

Background. Influenza infection in children can be severe, resulting in complications such as pneumonia, but may be mitigated by early recognition and administration of antivirals. In this study, we identified risk factors for hospitalization and pneumonia in a pediatric population presenting with influenza-like illness (ILI) in Thailand.

Methods. Our study included pediatric patients (age < 18 years) presenting with ILI to inpatient and outpatient departments at a public hospital in Bangkok, Thailand, from 2009 to 2016. ILI was defined as fever plus cough or sore-throat, and pneumonia was defined as either lung radiographic or pulmonary examination abnormalities. Demographic and clinical data, as well as nasal and throat swabs, were collected during a one-time interview with patients presenting with ILI. Influenza infections were confirmed via RT-PCR testing of respiratory specimens. Retrospective chart review was used to collect data on individuals with influenza admitted for inpatient care.

Results. 5,968 children (33.6%) were enrolled with ILI, of whom 1,530 (25.6%) were confirmed to be influenza by RT-PCR, of which 25.5% were influenza A(H1N1) pdm09, 31.5% influenza A(H3N2), and 43.0% influenza B. 124 (8.1%) patients were admitted, and 41 of these children (33.1%) developed pneumonia. Predictors of hospitalization included younger age (4.1 yrs for inpatients vs. 5.6 yrs) and higher presenting temperature (38.6C for inpatient vs. 38.0C) (both $P < 0.05$). Among children hospitalized with influenza, influenza subtype was not associated with pneumonia risk. Co-detection of *Klebsiella pneumoniae* was associated with an increased risk of pneumonia ($P < 0.05$). Patients with pneumonia were younger (4.1 yrs with vs. 6.4 yrs, $P = NS$), had a longer interval from fever onset to presentation at the hospital, and required longer hospital stays. Risk of pneumonia was decreased in patients who received oseltamivir within 48 hours of fever onset (odds ratio 0.36, 95% confidence interval 0.16–0.91).

Conclusion. Post viral pneumonia is a potentially serious complication of influenza, requiring longer hospitalization stay and affecting more than one-third of hospitalized pediatric patients with influenza. The risk of pneumonia can be reduced with early presentation for clinical care and prompt administration of oseltamivir following fever onset.

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715. Increase in Reported Respiratory Syncytial Virus Cases Among Adults in the Minneapolis-St. Paul Metropolitan Area, 2014–2018

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Background. Respiratory syncytial virus (RSV) is a common cause of respiratory infection, typically causing severe disease in young children. We were interested in evaluating trends of severe RSV infections in adults.

Methods. The Minnesota Department of Health conducts active surveillance for laboratory-confirmed RSV in hospitalized patients in the Minneapolis-St. Paul metropolitan area as part of the CDC Emerging Infections Program. Adults (≥18 years) cases identified during the RSV season (10/1–4/30) from 2014 through 2018 were analyzed and surveys of catchment-area hospital laboratories were conducted regarding respiratory virus panel (RVP) testing.

Results. Twenty-three catchment area hospitals serve adults. Four hospitals offered RVP during the 2014–2015 and 2015–2016 seasons; eight offered RVP during the 2016–2017 and 2017–2018 seasons. Three hundred and fifty-five cases were identified. Three hundred and nine (87%) were reported from four hospitals where RVP was offered throughout the study period. Case increases were observed at three hospitals; all of these hospitals offered RVP throughout the surveillance period; increases were not observed at hospitals where RVP was added for the 2016–2017 and 2017–2018 seasons. Cases increased from 42 in 2014–2015 to 198 in 2017–2018 ($\chi^2 = 125.51$, $P < 0.01$), the proportion of cases reported by year was 12%, 15%, 17% and 56% during consecutive seasons. Cases by age groups over time generally did not differ; however, cases ≥85 years increased from 7% of total cases in 2014–2015 to 19% in 2017–2018 ($\chi^2 = 6.14$, $P = 0.01$). Overall, 23% of cases were admitted to the ICU and 7% died during hospitalization. The proportion of ICU admissions and deaths did not change over time.

