

# Respiratory viruses associated admissions during four consecutive seasons (2012/13 – 2015/16) in the Global Influenza Hospital Surveillance Network (GIHSN)

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## INTRODUCTION

Acute respiratory infection (ARI) is the main cause of morbidity and mortality worldwide. Influenza, respiratory syncytial virus (RSV), rhinovirus/enterovirus (RhV/EV) and coronavirus (CoV) play a significant role in respiratory pathology. The aim of this study was to determine the aetiology and seasonality of respiratory viral infections among patients with acute respiratory disease.

## METHODS

- The GIHSN conducted a prospective, active-surveillance, hospital-based study over 4 consecutive seasons. Data were collected in 8 hospitals (3 from Saint Petersburg and 5 from Valencia) during the 2012/13 season, 16 hospitals (3 from Saint Petersburg, 7 from Turkey and 6 from Valencia) during the 2013/14 season, 19 hospitals (3 from Saint Petersburg, 5 from Turkey, 10 from Valencia and 1 from Fortaleza) during the 2014/15 season and 11 hospitals (3 from Saint Petersburg, 4 from Valencia and 4 from Mexico) during the 2015/16 season. Saint Petersburg, Turkey, Valencia and Mexico included patients of all ages and Fortaleza included only patients under 18 years old.
- All consecutive consenting admissions of non-institutionalised patients who were residents (at least, during 6 months) in a participating hospital's catchment area and were not discharged from a hospital within 30 days were considered in the study. Moreover, for patients ≥5 years of age the presence of, at least, one systemic symptom (fever, headache, myalgia or malaise) and, at least, one respiratory symptom (cough, sore throat or shortness of breath) was required. Patients, of all ages, were included in the study if admitted to hospital within 7 days of the onset of symptoms.
- Demographic and clinical information was collected by face-to-face interview or by clinical records searching. Swabs were obtained and were tested by real-time reverse transcription polymerase chain reaction (RT-PCR).
- Logistic regressions were performed comparing PCR-negatives with positives for influenza, RSV, RhV/EV or CoV considering in univariate analysis: age, sex, presence of chronic conditions, smoking habits, hospitalisations and general practitioner consultations in last 3 months, socioeconomic class, obesity, prematurity (<5 years old), birth weight (<5 years old) and breastfeeding (<5 years old). Significant covariates were considered in final models, also adjusted by epidemiological week at admission, days from onset to swab, site and season.

## RESULTS

### Characteristics of included patients

- During four consecutive seasons, 43,933 subjects were screened with processes possibly related to a respiratory viral infection. After applying exclusion criteria, laboratory results were obtained from 21,589 (49%) individuals: 39% were under 5 years old and 33% were 65 years old or over.
- Pathogens were detected in 9,442 (44%) of admitted patients. Most common viruses were influenza (N=3639; 17%), RSV (N=2000; 9%), RhV/EV (N=1244; 6%) and CoV (N=484; 2%).

Table 1. General description of included patients with PCR result by site.

