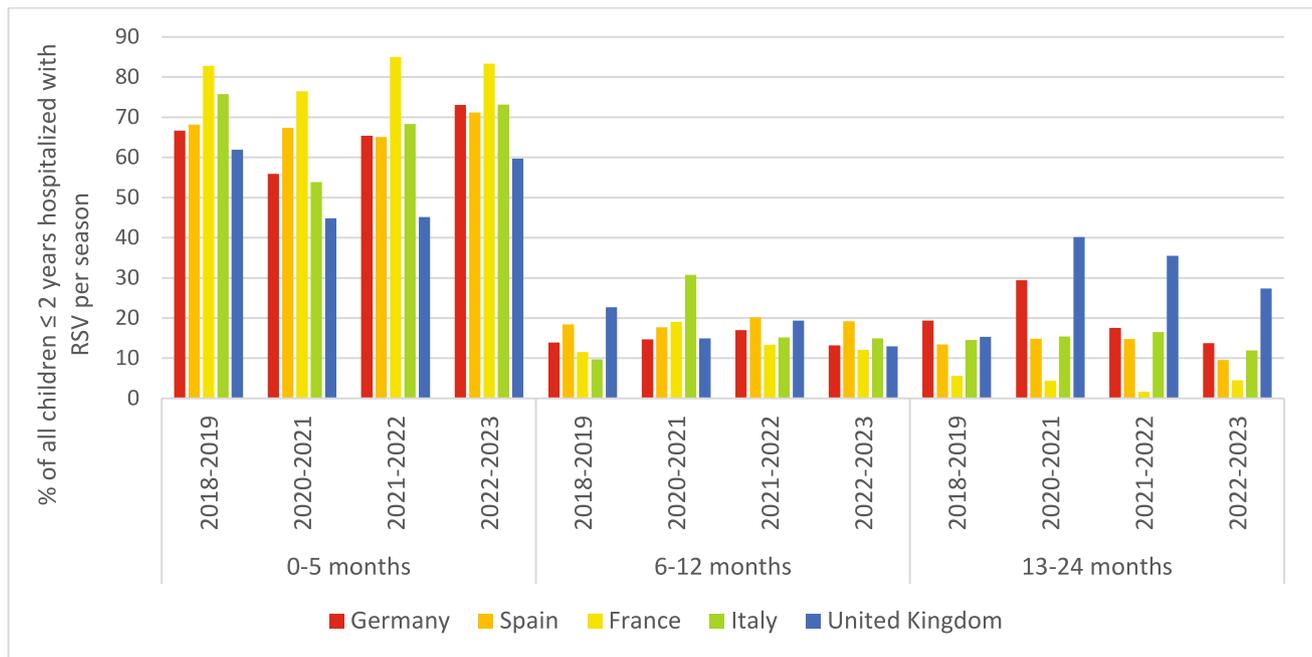
Fig. 1 Country-specific age distribution of RSV hospitalizations by season

Distinct patterns of RSV resurgence across five European countries

During the first year of the COVID-19 pandemic, the RSV season experienced significant disruptions in all five countries included in the study. However, as later seasons unfolded, the re-emergence of RSV activity varied across the five countries (Fig. 3 and Supplemental Fig. 1).

In France, RSV hospitalizations first peaked in March 2021, three months later than the peak in the pre-pandemic season (December 2018). The hospitalization rate was low through the summer of 2021, followed by an increase in cases during the fall and a second peak in November 2021. France was the only country to report a significant number of hospitalizations ($n = 230$) during the typical RSV season (from October to April) in 2020–2021. In comparison, the other four countries reported 0–5 RSV hospitalizations during the same period. In November 2022, RSV hospitalization rates peaked again, followed by a rapid decline starting from January 2023 onwards. This decline occurred earlier compared with the pre-pandemic season.