Conclusion. We found an increase in adult RSV hospitalizations from 2014 to 2018, especially among the oldest age group. This increase was observed only at hospitals where RVP testing was offered throughout the surveillance period. It is unclear if this represents a true increase in RSV or a change in testing practices. However, it does illustrate that RSV should be considered as a cause of severe respiratory illness (SARI) in adults, particularly among the elderly. A more systematic approach in identifying the causes of SARI in adults would be informative, particularly as RSV vaccines and antivirals approach licensure.

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716. Molecular Epidemiology of Respiratory Syncytial Virus in Children and Adults in Seattle, WA

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Background. Respiratory syncytial virus (RSV) is the most important cause of pneumonia in children <5 years worldwide and may cause severe disease in elderly and high-risk adults. Multiple RSV strains co-circulate and evolve over seasons. We seek to describe the evolution of RSV over five seasons in Seattle, WA, USA with two seasons reported here.

Methods. From 2014 to 2016, subjects 6 months and older seeking outpatient care for acute respiratory illness at Kaiser Permanente Washington were enrolled in the Influenza Vaccine Efficacy Network (Flu VE Network) and a respiratory swab was collected. Real-time polymerase chain reaction (RT-PCR) was performed to test and quantify RSV and subtype positive samples. A subset of RSV samples with cycle threshold (CT) value <30 will be sequenced using a metagenomic next-generation sequencing (NGS) approach. Specific RSV genotypes will be associated with severe disease, defined as requiring emergency department care or hospitalization, or chest radiographic findings.

Results. A total of 8,730 patients were enrolled in the Flu VE Network and PCR testing of seasons 2014/2015 and 2015/2016 resulted in 562 of 4,137 (13.6%) RSV-positive specimens. Of patients with RSV-positive specimens, 204 (36.5%) were adults 18–64 years and 112 (20.0%) were 65+ years. RSV-B predominated in the 2014/2015 season ($n = 298$; 83.7%), whereas RSV-A was more common in the 2015/2016 season ($n = 154$; 79.8%) (Figure 1). The median (IQR) CT value for RSV-A specimens was 26.7 (23.3–29.9) compared with 27.9 (25.2–31.3) for RSV-B.

Conclusion. One RSV subtype predominated within each season. Similar RSV subtype distributions were seen across age categories. With multiple RSV vaccine candidates in development, understanding the genetic diversity and circulation of RSV various viruses within a population is important for analyzing the effects of a vaccine on the evolution of RSV.

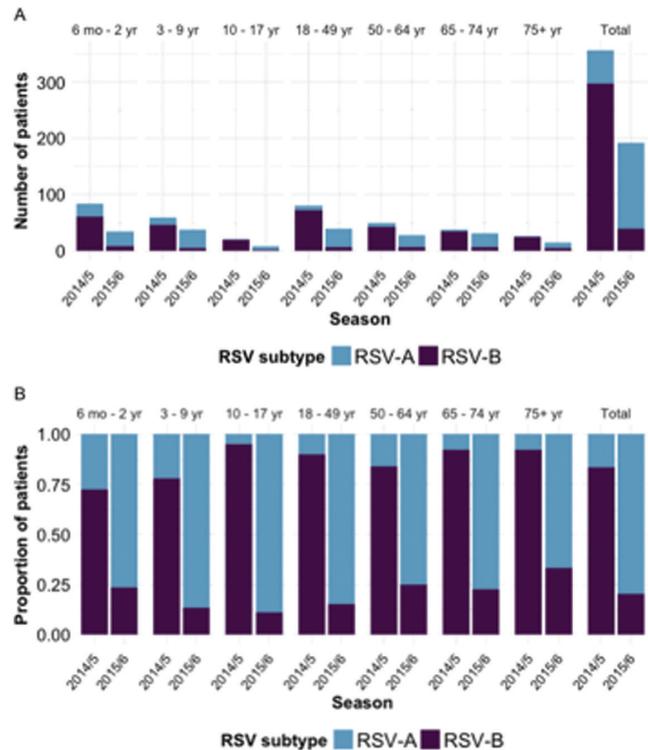


Figure 1. Total counts (A) and proportions (B) of RSV-A and RSV-B specimens collected from study patients in Seattle, WA during 2014/2015 and 2015/2016 seasons, by age category.

