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Original Article

The impact of influenza and respiratory syncytial virus on hospitalizations for lower respiratory tract infections in young children: Slovenia, 2006–2011

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Background Influenza and respiratory syncytial viruses (RSV) are important viral pathogens in childhood.

Objectives Our aim was to estimate the effect of influenza and RSV on excess hospitalizations for acute lower respiratory tract infections (ALRTI) in children aged ≤5.

Methods Retrospective, population-based study was performed for five seasons (2006–2011). Slovenian national hospital discharge data and surveillance data were used to estimate the effect of influenza and/or RSV on ALRTI hospitalizations (acute bronchiolitis, pneumonia, and acute bronchitis) using rate difference method.

Results An excess was observed in average weekly ALRTI hospitalizations per 100 000 among children aged ≤5 in all five seasons during influenza and/or RSV active period. During three seasons, there was higher excess in ALRTI hospitalizations in the period when influenza/RSV cocirculated compared with the RSV period. In pandemic season (2009/2010), the only one without influenza/RSV overlap, excess hospitalization was higher in RSV period. The highest excess of hospitalizations was found among the youngest children (0-5 months old). In all five seasons, acute bronchiolitis was the most common ALRTI recorded in hospitalized young children.

Conclusions Respiratory syncytial viruses was leading viral pathogen associated with ALRTI hospitalizations in children aged ≤5. The cocirculation of influenza virus increased the burden of ALRTI hospitalizations especially in seasons with A(H3) predominance.

Keywords Children, hospitalizations, influenza viruses, respiratory syncytial viruses, respiratory tract diseases, Slovenia.

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Introduction

Many respiratory viruses can affect young children, with influenza viruses and respiratory syncytial virus (RSV) being most recognized and important cause of disease of varying severity.[1,2] Excess morbidity and mortality caused by seasonal influenza have clearly been shown in persons over 65 years or having chronic medical condition. During the past decade, accumulated data on the impact of influenza-related diseases in children have become available. The spectrum of symptoms caused by influenza viruses in children is highly divergent and may lead to the hospitalizations for lower respiratory tract disease or other complications.[1] Respiratory syncytial virus has been recognized as one of the most common causes of serious lower respiratory tract infections worldwide and causes a large disease burden among infants and young children <2 years of age.[2] While the greatest risk of severe disease occurs in infants and children with known high-risk conditions, most infants who are hospitalized with or die of RSV-related causes have no underlying medical conditions.[2]

Effective preventive measures are available for several years against influenza and RSV for high-risk children.[1,2] In last decade, Slovenian national immunization program recommends vaccination against influenza to children who are diagnosed with chronic medical conditions and are at high risk of developing influenza-related complications. The vaccination program has been expanded in 2009 when influenza vaccine was recommended to healthy children aged from 6 to 23 months. Despite the recommendations, the vaccination coverage remains <1% in children younger than 5 years of age.[3] From 2006 onward, children with serious congenital heart disease, chronic pulmonary disease, or born prematurely (before 29th week of gestation) are given in their first year of life human monoclonal antibodies against RSV (palivizumab) during the RSV season.[3]

Influenza and RSV are important public health problems among children, as hospitalizations related to both pathogens

occur frequently with limited number of deaths in developed, industrialized countries.[1,2] Measuring the pediatric population-based disease burden of influenza is challenging. Using large databases and community influenza surveillance, population-based studies have documented excess hospitalizations, antibiotic use, and outpatient visits among children during the influenza season.[4,5] Respiratory syncytial virus often circulates concurrently with influenza viruses, and it is difficult to distinguish the impact of those two viruses on morbidity, hospitalizations, and mortality in cold part of the year in the temperate climate. In young children, the estimates of burden of the disease for influenza might be confounded by RSV and *vice versa*.[6]

We studied the excess hospitalizations for pneumonia, acute bronchitis, and bronchiolitis among children aged 5 years and younger in Slovenia during five influenza and RSV seasons in the period 2006–2011.

Methods

Hospitalization data

Nationwide retrospective, population-based study was performed to estimate the effect of influenza and/or RSV on acute lower respiratory tract infection (ALRTI) hospitalization. The study population comprised children who were 5 years or younger and hospitalized with pneumonia, acute bronchitis, and acute bronchiolitis from the period 2006–2011. Weekly data were extracted from the electronic diagnosis-related groups (DRG) database, run by the National Institute of Public Health (NIPH). The DRG system contains data on acute inpatient treatments and serves as a pricing system for hospital therapy. Data for the DRG system are collected by all Slovenian hospitals that treat acute cases (19 public hospitals and seven private acute care providers). At discharge, the physician describes individual treatment cases, assigns them to the DRG system using the International Statistical Classification of Diseases and Related Health Problems, 10th revision codes (ICD-10), and identifies the primary diagnosis, that is the diagnosis that necessitated admission to hospital. Secondary diagnoses refer to diseases and conditions existing before the admission or occurring during inpatient treatment.

