

The Global Epidemiology of RSV in Community and Hospitalized Care: Findings From 15 Countries

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Background. Respiratory syncytial virus (RSV) is one of the leading causes of acute respiratory tract infections. To optimize control strategies, a better understanding of the global epidemiology of RSV is critical. To this end, we initiated the Global Epidemiology of RSV in Hospitalized and Community care study (GERi).

Methods. Focal points from 44 countries were approached to join GERi and share detailed RSV surveillance data. Countries completed a questionnaire on the characteristics of their surveillance system.

Results. Fifteen countries provided granular surveillance data and information on their surveillance system. A median (interquartile range) of 1641 (552–2415) RSV cases per season were reported from 2000 and 2020. The majority (55%) of RSV cases occurred in the <1-year-olds, with 8% of cases reported in those aged \geq 65 years. Hospitalized cases were younger than those in community care. We found no age difference between RSV subtypes and no clear pattern of dominant subtypes.

Conclusions. The high number of cases in the <1-year-olds indicates a need to focus prevention efforts in this group. The minimal differences between RSV subtypes and their co-circulation implies that prevention needs to target both subtypes. Importantly, there appears to be a lack of RSV surveillance data in the elderly.

Keywords. epidemiology: RSV: respiratory infections; surveillance.

Respiratory syncytial virus (RSV) is one of the leading causes of acute respiratory tract infections (ARIs) in both children and adults [1, 2]. The 2016 Global Burden of Disease (GBD) study estimated that RSV is responsible for 24.8 million ARI episodes and 76 600 deaths each year [3]. By the age of 1, ~60%–70% of children have been infected with RSV, and 2%–3% of these infections result in hospitalization, making

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RSV a leading cause of mortality and morbidity in children age <5, particularly in low- and median-income countries [4, 5]. Although the incidence of RSV infection is generally lower in adults compared with young children [6], RSV has been increasingly recognized as an important cause of respiratory disease in adults. High hospitalization and mortality rates associated with RSV have been reported in the elderly and in high-risk adults [2, 7].

Over 30 potential vaccines and new monoclonal antibodies (mAbs) are currently being evaluated, and new prevention methods are anticipated in the coming years [8]. For an effective implementation of these preventive measures, a clear understanding of the epidemiology of RSV is required. Several studies have previously reported and compared epidemiological metrics on a regional or global level [1, 3, 9]. However, studies transcending the national level do not leverage national surveillance data, and few studies have focused on the overall

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age distribution of RSV. Though studies have reviewed the epidemiology of RSV subtypes [10], few studies have done so at global level [11].

An important challenge to understand the epidemiology of RSV is a lack of publicly available data [12]. While most influenza-endemic countries have an influenza surveillance system publicly available data, dedicated surveillance systems for RSV are lacking [13]. RSV cases are therefore mostly captured through influenza surveillance systems, which has inherent challenges, and no public platform consolidating these data exists. In 2016, the World Health Organization initiated a pilot study to evaluate the feasibility of incorporating RSV surveillance into the Global Influenza Surveillance and Response System (GISRS) platform [13]. Two studies that emerged from this initiative compared the seasonality of RSV and influenza and described clinical characteristics as well as the performance of case definitions [13, 14].

Although RSV data collected through influenza surveillance systems are not perfectly sensitive or specific for capturing RSV cases [14], they can be a valuable source to predict the timing and duration of RSV epidemics as well as help define risk groups. Therefore, the Global Epidemiology of RSV (GERi) network was launched in 2019 to examine the global epidemiology and timing of RSV epidemics based on virological surveillance data [15]. Here, we describe the surveillance systems used to collect RSV data in 15 countries. Importantly, through access to national surveillance data, we analyze the age distribution of RSV cases overall and examine whether they are differently distributed across care levels or RSV subtypes. Lastly, to better define the epidemiology of RSV, we explore the role of RSV A and B in terms of overall patterns (dominant seasons), per country, and per level of care.

METHODS

Collection of Surveillance Data

Focal points of 44 countries across the world (usually based at national influenza centers) were approached between January 2019 and January 2020 to identify whether the respective country conducted RSV surveillance, and if so, they were invited to participate in the GERi network. Those who agreed to participate were sent an Excel data collection template and were asked to provide national RSV surveillance data from 2000 onwards. Data requested included: weekly number of RSV cases, age of the cases, number of specimens tested, and, if available, the RSV subtype. In addition, countries were asked to stratify cases by the level of care from which cases were reported.