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717. Cumulative Incidence of Asthma/Wheezing Among Neonates/Infants/Toddlers Clinically Diagnosed with Respiratory Syncytial Virus Infection in the United States: A Retrospective Database Analysis

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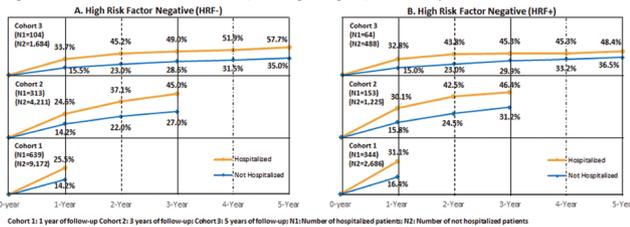
Background. The role of respiratory syncytial virus (RSV) in the development of asthma/wheezing (AW) has been evaluated in several studies, mostly among pre-term

infants or among infants after developing severe RSV-related disease. We describe the cumulative incidence (CI) of AW among hospitalized/ambulatory neonates/infants/toddlers after RSV/bronchiolitis infection diagnosis, in a large clinical database.

Methods. Using deidentified Optum Integrated commercial claims and electronic medical records, we identified patients (0–<3 years old) with a first clinical diagnosis of RSV/bronchiolitis infection from 01 January 2008–31 March 2016. Patients with a diagnosis of asthma/wheezing ≤30 days after first RSV/bronchiolitis diagnosis were excluded. Three cohorts were created with 1/3/5 years of follow-up time required, respectively. Patients were grouped by specific high-risk factors (HRF+/-), including pre-term births and predefined pre-existing disease. Descriptive statistics are reported, with comparisons made by logistic regression analyses.

Results. 9,811/4,524/1,788 patients with RSV/bronchiolitis infection and HRF- were included in the 1/3/5-years follow-up cohorts. 14.9%/28.2%/36.3% had AW events by the end of follow-up in the three cohorts. 6.5%/6.9%/5.8% were hospitalized for RSV/bronchiolitis. 3,030/1,378/552 patients with RSV/bronchiolitis infection and HRF+ were included in the 1/3/5-years follow-up cohorts. 18.1%/32.9%/37.9% had AW events by the end of follow-up in the three cohorts. 11.4%/11.1%/11.6% were hospitalized for RSV/bronchiolitis. The CI rates of AW in the 1/3/5-year HRF+/- cohorts, stratified by hospitalized for RSV/bronchiolitis Y/N, are shown in Figure 1.

Figure 1: Cumulative incidence rates of asthma/wheezing among RSV/bronchiolitis patients.



Logistic regression confirmed that hospitalization for RSV/bronchiolitis was associated with an increased ($P < 0.05$) likelihood of AW, for HRF+ and HRF- patients at each follow-up year.

Conclusion. Thirty-eight percent of RSV/bronchiolitis infants/neonates/toddlers HRF+, and 36% among infants/neonates/toddlers HRF-, developed AW in the 5 years after first RSV/bronchiolitis diagnosis. RSV/bronchiolitis hospitalization was associated with a significantly increased risk of AW development in 1/3/5 years of follow-up; confirming previous observational study results.

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718. Viral Coinfection and Nasal Cytokines in Children with Acute Bacterial Sinusitis (ABS)

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Background. ABS is one of the most common infections in childhood leading to antibiotic prescriptions, but remains a clinical diagnosis. Laboratory testing does not aid diagnosis and there are no predictors to identify those who will respond to therapy or develop complications. Thus, the tools to diagnose and manage ABS remain limited. Initial viral infection predisposes to development of ABS. However, there is poor understanding of the contribution of viral infection to pathogenesis, rate of complications, or the immune response to ABS. The objective of this study was to define bacterial upper airway colonization, viral co-infection and cytokine response in the upper airway during ABS.