Using ICD-10 codes, the patients aged 5 years or less hospitalized with ALRTI were classified into the following three groups: pneumonias (ICD-10 J12–18), acute bronchitis (ICD-10 J20), and acute bronchiolitis (ICD-10 J21). The ALRTI were selected as those diagnoses are related to influenza and RSV morbidity in children.

Influenza and RSV surveillance data

Influenza and RSV period were defined according to data from Slovenian National Influenza Sentinel Surveillance System and National RSV Laboratory Surveillance System.[7] Slovenian National Influenza Sentinel Surveillance System is based on network of primary care physicians (general practitioners and pediatricians), who weekly notify the number of patients consulting with ILI (influenza-like illness) or ARI (acute respiratory illness) in their reference population. Additionally, they regularly send throat and nose swabs from patients with ILI for virological confirmation with polymerase chain reaction (PCR) of influenza viruses to the National Influenza Center at NIPH. The sentinel surveillance system covers approximately 4% of Slovenian population.

National RSV Laboratory Surveillance System is based on the data derived from all public laboratories in Slovenia who perform the diagnostic tests for RSV on samples (with PCR or immunofluorescence) from patients with respiratory symptoms (mostly hospitalized children) and covers presumably all Slovenian population. The laboratories notify weekly the number of patients tested for RSV and the number of positive results.[7]

Study periods

We defined study periods for each season as follows:

1. Influenza period was defined as the interval of weeks between calendar weeks 40 and 19 with ILI incidence rate ≥25 per 100 000 population and ≥30% of samples tested positive for influenza virus.
2. Respiratory syncytial virus period was defined as the interval of weeks between calendar weeks 40 and 19, which started in the first of two consecutive weeks with ≥10% of samples tested positive for RSV and ≥20 samples tested and ended with the second of two consecutive weeks with ≤10% of samples tested positive for RSV and ≥20 samples tested.
3. Periseasonal period was defined as the interval between calendar weeks 40 and 19 without influenza and/or RSV period.
4. Summer period was defined as the interval between calendar weeks 20 and 39.

Statistical analysis

We calculated average weekly hospitalizations per 100 000 during each period separately, overall and for pneumonia, acute bronchitis, and acute bronchiolitis for children aged 5 years or younger and by three age-groups (0–5, 6–23, and 24–59 months). Excess hospitalizations were calculated as the difference between the average number of weekly hospitalizations per 100 000 children aged 5 years or younger in influenza and/or RSV period and periseasonal or summer period.

Size of Slovenian population for age-groups was obtained from Statistical Office of the Republic of Slovenia (http://www.stat.si/). The country population (app. 2·000 000 citizens) is relatively stable with practically no changes in

age structure in last years, and the population figures from 2009 were used as the denominator for all seasons (population at risk).

Results

Influenza and/or RSV periods

The length of influenza and RSV period fluctuated from season to season. In four of five seasons, influenza and RSV periods overlapped for 6, 5, 8, and 8 weeks in the season 2006/2007, 2007/2008, 2008/2009, and 2010/2011, respectively. In the pandemic season (2009/2010), the influenza peaked in November 2009 and ended in December 2009, while RSV period started in the second week of January 2010 (Figure 1).

Virological surveillance showed that influenza A predominated in the first four seasons. Influenza A (H3N2) virus was the dominant circulating subtype in the seasons 2006/2007 and 2008/2009. Influenza A (H1N1) predominated in the season 2007/2008. After the pandemic season (2009/2010) when barely influenza A (H1N1)pdm09 virus has been detected in sentinel (and non-sentinel swabs), pandemic influenza virus cocirculated with influenza B virus in the season 2010/2011 with nearly the same frequency.