	Valencia		Saint Petersburg		Turkey		Fortaleza		Mexico		Overall	
	N	%	N	%	N	%	N	%	N	%	N	%
<b>All study seasons</b>	<b>12008</b>	<b>100.00</b>	<b>7789</b>	<b>100.00</b>	<b>1187</b>	<b>100.00</b>	<b>427</b>	<b>100.00</b>	<b>178</b>	<b>100.00</b>	<b>21589</b>	<b>100.00</b>
<b>Season</b>												
2012/2013	2328	19.39	1701	21.84	0	0.00	0	0.00	0	0.00	4029	18.66
2013/2014	2566	21.37	1270	16.31	501	42.21	0	0.00	0	0.00	4337	20.09
2014/2015	4422	36.83	2747	35.27	686	57.79	427	100.00	0	0.00	8282	38.36
2015/2016	2692	22.42	2071	26.59	0	0.00	0	0.00	178	100.00	4941	22.89
<b>Age group</b>												
0 - <5 years old	2670	22.24	4999	64.18	448	37.74	354	82.90	36	20.22	8507	39.40
5 - <18 years old	330	2.75	874	11.22	174	14.66	73	17.10	21	11.80	1472	6.82
18 - <65 years old	2317	19.30	1749	22.45	227	19.12	0	0.00	91	51.12	4384	20.31
≥ 65 years old	6691	55.72	167	2.14	338	28.48	0	0.00	30	16.85	7226	33.47
<b>PCR result</b>												
Negative	8249	68.70	2981	38.27	623	52.49	242	56.67	52	29.21	12147	56.26
A(H1N1)pdm09	547	4.56	632	8.11	25	2.11	0	0.00	20	11.24	1224	5.67
A(H3N2)	666	5.55	492	6.32	89	7.50	11	2.58	14	7.87	1272	5.89
A not subtyped	100	0.83	140	1.80	0	0.00	0	0.00	4	2.25	244	1.13
B/Yamagata	209	1.74	403	5.17	57	4.80	8	1.87	2	1.12	679	3.15
B/Victoria	90	0.75	95	1.22	0	0.00	0	0.00	2	1.12	187	0.87
B not subtyped	16	0.13	18	0.23	0	0.00	0	0.00	0	0.00	34	0.16
RSV	641	5.34	1164	14.94	100	8.42	78	18.27	17	9.55	2000	9.26
Coronavirus	313	2.61	91	1.17	77	6.49	0*	0.00	3	1.69	484	2.24
Human metapneumovirus	217	1.81	64	0.82	29	2.44	0	0.00	8	4.49	318	1.47
Adenovirus	82	0.68	166	2.13	56	4.72	6	1.41	1	0.56	311	1.44
Bocavirus	71	0.59	63	0.81	13	1.10	0*	0.00	2	1.12	149	0.69
Parainfluenza	48	0.40	146	1.87	15	1.26	13	3.04	8	4.49	230	1.07
Rhinovirus/enterovirus	592	4.93	551	7.07	40	3.37	40	9.37	21	11.80	1244	5.76
Mixed respiratory infection	109	0.91	318	4.08	51	4.30	21	4.92	18	10.11	517	2.39
Mixed influenza infection	58	0.48	465	5.97	12	1.01	8	1.87	6	3.37	549	2.54

\*Not tested viruses

- RSV infected mostly young children (84% of RSV positives were children under 5 years old and median age was 1 year old) followed by RhV/EV (55% of RhV/EV positives were under 5 years old but 19% were elderly people, median age was 3 years old) and CoV (46% were under 5 years old and 34% were 65 years old or over, median age was 13 years old). Influenza infected mainly children under 5 years old (35%) and elderly people (28%). Negatives were principally (43%) individuals 65 years old or over.

- Co-infections were detected in 1066 (5%) admissions and were more common during the circulation of RSV. The most frequent co-infection was RSV with RhV/EV with 180 cases, representing 15% of co-infections, followed by RSV with A(H1N1)pdm09 (N=126, 10%), AdV with RhV/EV (N=73, 6%) and RSV with A not subtyped (N=66, 5%)