Initially our data collection template differentiated between 3 levels of care: primary, secondary, and tertiary care. Primary care was defined as day-to-day health care, that is, the first contact and principal point of continuing care within the health care system. This typically includes general practitioners (GPs) Participating countries were also given a questionnaire (Supplementary Data) focused on the functioning of their respective surveillance system(s). In addition, they were asked for supplementary literature outlining their surveillance system(s). Through this mechanism, information on case definitions, definitions of different levels of care, type of laboratory testing, and representativeness of the data were obtained.

Data Analysis

To be included in the analysis, each season was required to contain at least 50 cases. Seasons north of the Tropic of Cancer were defined as ranging from week 27 to week 26 of the next calendar year. For countries south of the Tropic of Cancer, seasons were defined as ranging from week 1 through week 52 of the same calendar year.

The age distribution of RSV cases was investigated by calculating a median and interquartile range (IQR) at the country level, per level of care, and per RSV subtype. Differences in median were tested for significance using a 2-sample Wilcoxon rank sum. At the country level, age was expressed in the form of a relative illness ratio (RIR). The RIR, used to account for different age structures between countries, was calculated as follows:

$$RIR = (\frac{C_i}{\sum C_i}) / (\frac{N_i}{\sum N_i})$$

Here, C_i represents the number of cases in a given age group (*i*), and N_i represents the population size in a given age group [16]. Age-specific population data were obtained from the United Nations population division [17].

A meta-analysis was performed to pool results on the proportion of specimen testing positive for RSV each season and per country to estimate this proportion per care level using the R package "metafor" [18]. Pooled estimates were calculated using logit transformation and the DerSimonian-Laird estimator for random effects.

Lastly, the distribution of RSV A and B cases across seasons was analyzed for both community and hospitalized care. Differences in proportions were tested using a z test.

The occurrence of RSV A or B dominant seasons was explored using a $\geq 60\%$ threshold to define a subtype as being dominant. All analyses were performed and figures created using the statistical program R, version 3.6.1 [19].

Representativeness	Data from 6 different regions out of 10	No hospitals in the southern region	10 HHS regions, with data from >500 state and local public health laboratories, commercial labs, and hospitals/universities	0.37% of GPs and all regions are covered	0.8% of the Dutch population	80–90 GP practices covering the whole of NZ; previously (<2015) only Auckland region was included	All regions	Facilities in 10 cities, each in every federal district; this pop- ulation compromises 16.2% of the population	All regions are covered	Conducted at 2 clinics in the country	Nationally	NA	Cities located in regions with the highest proportion of the popu- lation (80%)
Methods Detection	Real-time RT-PCR	Real-time RT-PCR + antigen detection	A	Antigen detection, virus isola- tion, and other; Biomerieaux	Real-time RT-PCR	Real-time RT-PCR: US CDC protocol	Real-time RT-PCR	Multiplex PCR	Antigen detection, gel-based RT-PCR, or multiplex syn- dromic panels	Real-time RT-PCR assay, Fast Track Diagnostics Flu/ RSV	Real-time RT-PCR	AA	Immunofluores- cence assay or RT-PCR
Case Definition	Outpatient: ILIHospitalized: SARI	None	NA	ILI/ARI	ILI/ARI	L	ī	ILI	ARI + fever ≥38°C and cough	ILI	SARI	AA	SARI
Care Level Definition	AA	Outpatients & hospitalized patients	Ą	GPs for adults and GPs for children	GPs in a sentinel network	GP-based surveillance	GP at health care centers or patients attending at emergency rooms	Patients attended a poly- clinic	Government-funded pri- mary clinics (20) & pri- vate GPs (30) covering all regions of the country	Primary health care clinic in the community	Hospitalized patients	NA	Cases are in hospitalized patients, may consult at ER
Type of Surveillance	Sentinel surveillance system in outpa- tient and hospitalized patients	Nonsentinel, laboratory surveillance#	Passive national laboratory surveillance (NREVSS)	Sentinel surveillance	Sentinel surveillance—subset of patients; at least 2 per week and GP sentinel practice, 1 of which should be a child age <10	Sentinel surveillance—subset of patients: all ILIs in Auckland and Wellington and the first patient with ILI from Monday to Wednesday for the rest of NZ	Sentinel surveillance₊	Sentinel surveillance	Sentinel surveillance,	Sentinel surveillance [#]	Sentinel surveillance [#]	NA	Sentinel surveillance [#]
Timing	Year round	Seasonal (~weeks 40-18)	Year round	Seasonal (weeks 40–20)	Year round	Seasonal (~weeks 18–40)	Seasonal (~weeks 40-18)	Year round	Year round	Year round	Year round	NA	Year round
Re- gional Strati- fication	oN	Yes	Yes	0 Z	No	o	Yes	Yes	oZ	0 Z	Yes	Yes	oN
Care Level ^a	Mix	Mix	Aix	Com- munity care	Com- munity care	Com- munity care	Com- munity care	Com- munity care	Com- munity care	Com- munity care	Hospital- ized care	Hospital- ized care	Hospital- ized care
	Cameroon	Portugal	United States of America	The Czech Republic	The Nether- lands	New Zealand	Portugal	Russian Federation	Singapore	South Africa	Bhutan	Brazil ^b	Chile