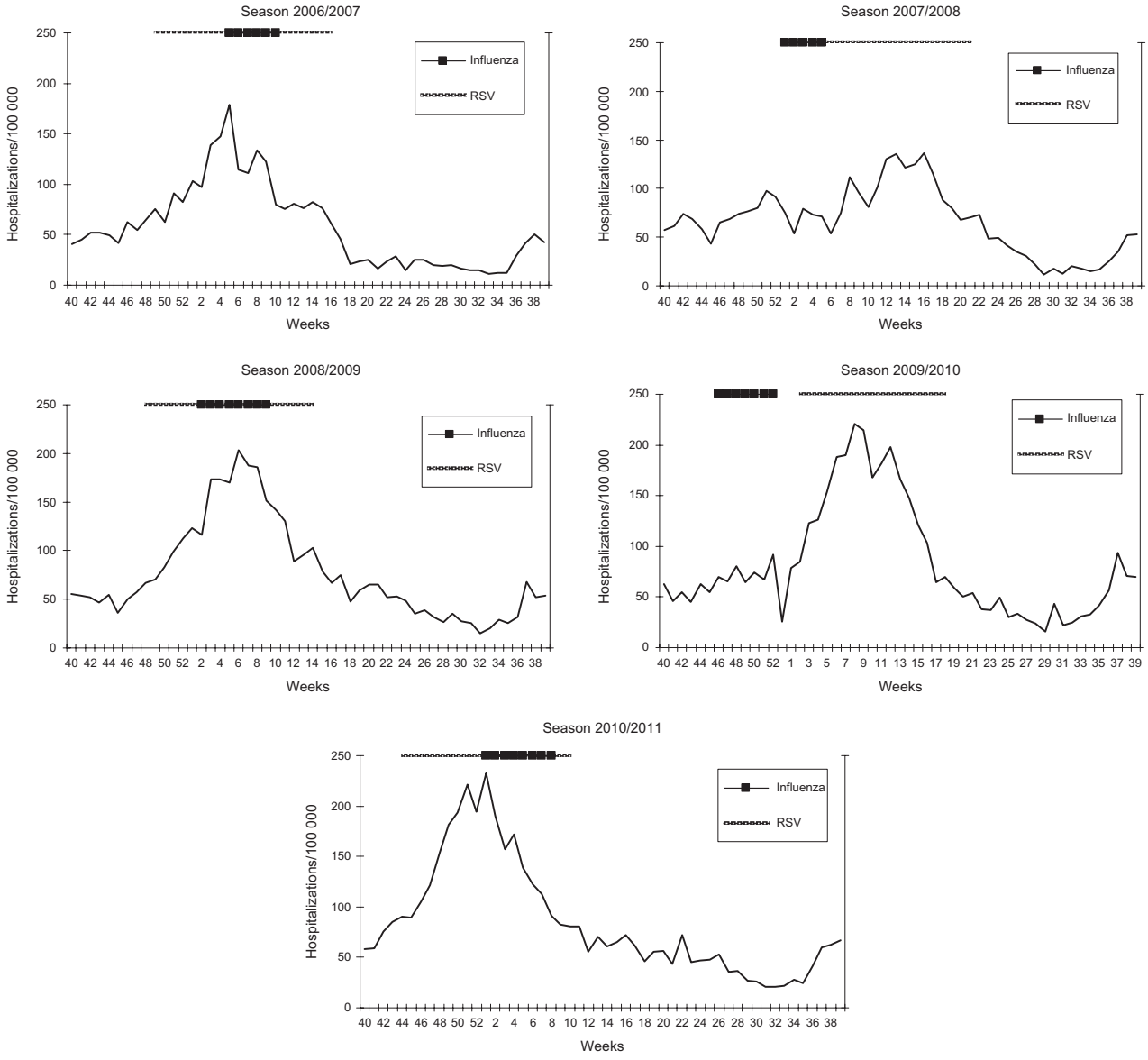

Figure 1. Weekly hospitalizations per 100 000 children aged 5 years or less for acute lower respiratory tract infections, and influenza and respiratory syncytial viruses periods, Slovenia, seasons from 2006/2007 to 2010/2011.

Hospitalization data

During all five seasons, there were 22 744 ALRTI hospitalizations in children aged ≤5 years registered in DRG system, with 3558, 4059, 4737, 5170, and 5220 hospitalizations per season 2006/2007, 2007/2008, 2008/2009, 2009/2010, and 2010/2011, respectively, regardless of the study period.

Average weekly hospitalizations for ALRTI per 100 000 children aged ≤5 years varied according to the period of the year. The highest average weekly hospitalizations were found in influenza/RSV overlapping periods in the season 2006/2007, 2008/2009, and 2010/2011 and in RSV only period in the seasons 2007/2008 and 2009/2010. As expected, the lowest weekly ALRTI hospitalizations were recorded during the summer period (Figure 1).

The excess hospitalization for ALRTI per 100 000 children aged ≤5 years was higher for all seasons when comparing periods with influenza and/or RSV circulation to summer periods than periseasonal periods (Table 1). The excess hospitalization was higher in influenza/RSV period compared with RSV only period in three seasons—in two seasons dominated by influenza A (H3N2) virus (2006/2007, 2008/2009) and in season 2010/2011 with influenza B and influenza A (H1N1)pdm09 virus cocirculation. In season 2007/2008 (with influenza A (H1N1) as predominant virus), the opposite has been observed—the excess hospitalization was higher in period when only RSV was present. In only season (2009/2010) when influenza period and RSV period did not overlap, the excess hospitalization was higher in RSV period compared with influenza period.