Figure 1. Age group distribution by virus

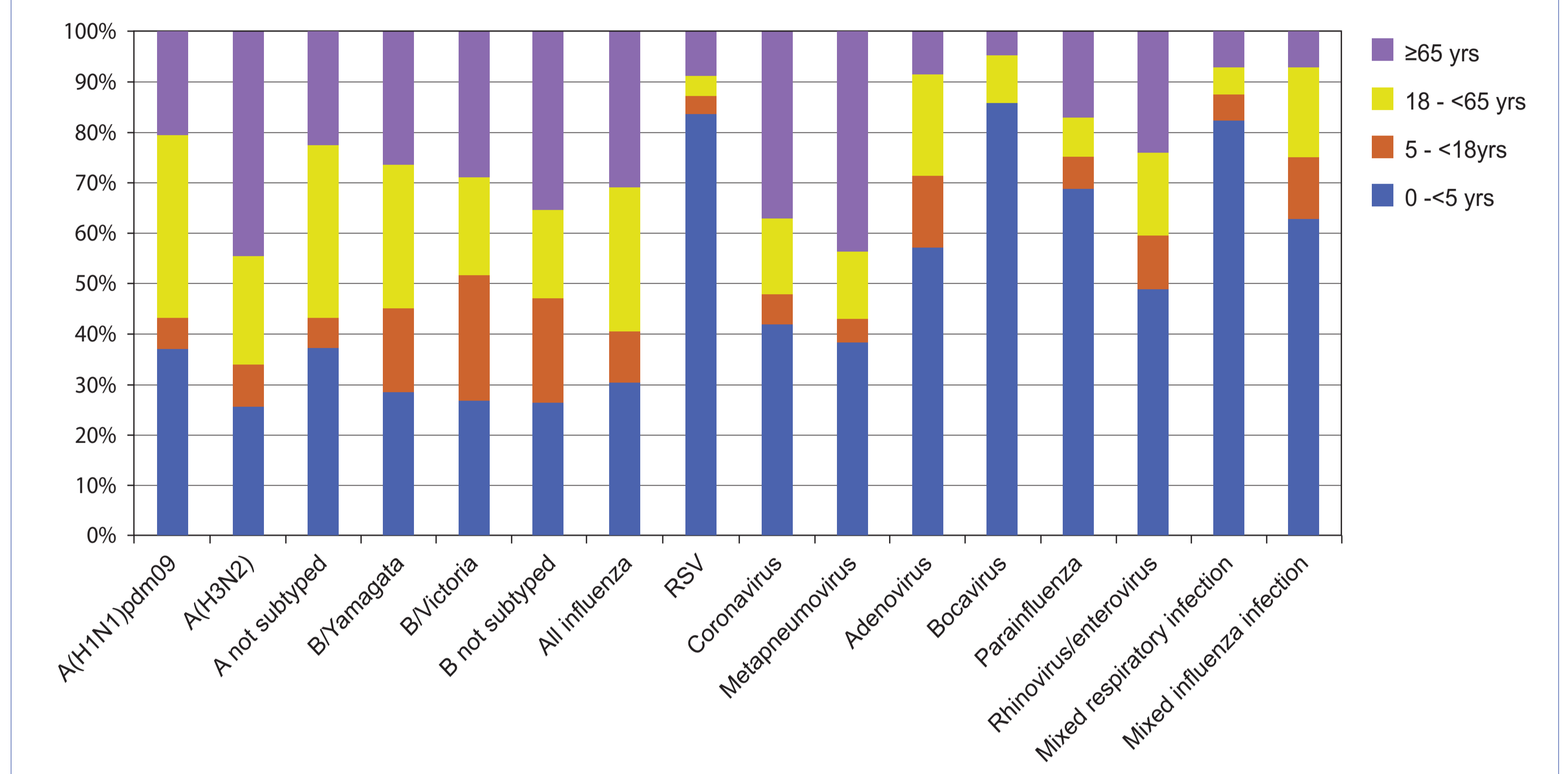
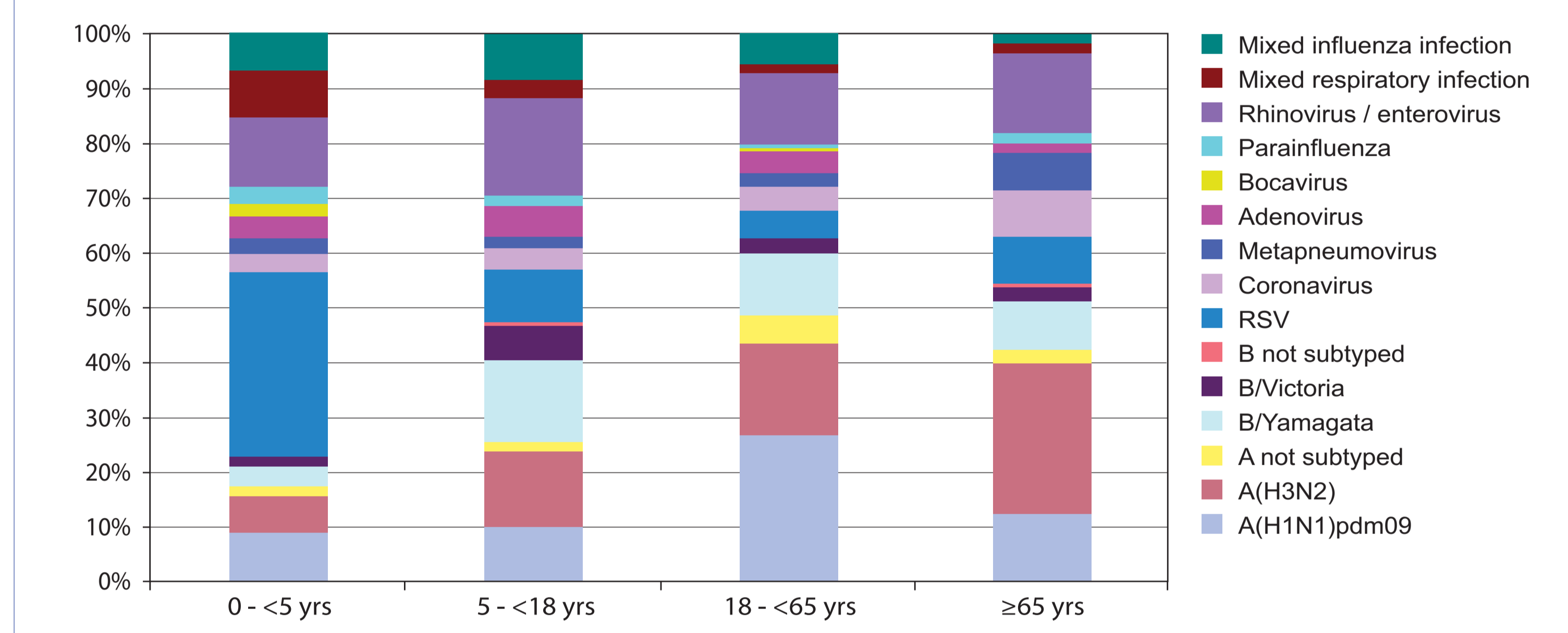