During the typical 2020–2021 season, Spain and England reported a negligible number of hospitalizations (five and four hospitalizations, respectively). In both countries, there was an increase in RSV hospitalizations between seasons, with peaks occurring in June and August 2021, respectively. In Spain, cases were almost absent during the summer of 2022, but started to rise from October onwards, peaking sharply in

November–December 2022, followed by a steep decline and minimal cases from March 2023 onwards. In England, there was continuous circulation of RSV throughout 2022, peaking in November 2022 and then declining from January 2023 onwards. Both countries experienced a final season that was comparable with the pre-pandemic season.

Germany did not report any RSV hospitalization cases during the typical RSV season in 2020–2021, while Italy reported one case. In both countries, RSV hospitalizations started to rise in the fall of 2021, which was four and two months earlier than the pre-pandemic season in those countries, respectively. The number of RSV hospitalizations peaked in October–November 2021, followed by a sharp decline and virtually no cases after February 2022. In Italy, RSV cases increased sharply during December and January of the 2022–2023 season. In Germany, hospitalizations peaked in December 2022, which was again earlier compared with the pre-pandemic season.

Discussion

This study is one of the few studies to compare RSV hospitalization incidence in different European countries during recent RSV seasons, including periods prior to and during the COVID-19 pandemic. The annual incidence rate in children 0–24 months was lowest during the 2020–2021 pandemic season (5.9/1000 child-years) but rebounded in the following seasons to rates higher than pre-pandemic levels.

Table 2 Annual incidence rates of RSV hospitalizations across countries, by season and age group

	Number of RSV hospitalizations (numerator)	Number of children in catchment area (denominator)[1]	Incidence rate per 1000 child-years (95% CI)
2018 Sept – 2019 Aug			
Age (months)			
0–5	887	25,487	34.8 (32.6–37.2)
6–12	190	29,925	6.4 (5.5–7.3)
13–24	161	54,591	3.0 (2.5–3.4)
0–12	1077	55,412	19.4 (18.3–20.6)
0–24	1238	110,003	11.3 (10.6–11.9)
2020 Oct – 2021 Sept			
Age (months)			
0–5	410	24,493	16.7 (15.2–18.4)
6–12	110	28,576	3.9 (3.2–4.6)
13–24	90	51,294	1.8 (1.4–2.2)
0–12	520	53,069	9.8 (9.0–10.7)
0–24	610	104,363	5.9 (5.4–6.3)
2021 Oct – 2022 Sept*			
Age (months)			
0–5	973	24,056	40.4 (38.0–43.1)
6–12	226	28,033	8.1 (7.1–9.2)
13–24	211	50,439	4.2 (3.6–4.8)
0–12	1199	52,089	23.0 (21.7–24.3)
0–24	1410	102,528	13.8 (13.0–14.5)
2022 Oct – 2023 Sept*			
Age (months)			
0–5	1421	23,889	59.5 (56.4–62.7)
6–12	276	27,836	9.9 (8.8–11.2)
13–24	214	49,905	4.3 (3.7–4.9)
0–12	1697	51,725	32.8 (31.3–34.4)
0–24	1911	101,630	18.8 (18.0–19.7)

[1]The number of children in the catchment area was adjusted for the market share of the participating hospital if there were other hospitals in the same catchment area

*Denominator numbers for various sites in Germany, France, the United Kingdom, Spain, and Italy were used from 2021 (sites 3401, 4401, and 4902) and 2022 (sites 3301, 3302, 3402, 3902, 4402, and 4901) due to unavailability of numbers for 2022 and/or 2023

RSV Respiratory Syncytial Virus, *CI* Confidence Interval, *Sept* September, *Aug* August, *Oct* October

The highest rate of 18.8/1000 child-years was observed in the 2022–2023 season.

There were remarkable differences in circulation between countries during the pandemic. Countries that experienced an early or interseason resurgence of RSV in the wake of the COVID-19 pandemic, had a prolonged period of RSV circulation, leading to persistent hospitalizations throughout the year, albeit at a low rate. In contrast, countries with a more delayed resurgence closer to the subsequent season followed a more typical seasonal pattern, with a sharp decline in RSV cases after reaching a peak. During the 2022–2023 season, all countries returned to a more or less normal RSV season. However, the overall annual incidence rate was higher compared with the pre-pandemic season, and the peak remained earlier than normal in France, Italy, and Germany. Higher PICU admission rates in young infants, and in some countries a higher proportion of older children being hospitalized due to RSV, was largely limited to 2020–2021.