In all five seasons, acute bronchiolitis was the most common ALRTI recorded in hospitalized young children (Figure 2). Proportion of all hospitalizations due to acute bronchiolitis regardless of the study period ranged from 39·1% (2024 cases) in 2009/2010 to 44·2% (2305 cases) in 2010/2011. Hospitalizations for pneumonia varied from 28·3% (1007 cases) in 2006/2007 to 31·0% (1602 cases) in 2009/2010 and for acute bronchitis from 25·8% (1345 cases) in 2010/2011 to 32·1% (1141 cases) in 2006/2007.

We observed excess hospitalization in children aged ≤5 years for all three diagnoses during all five seasons when influenza and/or RSV period were compared with the summer periods or the periseasonal periods with one exception. In the season 2007/2008, there was no excess hospitalization for pneumonia or acute bronchitis observed in influenza/RSV period compared with the periseasonal period (Table 1).

The ALRTI hospitalization rate was consistently higher in children aged 0–5 months compared with children aged 6–23, and 24–59 months in all five seasons (Figure 3). The same holds for the excess hospitalization in RSV, influenza, and RSV/influenza periods compared with the summer or the periseasonal period—it was higher in youngest children, with exception of season 2007/2008 (RSV/influenza period compared with summer or periseasonal period) and season 2009/2010 (influenza period compared with summer or periseasonal period) (Table 2).

Table 1. Excess acute lower respiratory tract infections average weekly hospitalizations per 100 000 children aged 5 years or younger, according to different study periods during five seasons from 2006 to 2011

		ALRTI*		Pneumonia		Acute bronchitis		Acute bronchiolitis	
Season	**Period**	**Summer**	**Periseasonal**	**Summer**	**Periseasonal**	**Summer**	**Periseasonal**	**Summer**	**Periseasonal**
2006/2007	Influenza	–	–	–	–	–	–	–	–
	RSV	63·2	40·1	14·3	10·3	18·4	8·0	30·5	21·8
	RSV+influenza	100·1	77·0	27·4	23·4	21·8	11·4	51·0	42·2
2007/2008	Influenza	–	–	–	–	–	–	–	–
	RSV	67·2	28·7	19·8	3·6	15·8	5·0	31·5	20·1
	RSV+influenza	38·1	−0·3	15·7	−0·6	10·2	−0·6	12·2	0·8
2008/2009	Influenza	–	–	–	–	–	–	–	–
	RSV	61·4	44·9	14·4	9·5	12·8	7·1	34·2	28·3
	RSV+influenza	130·2	113·7	28·9	23·9	28·1	22·4	73·2	67·3
2009/2010	Influenza	30·9	19·0	14·9	9·9	8·2	6·4	7·9	2·7
	RSV	105·9	94·0	29·5	24·6	21·9	20·1	54·5	49·4
	RSV+influenza	–	–	–	–	–	–	–	–
2010/2011	Influenza	–	–	–	–	–	–	–	–
	RSV	95·9	72·7	25·0	17·4	18·2	11·6	52·7	43·7
	RSV+influenza	110·3	87·0	29·9	22·3	16·5	9·9	63·9	54·8

*Pneumonia, acute bronchitis and acute bronchiolitis.