Table 1. Description of the RSV Surveillance Systems by Level of Care (eg, Mix, Community, or Hospitalized Care) of the 15 Participating Countries on the Basis of a Questionnaire

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Representativeness	All regions	Nationally	NA	14–21 laboratories across the Netherlands, covering 29%– 44% of the population	4 hospitals in Auckland (20% of NZ population)	10 cities, each in every federal district; this population com- promises 16.2% of the pop- ulation	All regions are covered	North of Vietnam only	Conducted at 7 hospitals in 5 out of 9 provinces	and the states of the states o
Methods Detection	Antigen detection, virus isola- tion, and other; Biomerieaux	Antigen detection	AN	Rapid antigen test, PCR	Real-time RT-PCR	Multiplex PCR	Antigen detection, gel-based RT-PCR or multiplex syn- dromic panels	Gel-based RT-PCR	Real-time RT-PCR assay, Fast Track Diagnostics Flu/ RSV	
Case Definition	NA	SARI	NA	NA	SARI	SARI	SARI	SARI	SARI (>5-y), LRTI (>2 d-<5 y)	uenza were tested for RSV.
Care Level Definition	Local (district) hospitals and regional hos- pitals + university hos- pitals	National sentinel surveil- lance hospitals	NA	Testing requested by GPs, clinical departments in hospitals, and outpatient clinics	Hospital-based surveil- lance + ICU	Hospitalized patients (spe- cial infectious disease hospitals)	Two pediatric departments in public acute care hospitals	Hospitalized patients	Hospitalized care & tertiary care facilities	samples that were negative for infl
Type of Surveillance	Nonsentinel/routinely—subset: ~500- 700 swabs each epidemic season	Sentinel surveillance [#]	AA	Passive national laboratory surveillance (virologische weekstaten)	Sentinel surveillance [#]	Sentinel surveillance ⁴	A	A	Sentinel surveillance system [#]	se definition reporting to the included facilities; , only
Timing	Seasonal (weeks 40–20)	Year round	NA	Year round	Seasonal (~weeks 18–40)	Year round	Year round	Year round	Year round	ents fitting the cas
gional Strati- fication	°N N	No	No	No	No	Yes	No	No	No	testing all pati
Care Level ^a	Hospital- ized care	Hospital- ized care	Hospital- ized care	Hospital- ized care	Hospital- ized care	Hospital- ized care	Hospital- ized care	Hospital- ized care	Hospital- ized care	llance aimed at t
	The Czech Republic	Ecuador	Spain ^b	The Nether- lands	New Zealand	Russian Federation	Singapore	Vietnam	South Africa	Symbols: #, survei

^aCare level definitions: community care = day-to-day health care usually provided by the first contact within the health care system, hospitalized care = both acute care received in the emergency department or intensive care unit and more specialized consultative health care usually concerning inpatients, mix = a combination of the 2. ^bBrazil and Spain did not return the questionnaire.