The persistent higher annual RSV hospitalization rates during the 2021–2022 and 2022–2023 seasons compared to the pre-pandemic season, has also been reported in Denmark, Canada and USA [19–21]. This increased hospitalization rate may suggest a prolonged period of "immunity debt" following the COVID-19 pandemic, which suggests that a larger proportion of the population may have reduced levels of immunity to RSV due to limited exposure, possibly including pregnant women. However, the varying patterns observed may be influenced by country-specific
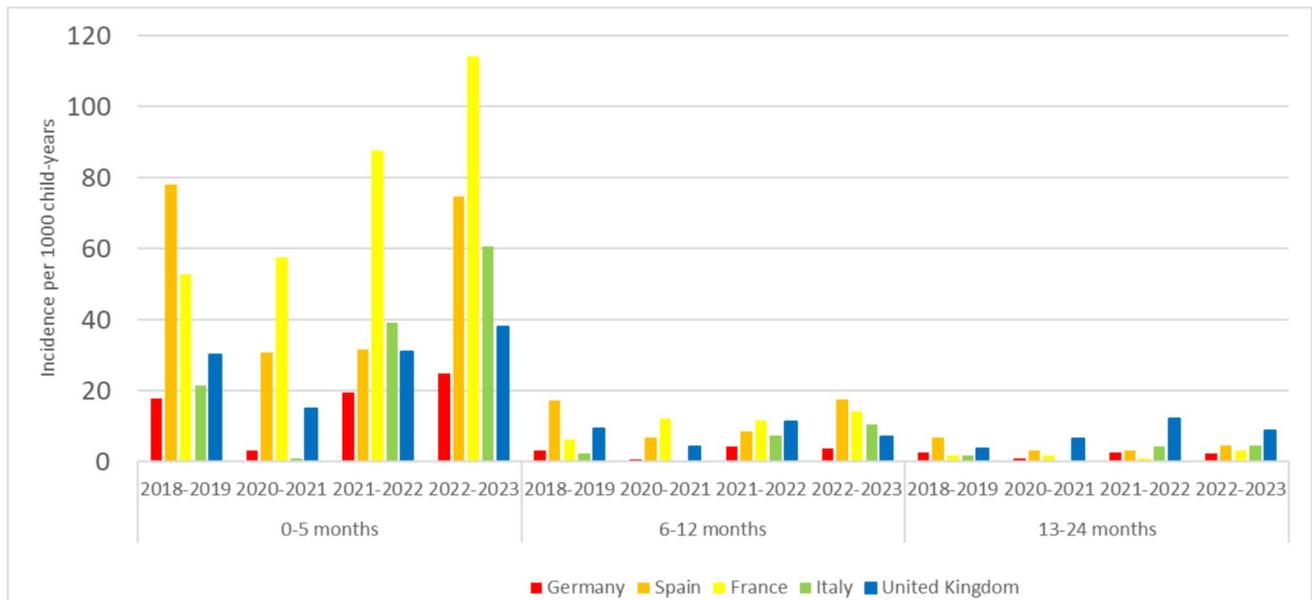
Denominator numbers for various sites in Germany, France, the United Kingdom, Spain, and Italy were used from 2021 (sites 3401, 4401, and 4902) and 2022 (sites 3301, 3302, 3402, 3902, 4402, and 4901) due to unavailability of numbers for 2022 and 2023.