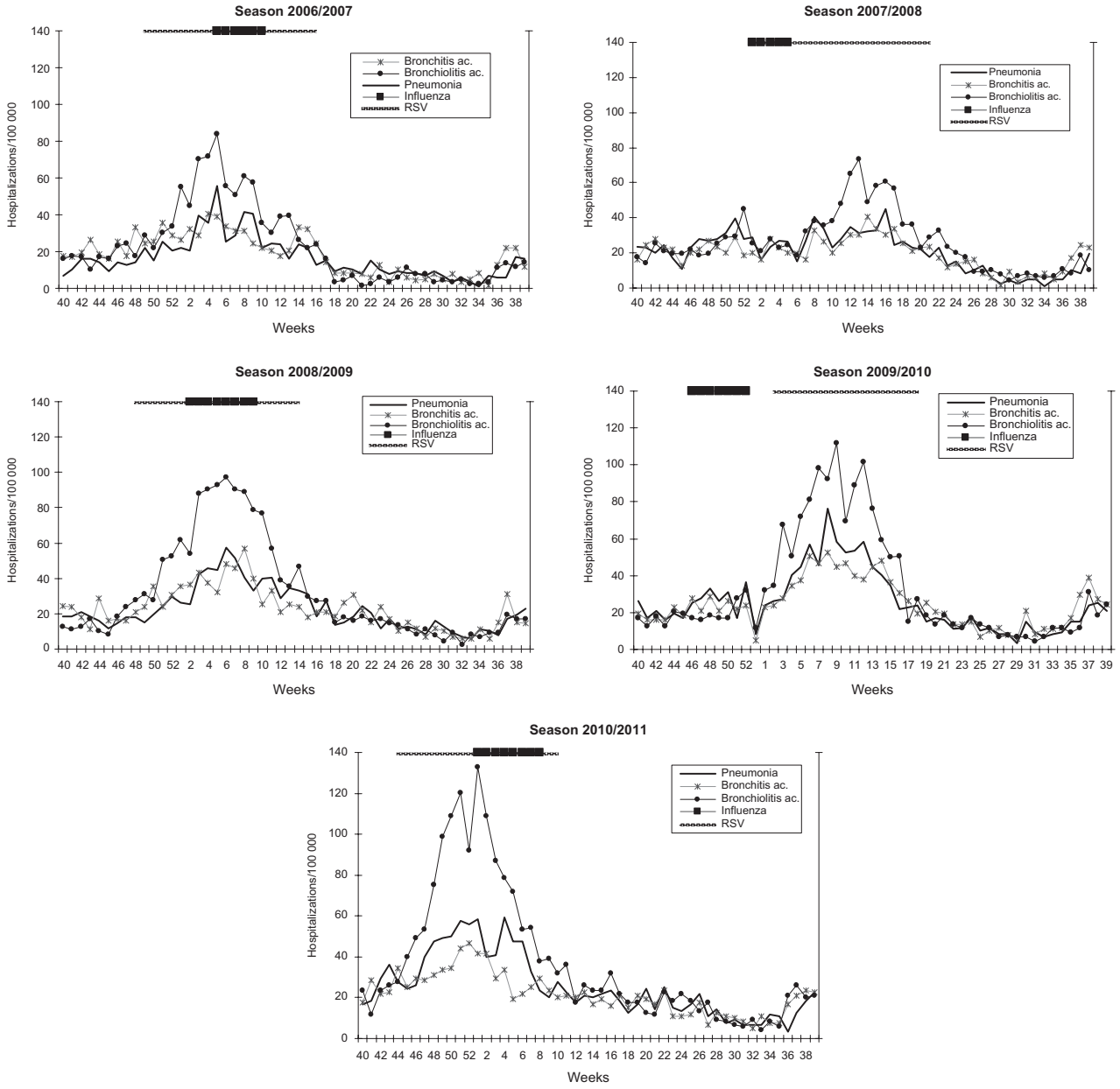

Figure 2. Weekly hospitalizations per 100 000 children aged 5 years or less for pneumonia, acute bronchitis and acute bronchiolitis, and influenza and respiratory syncytial viruses periods, Slovenia, seasons from 2006/2007 to 2010/2011.

Discussion

We observed an excess in average weekly hospitalizations for ALRTI (acute bronchiolitis, pneumonia, and acute bronchitis) per 100 000 among children aged 5 years or younger in all five seasons studied when influenza and/or RSV were present in Slovenian population. During three seasons (two predominated by influenza A (H3N2) and one by pandemic influenza A (H1N1) and influenza B virus combined), there was higher excess in the hospitalizations for ALRTI in the period when both pathogens (influenza and RSV) were circulating comparing with the period when only RSV was present. An excess of hospitalizations was highest among youngest children (0-5 months old).

Defining the cut offs for influenza and RSV season, periseasonal and summer period were one of the most challenging parts of our study. We carefully reconsidered certain approaches used in the previously published studies from the United States. In the first study, the beginning of influenza season was defined as the first week (between