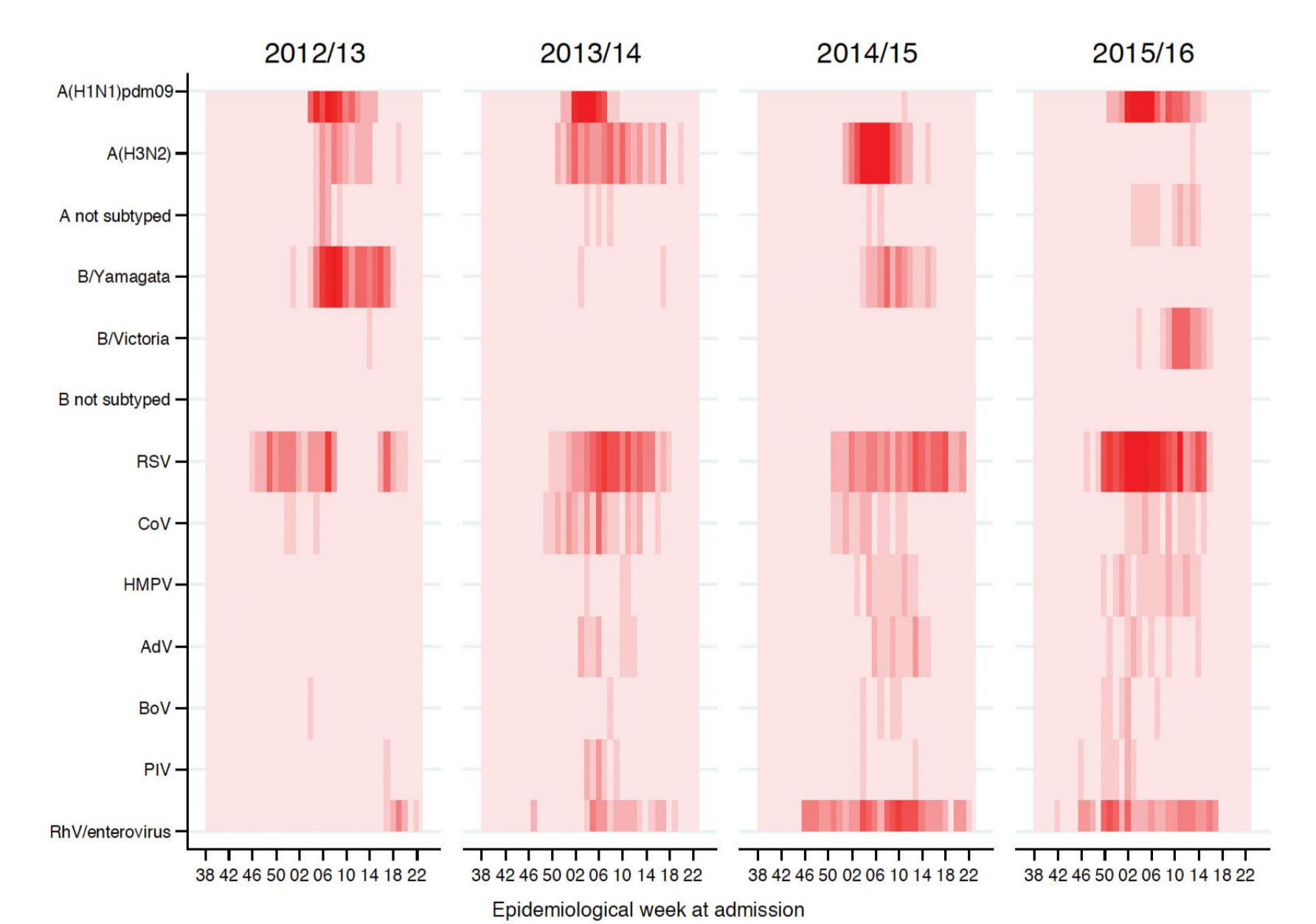
Figure 2. Virus distribution by age group