Fig. 2 Country-specific annual incidence rates of RSV hospitalizations by season and age group
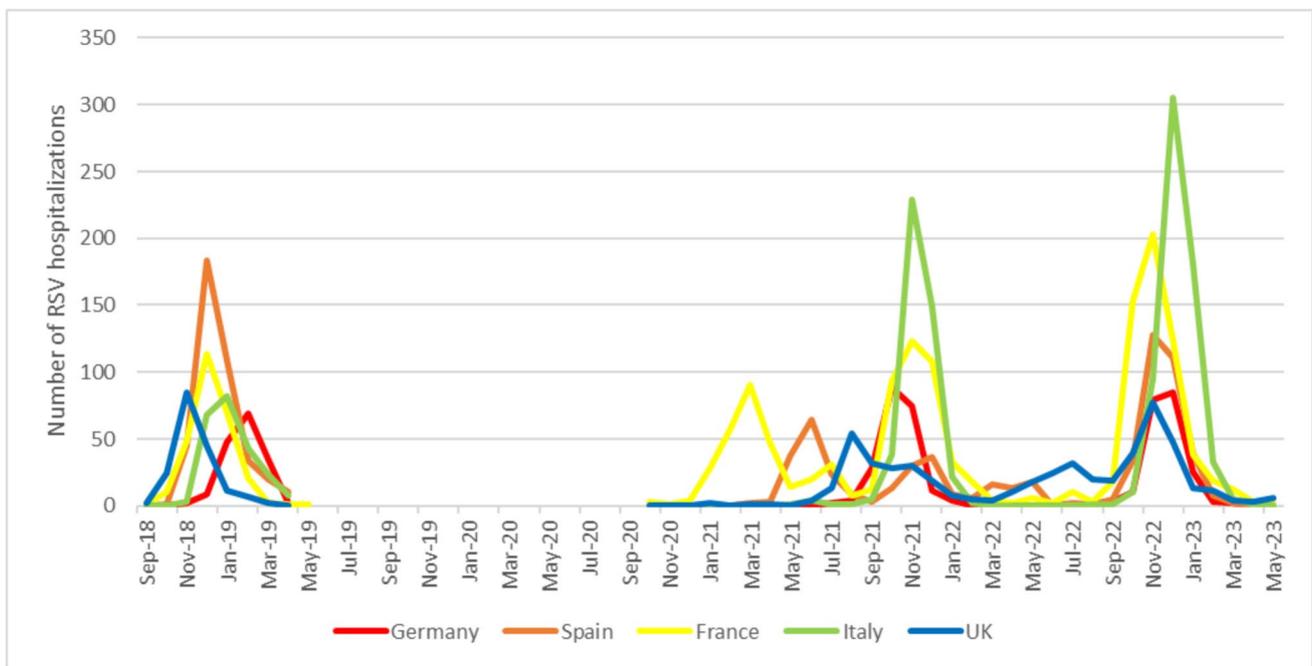
Fig. 3 Monthly distribution of RSV hospitalizations of children ≤2 years between September 2018 and April 2019 (pre-pandemic season) and October 2020 and May 2023

factors, particularly the COVID-19 restrictions and relaxations implemented. Factors such as school reopening and the reopening of international borders can also impact the transmission dynamics of RSV [16, 18, 22]. Furthermore, our study indicated that the pattern of the RSV resurgence had an impact on the relative incidence during different months of the season. This finding is consistent with previous studies conducted in the Netherlands [23] and United States [24].

We observed a shift in hospitalizations towards older ages in the 2020–2021 season in the United Kingdom and Italy only. Inconsistency in the age distribution of RSV hospitalizations has also been observed within and across countries. For example, a recent nationwide study conducted in Canada found no change in the age distribution of hospitalized RSV cases [25], while a single center study in British Columbia reported an increase in age during the 2020–2021 season [20], indicating regional differences. A nationwide study in Denmark found the highest increase in the risk of hospital admission in children 24–60 months [26], not included in the study presented here. This observation could also potentially be attributed to the concept of "immunity debt" in older children.

Most studies have found no significant difference in the severity of RSV disease during the COVID-19 pandemic [16, 19–21, 25–27]. However, in the current study, a higher percentage (29.5%) of hospitalized children were admitted to the PICU during the 2020–2021 period compared to the pre-pandemic period (20%), particularly in the youngest age group (0–2 months), although the absolute numbers of overall hospital and PICU admissions were considerably lower compared with other seasons (50% fewer overall hospital admissions and 25% fewer PICU admissions compared to the pre-pandemic season). One possible explanation could be a modified threshold for admitting children to the PICU during the COVID-19 pandemic.