RESULTS

Structure of RSV Surveillance in Participating Countries

Of the 44 invited countries, 15 countries (Supplementary Figure 1) provided data, and 13 of these completed the questionnaire (Supplementary Data). A summary of questionnaire results can be found in Table 1. Seven countries provided community care surveillance data, 12 provided data from hospitalized care, and 4 provided data on a combination of both. Cases were recorded as part of sentinel surveillance for all 7 countries providing data on community care and 6 out of 12 countries providing data on hospitalized care. The remaining countries recording cases in hospitalized care take a more passive and voluntary approach, where testing is usually driven by diagnostic needs. Definitions of community and hospitalized care largely overlapped on a country level. Most of the community care data are provided by GPs; however, the data from Portugal included emergency room visits. In some countries, data could not be categorized into level of care. The data from the United States, for example, stemmed from national laboratories that receive data from a variety of public health institutions, and some data from Portugal and Cameroon included both out- and inpatients [20].

The predominant case definition used to capture RSV was influenza-like illness (ILI) in community care and severe acute respiratory infection (SARI) in hospitalized care, with the exception of the Netherlands and Portugal, where ILI was combined with other acute respiratory infection (ARI) in community care. In most countries, RSV is 1 of several respiratory infections tested for by real-time RT-PCR.

The largest variation between countries was seen when comparing representativeness by country. Most of the countries provided data at the national level, with the exception of Chile, Portugal, and New Zealand. Four countries provided regional data (Bhutan, Brazil, Portugal, and the United States). Another factor influencing the representativeness of the data and comparability across countries was testing policy. Where some countries test a predetermined subset of patients (eg, 1 child and 1 adult per week) presenting with ILI or SARI (the Netherlands: community care; New Zealand: community care; and Portugal: mix), others test all patients presenting with ILI or SARI symptoms (Cameroon, the Czech Republic, Portugal: community care; Russian Federation, South Africa, Bhutan, Chile, Ecuador, New Zealand: hospitalized care). In 2 out of 15 countries, specimens collected are first tested for influenza, and testing for other respiratory viruses only occurs if negative for influenza (Portugal and Singapore). However, most surveillance data were collected year-round.

Overview RSV Surveillance Data

Surveillance data shared by the 15 participating countries are summarized in Table 2. Supplementary Figures 2 and 3 show the available national surveillance data over time. Countries provided data for a median (range) of 7 (1-19) seasons, with

a median (IQR) of 1641 (552–2415) RSV cases per season. Apart from Brazil, all countries provided a weekly number of specimens tested, with a median (IQR) of 6420 (3473– 22777) specimens tested per season. The majority of cases (97%) were recorded in hospitalized care, both overall and in countries with data available from both community and hospitalized surveillance. For the United States, no age data were available.

The percentage of RSV-positive cases varied widely across countries. The proportions are consistent from season to season at a country level in community care, but there was great variation in hospitalized care. Overall, the percentage of positive cases was higher in hospitalized care (SARI; 12%; 95% CI, 11%–13%; $I^2 = 99\%$) than in community care (ILI or ARI; 6%; 95% CI, 5%–6%; $I^2 = 91\%$). Forest plots on RSV positivity in community and hospitalized care are shown in Supplementary Figures 4 and 5, respectively.

Age Distribution of RSV Cases

The median age of RSV cases was available for 10 countries, and 4 countries provided cases per age category (Table 3). Portugal provided both exact and categorical age data; however, due to the small number of cases with the exact age (105/4902), Table 3 only presents the categorical data. Spain, not presented in Table 3, provided data stratified as <15- and \geq 15-year age categories.

Overall, the median age (IQR) was 0.78 (0.3–2.6), but this differed greatly across countries (Table 3). The RIR was consistently higher in the youngest age category compared with the \geq 5-year age category, where the RIR remained consistently below 1 (~20–800 fold). For Spain, the RIR showed a similar pattern, with the highest RIR (IQR), 5.4 (4.9–6.2), in the <15-year-old age category, compared with 0.2 (0.1–0.3) in the \geq 15-year-old age category. All countries included RSV cases in those aged 65 or older, comprising ~8% of all cases. This proportion ranged from 1% in Chile, Ecuador, Portugal, and South Africa to 20% in Portugal.

As the majority of cases (n = 9287, 55%) were found in the <1-year-old category, we decided to focus on this group. The monthly age distribution for this category in community and hospitalized care is depicted in Figure 1A–B. In hospitalized care (1B), the number of cases peaked in the 1–2-month age group, after which the number of cases declined for older age groups. In this age category and setting, 70% of cases were ≤ 6 months of age. The sample size for the <1-year-old age category in community care was substantially smaller (n = 422) than in hospitalized care (n = 8864). The age distribution found in hospitalized care did not appear to repeat itself in the community care setting for cases aged <1 year (Figure 1A).