### Risk factors

- Among children less than 5 years old, the risk of being hospitalised with RSV decreased with age and those children who were not breastfed had 27% higher risk in comparison with those breastfed for at least 6 months. Children aged 2 to 5 years old had a reduced risk of being hospitalised with CoV than other age groups.
- Among those individuals 5 years old or over, the oldest adults (≥85 years old) had the highest risk of being admitted with influenza. Hospitalised subjects with chronic conditions were more likely to be positive for RhV/EV than those without underlying chronic conditions (after adjusting by age).

Figure 3. Probability of being positive for each virus in the four consecutive seasons



### Seasonality

- Although most of ARI occurred from November to May, different patterns of viruses' circulation were observed across seasons.
- RSV activity appeared earlier during 2012/13 and 2015/16 seasons and later in 2013/14 and 2014/15 seasons and RSV usually preceded the influenza wave. RhV/EV was more common in the 2014/15 season and its wave was wider than the wave of any other virus.

## CONCLUSIONS

Respiratory infections affected mainly the youngest and the elderly, RSV and influenza respectively. Seasonality patterns and risk factors vary according to the different viruses. Different virus distributions between sites were found due to age differences in the study population. Further research is necessary for better understanding and characterization of these respiratory viruses to make appropriate healthcare policy decisions.

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