In Spain, France, and England, the percentage in PICU admissions exceeded 20% during all seasons, which is higher compared with other literature focused on the pre-pandemic era [28–30]. One plausible explanation for this difference is that our study specifically targeted hospitals with a PICU, which may have resulted in an overrepresentation of PICU admissions as children from hospitals without a PICU would be referred to these selected hospitals. Nonetheless, it is important to acknowledge that most other studies of RSV hospitalizations have been conducted in tertiary hospitals. Additionally, our study found that the average length of hospital stay was consistent at around 5–6 days across countries and seasons, similar to other studies conducted in Germany and Italy [29, 30]. However, it is essential to note that our aggregated dataset only allowed for the calculation of the mean, not the median, which could have been lower.

In our study, more than 80% of children hospitalized with RSV did not have any underlying medical condition. We did not observe an increase in the proportion of premature children or children with underlying medical conditions hospitalized due to RSV during the COVID-19 pandemic, consistent with previous reports [20, 21, 26]. This is likely attributed to the continued use of immunoprophylaxis in these vulnerable populations.

The BRICE study has several strengths and limitations. One strength is the inclusion of sites that routinely test children ≤ 2 years hospitalized for acute respiratory tract infections. This allowed for the inclusion of a control season prior to the pandemic and minimized the risk of underestimating RSV hospitalizations. Importantly, the identification of cases were standardized during the prospective seasons, enabling comparisons among countries. However, thresholds for admitting children to hospitals and to the PICU can vary by country, as reflected in the differing incidence and prevalence estimates between countries. A more granular severity index, along with an understanding of incidence rates of outpatient RSV—which was not collected in our study—could have provided a better insight into hospitalized cases in each country. In addition, testing practices and propensity were dynamic during the COVID-19 pandemic. Routine nasal swab testing has become more common during the pandemic period, and it may have subsequently increased the testing rate for RSV. Also, a few hospitals used rapid antigen detection (RAD) in conjunction with PCR. Since the sensitivity of RAD is known to be lower than that of PCR [31], our incidence rate might have been slightly underestimated. Additionally, during the retrospective season, not every child may have been tested, potentially leading to an underestimation of the true incidence. A previous study with routine testing estimated that the rate of missed testing could be up to 15% [2]. We compared RSV incidence during the study period with only one prepandemic season (2018–2019). This may have resulted in an under- or overestimation of prepandemic incidence, as it is known that RSV circulation varied between seasons before the pandemic. However, this variation is considered minimal compared to the changes in RSV seasonality during the COVID-19 pandemic. Second, there were variations across sites in determining the denominator for calculating incidence rates, mainly due to limited data availability regarding the exact market share of hospitals. However, the pre-pandemic annual incidence in this study aligns with other literature [2, 32–35]. While children from outside the catchment area, such as those on vacation, could have been included in the numerator, the impact on the incidence rate is likely minimal. Third, the study did not specifically examine co-infections with other viruses. Differences in co-infection rates during the COVID-19 pandemic could potentially impact the severity of RSV disease and hospitalization rates. However, previous studies have not consistently demonstrated a clear association between co-infection and more severe RSV disease [36–39]. Fourth, underlying medical conditions were unknown in 15–27% of hospitalized children. This primarily stemmed from missing data at one site, whereas the data from the other sites was almost complete. Finally, despite the geographic span of participating sites, incidence rates may not fully represent the entire country.

Conclusion

The population-based incidence of RSV hospitalization in children ≤2 years is substantial. Considerable variation in incidence was observed between 2020 and 2023, with an initial decline during the COVID-19 pandemic followed by a rebound in the subsequent seasons. Our study underscores the importance of RSV surveillance and flexibility in RSV preventive strategies.

Declarations

References

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