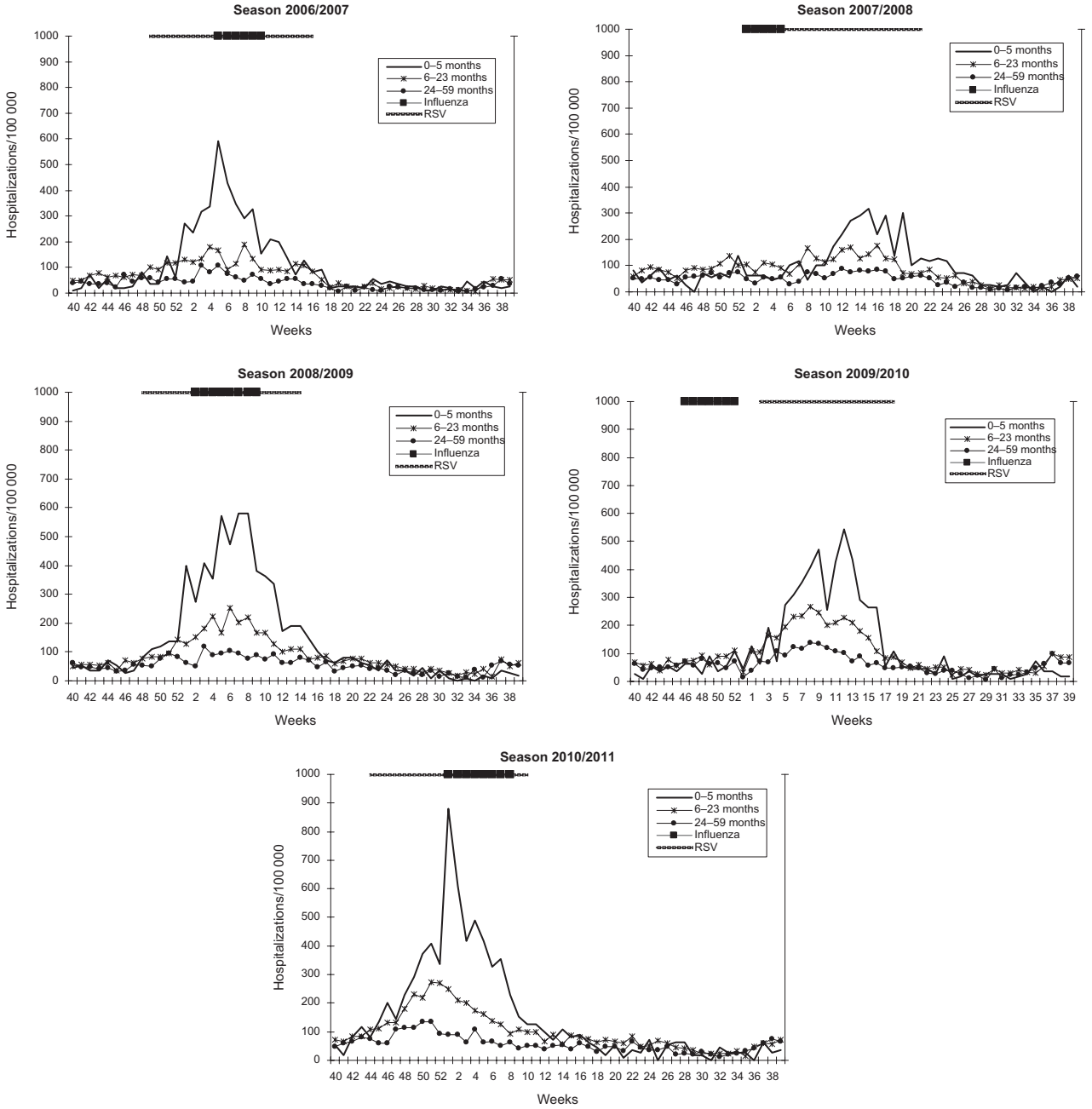

Figure 3. Weekly hospitalizations per 100 000 children for acute lower respiratory tract infections in three age-groups 0–5, 6–23, and 24–59 months of age, influenza and respiratory syncytial viruses periods, Slovenia, seasons from 2006/2007 to 2010/2011.

November 1 and April 30) with at least one positive sample in pediatric population consulting at hospital.[5] Main disadvantage of such definition is that a single patient with imported influenza from Southern Hemisphere could be a "starter" of the season. In two other studies, the influenza season was defined as any period of two or more consecutive weeks (between October and May) with influenza accounting for ≥5% of the season's total number of influenza isolates and less than 5% of RSV isolates.[8,9] When we tried to apply this methodology to our virological surveillance data, the weeks with intensive influenza circulation in the community (high percentage of samples positive for influenza and high ILI incidence rate) were not classified as influenza virus period as RSV was cocirculating even more intensively.

We believe that both epidemiological and virological data should be a part of influenza season definition. At the start of

Table 2. Excess acute lower respiratory tract infections average weekly hospitalizations per 100 000 in three age-groups of children, according to different study periods during five seasons from 2006 to 2011

		0–5 months		6–23 months		24–59 months	
Season	**Period**	**Summer**	**Periseasonal**	**Summer**	**Periseasonal**	**Summer**	**Periseasonal**
2006/2007	Influenza	–	–	–	–	–	–
	RSV	130·2	124·4	82·0	50·0	32·2	14·1
	RSV+influenza	328·4	322·7	105·7	73·7	49·3	31·2
2007/2008	Influenza	–	–	–	–	–	–
	RSV	131·7	120·1	86·0	33·7	38·6	9·0
	RSV+influenza	8·2	−3·4	60·9	8·7	21·8	−7·8
2008/2009	Influenza	–	–	–	–	–	–
	RSV	172·2	139·5	65·8	48·4	35·9	23·3
	RSV+influenza	422·0	389·3	149·7	132·3	53·6	41·0
2009/2010	Influenza	30·9	14·1	36·8	20·7	25·4	18·4
	RSV	272·9	256·1	132·3	116·2	52·5	45·5
	RSV+influenza	–	–	–	–	–	–
2010/2011	Influenza	–	–	–	–	–	–
	RSV	191·8	149·9	122·4	92·9	51·8	38·2
	RSV+influenza	431·8	390·0	121·5	92·0	35·6	22·0