Methods. In the context of an ongoing larger prospective clinical study, children were enrolled who were diagnosed with ABS using standardized clinical criteria. Nasopharyngeal (NP) samples were processed for bacterial culture for *S. pneumoniae*, *H. influenzae*, *S. pyogenes* and *M. catarrhalis*; real-time PCR viral testing and cytokine measurement by qPCR. We correlated these findings with clinical symptoms at the time of presentation.

Results. Of 184 enrolled children (median age 4.9 years), 134 (72.8%) had a positive bacterial culture for potentially pathogenic bacteria and 50 (27.2%) had growth of normal flora. A total of 129 (70.4%) subjects tested positive for a virus. The most common virus detected was rhinovirus ($n = 86$) followed by influenza virus ($n = 23$) and adenovirus ($n = 21$). A total of 102 patients (70.4%) had both a positive pathogenic bacterial culture and viral detection. Patients who had a bacterial pathogen plus a viral detection had a significantly higher expression of IL-6, IL-8 and IL-25 ($P < 0.001$). Univariable analysis found no correlation between clinical presentation with viral and/or cytokine expressions.

Conclusion. Children meeting clinical criteria for ABS and a NP swab with a pathogenic bacteria plus viral detection demonstrated higher expression of inflammatory cytokines compared with subjects whose culture had normal respiratory flora.

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719. The Respiratory Pathogen Panel and Antibiotic Utilization in the Emergency Department

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Background. The multiplex polymerase chain reaction respiratory pathogen panel (RPP) is used frequently in emergency departments (EDs) for the rapid identification of viruses and atypical bacteria of the respiratory tract. Its clinical value is unclear, as numerous studies have demonstrated that its use has a limited impact on antibiotic prescribing. We aimed to describe the relationship between RPP results and antibiotic prescribing rates for ED patients in our large academic medical center.

Methods. We retrospectively analyzed the charts of 1,061 patients aged 18–90 who were treated and released from two EDs from January 1, 2015 to January 31, 2018 and underwent RPP testing. Patients with evidence of bacterial infection were excluded based on RPP detection of atypical bacteria and microbiological analysis of blood, urine, wound, and sputum specimens. The results of the RPP and the rates of subsequent respiratory pathogen-directed antibiotic prescribing (including ED and outpatient pharmacy orders) were compared.

Results. Antibiotic prescription rates were 21.5% in patients who tested negative for any respiratory virus, compared with 14.5% in patients who tested positive (OR 0.70, $P < 0.01$). When positive RPPs were subdivided based on virus type (influenza and non-influenza) and compared with negative RPPs, only influenza-detection was associated with a significant reduction in antibiotic prescriptions (Table 1).

Conclusion. In our study population, the presence of a respiratory virus detected by the RPP was correlated with a significant decrease in antibiotic prescribing. This effect was largely driven by influenza detection. This demonstrates that at our institution, the RPP may have a role in reducing unnecessary antibiotic utilization, but providers need further guidance in the interpretation of non-influenza respiratory virus positivity.

Table 1. Antibiotic Prescription Rates by RPP Result, Subdivided by Virus Type

RPP Result	N	No. of Patients Given Antibiotics	Odds Ratio (95% CI)	P-value
Negative	628	135 (21.5%)	Reference	
Positive	433	63 (14.5%)	0.70 (0.56–0.88)	<0.01
Influenza*	169	20 (11.8%)	0.49 (0.30–0.81)	<0.01
Non-influenza virus(es)	264	43 (16.3%)	0.71 (0.49–1.04)	0.08

*Includes RPPs that were positive for multiple viruses if influenza was present.

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720. Respiratory and Nonrespiratory Complications Among Patients Hospitalized with Influenza, FluSurv-NET, 2016–2017

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Background. Influenza is most commonly associated with respiratory complications; however, nonrespiratory complications occur frequently among patients hospitalized with influenza. We used data from the Influenza Hospitalization Surveillance Network (FluSurv-NET) to describe complications recorded on discharge summaries of patients hospitalized with influenza.

Methods. We included children (0–17 years) and adults (≥18 years), who resided within a FluSurv-NET catchment area and were hospitalized with laboratory-confirmed