Three countries (New Zealand, Russian Federation, and South Africa) provided exact age data for both levels of care, representing 16 934 RSV cases (Supplementary Figure 6). The median age among community care cases (IQR) was 5.5 (1.9–43.6) years, substantially and significantly higher than

spitalized)	Average % Posi
r Level of Care (eg, Community or Hos	Cases per Season, Median (IQR)
her Specified fo	Care Level
narized on a Country Level and Furt	Median Cases per Season (IQR)
Countries; Data Are Sumr	Subtyped Data, %
lance Data of the 15 Participating	Seasons, No.
Summary of Available Surveil	Country
Table 2.	

	Country	Seasons, No.	Subtyped Data, %	Median Cases per Season (IQR)	Care Level	Cases per Season, Median (IQR)	Average % Positive
Africa	South Africa	10 (2009–2018)	36	604 (524–824)	Community	81 (80–95)	9
					Hospitalized	693 (515-824)	14
	Cameroon	1 (2018–2019)	0	22	Community	22	13
					Hospitalized	NA	NA
Americas	United States of America	14 (2005/2006-2018/2019)	0	18 007 (5510–37 834)	Community	NA	NA
					Hospitalized	NA	NA
	Chile	7 (2012–2018)	0	4923 (4846–5490)	Community	138 (124–146)	ω
					Hospitalized	4773 (4722–5361)	17
	Ecuador	7 (2012–2018)	0	482 (365–615)	Community	NA	NA
					Hospitalized	482 (365–615)	13
	Brazil	5 (2014–2018)	0	2208 (1337–2520)	Community	NA	NA
					Hospitalized	2208 (1337–2520)	NA
Europe	Portugal	8 (2011/2012–2018/2019)	14	529 (247–783)	Community	13 (7–13)	4
					Hospitalized	NA	NA
	The Netherlands	19 (2000/2001-2018/2019)	100	1980 (1766–2219)	Community	73 (53–98)	4
					Hospitalized	1959 (1732–2195)	NA
	The Czech Republic	4 (2014/2015–2017/2018)	ო	233 (202–345)	Community	22 (17–26)	4
					Hospitalized	213 (189–319)	ო
	Spain	13 (2006/2007–2018/2019)	0	2060 (1638–2969)	Community	NA	NA
					Hospitalized	2060 (1638–2969)	13
	Russian Federation	5 (2014/2015–2018/2019)	0	133 (104–176)	Community	66 (48–88)	4
					Hospitalized	67 (56–78)	9
South East Asia	Bhutan	3 (2015/2016–2017/2018)	0	98 (82–218)	Community	NA	NA
					Hospitalized	41 (33.5–64)	38
Western Pacific	Singapore	8 (2011–2018)	4	1786 (1647–2076)	Community	90 (75–105)	7
					Hospitalized	1710 (1574–1968)	10
	New Zealand	6 (2013–2018)	39	610 (533–682)	Community	101 (82–128)	7
					Hospitalized	466 (450–566)	16
	Vietnam	2 (2017–2018)	0	39 (26–41)	Community	39 (26–41)	10
					Hospitalized	NA	NA
Average	Average	7		1463 (512–2335)	Community	78 (37–110)	8
					Hospitalized	747 (435–1807)	17
Abbreviations: IQR, in	iterquartile range; NA, not available.						