the season, sentinel doctors are keen to take samples (and are advised to do so) to detect influenza virus as soon as possible —consequently, the number of samples taken is usually high, and the percentage of positives reflects the intensity of the season well. In the middle of the season, not so many samples are taken (percentage of positives usually peaks) and ILI incidence rates are also high. As influenza season is approaching to its end, only few samples are tested, and most of them positive for influenza, with a sharp drop in ILI incidence rates.

Combining virological and epidemiological cut offs enabled us to exclude weeks with high ILI incidence rates due to other respiratory viruses but without confirmed flu (in the reality, high ILI incidence rates were always accompanied by high percentage of flu-positive samples). Inversely, weeks with high percentage of flu positives (as a consequence of very few samples tested) but without elevated ILI incidence rates were excluded too. The epidemiological cutoff value (incidence rate ≥25/100·000) has been chosen on our observation that in the following week after the cutoff was reached ILI incidence rate doubled (three seasons) or even tripled (two seasons). This empirical observation was not far from a modeled value created on our sentinel surveillance data.[10]

For defining the RSV season, we applied the criteria used for regular "Respiratory Syncytial Virus Activity—United States" reports.[11]

Global burden of acute lower respiratory tract infections is high and remains a leading cause of morbidity in young children worldwide. It has been estimated that around 150 million new episodes of ALRTI arise every year globally.[12] Respiratory syncytial virus is most prevalent pathogen in children less than five causing app. 20% of all ALRTI (mostly acute bronchiolitis and acute bronchitis) in this age-group. Majority of children are infected with RSV by 2 years of age, but reinfections can occur throughout of life. There is a considerable annual variation in number of hospitalizations caused by RSV with regular biennial rhythm observed in some studies—a modest RSV season is followed by a more severe one.[13] Moreover, the precise time of RSV activity cannot be foreseen and appears to be an effect of weather and behavior change in cooler part of the year in the temperate climate zones.[14,15] In our study, the start of RSV seasons differed considerably from year to year as did the duration of RSV circulation.

Studies in the past decade suggested that the burden of ALRTI hospitalization in small children caused by influenza virus is substantial, too.[16,17] The recent meta-analysis showed that at least 13% of pediatric ALRTI and 7% of severe ALRTI in children are caused by influenza virus.[16] Circulation of influenza viruses starts early in some seasons and late in others without an anticipated pattern. Higher morbidity and mortality was usually generated by influenza A (H3N2) predominance in the elderly, in the patients with chronic conditions, and in small children as well.[18] Less-intensive seasons were observed when influenza B virus or influenza A (H1N1) virus prevailed.[16,19]

Disentangling the effects of influenza from those of RSV remains a challenge in epidemiological studies like in our study which use an ecological approach to assess the influence of viruses on healthcare utilization. In some previous studies, the effects of influenza or RSV only on

the consultation or hospitalization rates were analyzed separately simply by defining a week in a season as an influenza week if influenza virus predominated in virological samples or RSV week when higher percentage of RSVs were found.[5,8] This approach does not completely eliminate confounding by either RSV or other respiratory pathogens that may occur during the same period as influenza. Thus, there may be an overestimation of actual burden associated with influenza circulation in hospitalization rates reported. As shown in many studies as well as in ours, both pathogens (RSV and influenza) along with other viruses circulate concomitantly. Therefore, we did not attempt to separate the effects of influenza on hospitalizations in children aged ≤5 years from those of RSV, and we analyzed our data also for the period when both pathogens were present.

Only in the pandemic season (2009/2010), we were able to investigate the effect of influenza and RSV on the hospitalizations separately. The results of our study are consistent with the finding that RSV, not influenza, is associated with higher rates of the hospitalizations for lower respiratory tract disease in infants and young children.[5,17,20] The burden caused by RSV appeared to be considerably higher also in similar study from the Netherlands, where the total winter excess of hospitalization per 100 000 population (seasons 1997–2003) was estimated to be 142·7 (influenza versus summer baseline period) among children <1 year of age compared with 608·2 (RSV versus summer baseline period), and among children from 2 to 4 years, 19·8 compared with 34·6, respectively.[21]

The rate-difference model for determining the excess hospitalizations during influenza periods compared with base-line periods with lower or no influenza activity used in our study has been applied before.[5,8,21,22] It is less complicated and allows the insight to broader public than more sophisticated statistical models addressing this problem. The use of different definitions of study periods, various definitions of end points, and differences in healthcare systems make the published studies difficult to compare.

Our study implicates that influenza and RSV are associated with substantial increase in burden of the hospitalizations in children aged 5 years or less during the periods when those pathogens are detected compared with periseasonal or summer period. The results of this study are also in agreement with past studies that concluded that RSV and influenza virus account for significant morbidity in young children.[1,5,20,21,23] The youngest children (0-5 months old) were the most vulnerable for hospitalization compared with older age-group during the presence of RSV and/or influenza, as has been shown in the previous studies. The hospitalizations for acute respiratory infections were less frequent with increasing age.[1,5,20,21,23]

This study of excess hospitalizations estimates an effect of influenza virus and/or RSV infections on young children in Slovenia. The highest excess of hospitalizations in our study was found among the youngest children aged <6 months. The second most affected group were children aged 6–23 months. These results additionally support recommendations for preventive measures available. Only influenza virus infection is currently vaccine preventable, but vaccination coverage against influenza among children has been low in our country, and increased use of influenza vaccine could reduce the hospitalizations in this population group during winter months.[24] For reducing the hospitalizations among children aged <6 months, the population group without approved vaccine, the "cocoon strategy" of vaccinating pregnant women or new mothers, and family members of newborns with influenza vaccine should be recommended.

Much effort has been focused on prophylaxis of high-risk children for severe RSV disease with the highest burden on healthcare resources, but those control strategies have a limited effect on the total disease burden of RSV infection in the population.[21,25,26] The effective and safe vaccine against RSV infection is still under development and has the potential to markedly reduce the pediatric morbidity from acute respiratory infections.[6,19]

The importance of RSV as a driving force for ALRTI hospitalizations especially in children aged <6 months and the lack of vaccine reveal the need to intensify the education of young parents on how to avoid respiratory infections in newborns—keep them away from crowded places (e.g., shopping malls), not to send elderly siblings to kindergarten while mother is still on maternity leave (of 12 months in Slovenia), and to cease smoking in the proximity of the baby. These simple preventive measures are often ignored but can have an impact on reduction of morbidity.[2]

There are some limitations we should be aware of when we interpret the results from an ecological study like ours. We may have overestimated the excess burden of influenza and/or RSV on the hospitalizations. Our hospital registry (DGR) does not include information on laboratory confirmation, and we were not able to estimate the real number of the hospitalizations from influenza or RSV infections. Part of the hospitalizations that we considered to be associated with influenza or RSV might in fact be a potential confounding factor due to other respiratory viruses like parainfluenza virus, rhinovirus, coronavirus, human metapneumovirus, human bocavirus, enterovirus, and adenovirus. But on the other hand, other respiratory viruses may have contributed to the hospitalizations during base-line periods and could also be the source of confounding.

We were also not able to account for readmissions for the same disease in the same patient and therefore a possible overestimation of the hospitalizations. However, as this limitation is present in all five seasons studied, the results obtained are still comparable between them.

The analysis in this study was limited to the hospitalizations focused on ARLTI. We did not attempt to estimate the total increase in the hospitalizations attributable to influenza and may also underestimate the true burden of this disease. The hospitalizations for other conditions, including sepsis-like illness, acute neurological conditions, exacerbation of asthma, may increase among children during influenza seasons.[27]

The impact of RSV and influenza on ALRTI hospitalizations varied significantly from season to season. RSV was a leading viral pathogen associated with ALRI hospitalizations in children aged ≤5. The cocirculation of influenza virus increased the burden of ALRTI hospital admissions, especially in seasons with influenza A (H3N2) predominance. The RSV and influenza periods overlapped in four of five seasons, which made their impact on excess hospital burden of ALRTI inseparable. To our knowledge, this is also the first comparative study of influence of the pandemic influenza and RSV on excess hospitalization for ALRTI among young children and indicates the greater impact of RSV.

Competing interests

The authors have no competing interests.

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Supporting Information

Additional Supporting Information may be found in the online version of this article:

Table S1. Influenza virus and respiratory syncytial virus activity in Slovenia, during five seasons from 2006 to 2011.

Table S2. Acute lower respiratory tract infections weekly hospitalizations per 100 000 children aged 5 years or younger during five seasons from 2006 to 2011.

Table S3. Acute lower respiratory tract infections average weekly hospitalizations per 100 000 children aged 5 years or younger, according to different study periods during five seasons from 2006 to 2011.

Table S4. Acute lower respiratory tract infections average weekly hospitalizations per 100 000 in three age-groups of children, according to different study periods during five seasons from 2006 to 2011.