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Age Category

			<1 y		1-4 y		≥5 y		
	No. of Cases	Median Age (IQR), y	No. of Cases	Median RIR (IQR)	No. of Cases	Median RIR (IQR)	No. of Cases	Median RIR (IQR)	No. of Years
Bhutan	320	1.00 (0.42–2.00)	156	28.5 (22.4–29.8)	125	5.6 (4.8–6.5)	39	0.1 (0.1–0.1)	e
Cameroon	35	1.00 (0.33-4.50)	15	NA	11	NA	თ	NA	0
Chile	358	0.92 (0.42–1.00)	189	42.8 (42.6–43.1)	137	7.3 (7.1–7.6)	32	0.1 (0.1–0.1)	2
The Czech Republic	141	6.00 (3.00-43.00)	13	NA	46	NA	82	NA	0
Ecuador	3361	0.58 (0.25–1.00)	2179	31.7 (29.0–33.1)	1051	4.0 (3.8-4.6)	131	0.0 (0.0-0.1)	7
The Netherlands	975	14.82 (1.64–55.66)	157	14.3 (11.9 –18.2)	253	6.2 (5.8–7.0)	565	0.6 (0.5–0.6)	13
New Zealand	3996	1.00 (0.25–5.17)	1992	38.4 (35.8-44.5)	994	4.6 (4.0–5.0)	1010	0.3 (0.1–0.3)	7
Russian Federation	781	3.00 (1.00-8.00)	160	13.8 (6.7–16.5)	371	9.4 (9.0–9.5)	250	0.4 (0.3-0.4)	9
South Africa	6646	0.51 (0.21–1.53)	4416	28.9 (16.5–35.0)	1385	2.4 (2.3–2.5)	845	0.1 (0.1–0.2)	10
Vietnam	78	2.00 (1.50-4.00)	10	NA	50	NA	18	NA	0
Countries With Informs	ation on Age Provide	d Only in Categories			<5 y		≥5 y		No. of Years
					No. of Cases	Median RIR (IQR)	No. of Cases	Median RIR (IOR)	
Brazil	11 460	<2 y#	NA	NA	10 318	12.7 (12.6–12.7)	1142	0.1 (0.1–0.1)	Ð
Portugal	4902	0-4	NA	NA	2973	7.3 (0.7–18.6)	1859	0.4 (0.2-0.6)	7
Singapore	716	1–2	NA	NA	523	18.6 (18.1–19.9)	193	0.3 (0.1–0.3)	8
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Symbol: ", median age category, as exact ages were not available. Abbreviations: IOR, interquartile range; NA, not available; RIR, relative illness ratio; RSV, respiratory syncytial virus.



Figure 1. A–B, Number of RSV cases per month in the <1-year-old age category in community and hospitalized care. "Age, mo" on the x-axis refers to the age of the child. The overall number of cases in the <1-year-old category was taken to calculate the proportion of cases in a given month. Abbreviation: RSV, respiratory syncytial virus.

the median age (IQR) in hospitalized care (0.6 [0.2-1.4] years; P < .001). The same level of significance (P < .001) was found when comparing age per care level on the individual country level.

RSV Subtype Distribution

Six countries (the Czech Republic, the Netherlands, New Zealand, Portugal, Singapore, and South Africa) provided subtyped RSV data. In the Netherlands, Singapore, and South Africa, \geq 90% of RSV cases were typed, whereas this was 3%, 14%, and 39% for the Czech Republic, Portugal, and New Zealand, respectively. These countries reported a total of 6148 RSV subtyped cases, of which 3155 were typed as RSV A cases (51%) and 2993 were typed as RSV B cases (49%). There were 34 seasons containing sufficient subtyped RSV cases to be included in the analysis. The distributions of RSV subtypes for

these seasons (from 2010 to 2019) stemmed from 5 countries (the Netherlands, New Zealand, Portugal, Singapore, and South Africa) and are summarized in Figure 2. The figure shows a slightly higher median (IQR) for RSV A (54% [38%–65%]) compared with RSV B (46% [35%–62%]).

There were 12 out of 34 seasons where RSV A was dominant and 10 seasons where RSV B was dominant. Subtype dominance reached \geq 80% twice in the Netherlands for RSV B for the 2017/2018 and 2018/2019 seasons, once in New Zealand for RSV A in the 2012 season, and once in Portugal for RSV B in the 2014/2015 season.

For 2 countries (New Zealand and South Africa), subtyped RSV data (n = 2180) were available in both community and hospitalized care. Overall the proportion of RSV A was lower in community care (46%, 264/570) compared with hospitalized care (53%, 859/1610; P < .001). At the country level, the





proportion of RSV A was 40% (107/269) in community care in South Africa and 54% (232/433) in hospitalized care (P < .001); in New Zealand this difference was 52% (157/301) compared with 53% (627/1177; P = .78) in community and hospitalized care, respectively.

The age distribution of RSV by subtype was available for a total of 4911 cases distributed across 5 countries (the Czech Republic, the Netherlands, New Zealand, Portugal, and South Africa). The global median age for RSV A (IQR) was 0.9 (0.3–4.3) years compared with 0.9 (0.3–5.2) years for RSV B (P = .96). Similar results were seen at the country level, the only exception being the Netherlands, where RSV B cases had a median age (IQR) of 24.4 (1.7–58.2) years compared with 6.4 (1.6–52.8) years for RSV A cases (P = .02) (Supplementary Figure 7).

DISCUSSION

This study describes for the first time age- and care settingspecific surveillance data at a global level. Importantly, it also provides insight into current RSV surveillance practices at a national level. The GERi network currently encompasses 15 countries and includes 112 seasons of RSV surveillance data between 2000 and 2020. We found several differences in data collection practices and demonstrated that the highest incidence of RSV cases requiring medical attention was found in the <1-year-old age category. In addition, our data set contained very few infections in the 65+ age group (8%).

Though it is well established that RSV is an important cause of respiratory disease requiring medical attention in the very young [5], the impact of RSV on the overall population is not well studied. Though the RIR is consistently higher in the <1-year-old age category, the lack of cases in the elderly might reflect that this group is disproportionately captured by the surveillance systems. In our study, only 8% of total surveillance cases were found in the >65-year-old age category (ranging from 1% in Chile, Ecuador, Portugal, and South Africa to 20% in Portugal). Based on previously published populationbased RSV estimates, we would expect this age group to represent between 19% and 33% of total surveillance cases in the United States, 37% in the United Kingdom, 25% in Canada 16% in Thailand, and <1% in Madagascar [21-26]. Studies in the United States have also reported incidence rates of RSV in the elderly that were nearly twice that of influenza A and that RSV had a high disease severity in the elderly [2]. These data

suggest that, at least for developed countries with relatively large elderly populations, surveillance systems may not be sufficiently picking up RSV cases in the \geq 65-year-old age group. This could be influenced by a variety of factors, including an atypical clinical presentation in older adults or lower viral titers, which might hinder RSV detection by rapid antigen tests [27].

RSV patients in community care were older than those in hospitalized care, underlined by South Africa and New Zealand—in which all ILI as well as SARI cases are tested. Data from both countries show that cases in hospitalized care were substantially younger. This could be due to the previously demonstrated higher risk of hospitalization in younger individuals [28]. The percentage of cases testing positive for RSV was consistently higher in hospitalized patients, suggesting that RSV might play a larger role among other causes of respiratory infections in the hospitalized setting than in the community setting. Several studies found similarly high proportions of RSV positivity among hospitalized patients [29, 30].

No evidence for age differences between RSV subtypes was found. In most seasons analyzed, both RSV subtypes co-circulated (<80% threshold) and no clear pattern per country or from season to season was found. Though the RSV subtype remained unknown for a large subset of cases, this would likely not impact the proportion of RSV A or B per season found in our study. While among subtyped cases the proportion of RSV A was higher in hospitalized care compared with community care, the evidence was limited. A difference in this distribution could indicate an increased severity for those infected with RSV A [11].

The strengths of the GERi network lie in the size of the data set, the global distribution of the countries, the stratification by level of care, and additional information gained through our questionnaire. This study also comes with several limitations. Although surveillance data are an effective way to determine timing and seasonality of epidemics, it is important to note that only medically attended cases are included in the data set. In addition, influenza surveillance systems-a common foundation for RSV testing-commonly use the ILI case definition, which requires a fever, a clinical symptom not universally and globally represented in RSV cases [14]. Another limitation of the GERi network is the diversity in surveillance systems. The information gathered through the questionnaire, in combination with the size of the database, enables a better interpretation of results. Not all regions and Income categories are equally represented in the database. In line with previous studies that have assessed global data sets, high-income countries tend to provide more data and data that have greater detail [31].

Our results have important public health implications as well as implications for the development of future prevention methods. They highlight and support previous findings on the age groups that need to be targeted to prevent and control infections, with <1-year-olds being of greatest importance. The co-circulation of both RSV types also implies that for a prevention method to be effective it should target both types. This is especially relevant, as neither of the types appears to be overly represented in hospitalized cases.

CONCLUSIONS

The GERi network is the most substantial assessment of RSV surveillance data to date. Importantly, we found several differences in RSV surveillance systems across countries, underlining the need to harmonize surveillance activities for RSV around the world to make the data more comparable and to draw firmer conclusions for prevention and control measures. While our analysis found that the incidence of RSV is highest in the <1-year-old age category, more surveillance data in the elderly may be required, especially in developed countries, to support prevention efforts in this age group.

Supplementary Data

Supplementary materials are available at *Open Forum Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

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