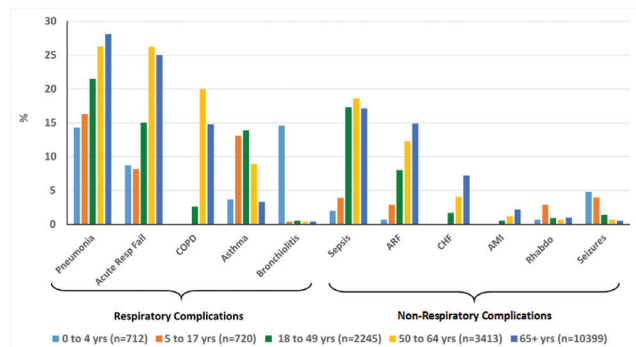


influenza during 2016–2017. We abstracted data on underlying conditions and discharge diagnoses from medical charts. We calculated the frequency of respiratory and nonrespiratory complications in all age groups and used univariate and multivariable logistic regression to examine factors associated with select complications among adults.

**Results.** Among 17,489 patients, the most common respiratory complications were pneumonia (26%) and acute respiratory failure (23%) and the most common nonrespiratory complications were sepsis (16%) and acute renal failure (ARF) (12%). Complications varied by age group (figure). Pneumonia was the most common respiratory complication in all age groups except 0–4 years; among children aged 0–4 years bronchiolitis was most common (104/712; 15%). Among 97 children aged 0–4 years with bronchiolitis who underwent testing for respiratory syncytial virus (RSV), 37% had RSV. The most common nonrespiratory complication was seizures in children aged 0–17 years (17% had a history of prior seizures) and sepsis in adults. Among adults ( $n = 16,057$ ), factors most strongly associated with ARF included chronic renal disease (adjusted odds ratio (AOR) 2.5; 95% confidence interval (95% CI) 2.2–2.8), male sex (AOR 1.5 95% CI 1.4–1.7) and age  $\geq 65$  years (AOR 1.4 95% CI 1.2–1.7); the factor most strongly associated with sepsis was chronic neuromuscular disease (AOR 1.5 95% CI 1.3–1.8).

**Conclusion.** Influenza hospitalizations are associated with a broad spectrum of complications including pneumonia, respiratory failure, sepsis, ARF and seizures. During the influenza season, astute clinicians should keep influenza in the differential diagnosis for patients with a wide range of presentations.

Figure. Respiratory and Non-Respiratory Complications by Age Group, FluSurv-NET, 2016–17



\*Acute Resp Fail = Acute Respiratory Failure; COPD = Exacerbation of Chronic Obstructive Pulmonary Disease; ARF= Acute Renal Failure; CHF= Exacerbation of Congestive Heart Failure; AMI= Acute Myocardial Infarction; Rhinobdo= Rhabdomyolysis

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### 721. Clinical Respiratory Syndromes and Association with Influenza Clinical Diagnostic Testing and Antiviral Treatment among Children Hospitalized with Acute Respiratory Illness, 2015–2016

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**Background.** We investigated clinical influenza testing and treatment in children hospitalized with acute respiratory illness (ARI) who had distinct respiratory syndromes.

**Methods.** Children <18 years old with ARI were enrolled at seven hospitals in the New Vaccine Surveillance Network (NVSN) between November 1, 2015–June 30, 2016. ICD10 admission diagnosis codes were grouped to define syndromes of bronchiolitis, asthma, pneumonia, and croup. At clinician discretion, influenza testing with a rapid influenza diagnostic test or molecular assay was performed on respiratory

samples. As part of the study, each site performed influenza testing using molecular assays on mid-turbinate nasal and throat swabs from all enrolled children. Analysis was restricted to influenza season; children who received antivirals before hospitalization were excluded.

**Results.** Among 2,134 children with available ICD10 codes, on preliminary analysis 1,119 (52%) had influenza testing ordered by a clinician: 111 (10%) were positive, and 57 (51%) of 111 received antiviral treatment. Of the 2,134, 858 (40%) had one of the four mutually exclusive syndromes (table). Hospital clinical testing per clinician discretion was influenza positive in 16 of the 858 children (percent positivity per syndrome ranged from <1% to 38%; table). Research study testing of children not undergoing clinical influenza testing identified 11 additional positives. Antiviral treatment was highest for pneumonia patients.

**Conclusion.** Understanding testing and treatment practices by clinical syndrome may help to identify missed opportunities for influenza diagnosis and treatment.

Table:

	Bronchiolitis		Asthma		Pneumonia		Croup
	n = 392		n = 320		n = 117		n = 29
	n	%	n	%	n	%	n %
<b>Age &lt;5 years</b>	391	>99	156	49	76	65	23 79
<b>&lt;2 days from illness onset to admission</b>	87	22	171	54	28	24	15 52
<b>&gt;1 known underlying condition</b>	84	21	277	87	62	53	6 21
<b>Hospital clinical testing performed</b>	209	53	90	28	68	58	8 28
Positive influenza	1	<1	4	4	8	12	3 38
Antiviral treatment	0		1		6		0
<b>Research study result in children without hospital clinical testing</b>							
Additional positive influenza	1		3		5		2
Antiviral treatment	0		0		3		0

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### 722. Normal Clinical Signs and Duration of Antibiotics in Hospitalized Patients with Pneumonia

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**Background.** The most common reason for antibiotic prescribing in hospitalized patients is suspected respiratory tract infection. In many cases, however, antibiotics may be started when the diagnosis is unclear and continued for a fixed course regardless of patients' clinical trajectories. We sought to characterize the distribution of clinical signs in patients started on antibiotics for possible pneumonia, number of days to normalization of clinical signs, and duration of antibiotics beyond when signs normalized.

**Methods.** We performed a retrospective analysis on 43,820 consecutive adults admitted to Brigham and Women's Hospital from May 2017 to January 2018. We identified all nonventilated patients started on antibiotics for pneumonia using clinicians' stated indications in their medication orders. We analyzed the distribution of clinical signs indicative of pneumonia (maximum temperature, maximum white blood cell count, median respiratory rate, and supplemental oxygen need) on the first day of antibiotics. We then calculated median days to normalization for each sign, total days of antibiotics for pneumonia, and duration of antibiotics beyond when all signs normalized.

**Results.** We identified 2,754 nonventilated patients started on antibiotics for pneumonia. On the first day of antibiotics, 38% had oxygen saturations  $\geq 95\%$  without supplemental oxygen, 78% had normal temperatures, 63% had normal white blood cell counts, and 79% had median respiratory rates <22 breaths/minute. All signs were normal in 25% of patients. Amongst those with at least one abnormal clinical sign on the first day of antibiotics, all signs returned to normal within a median of 3 days (IQR 2–7 days). Antibiotics were nonetheless continued for  $\geq 3$  more days in 33% of these patients.

**Conclusion.** Pneumonia is a major driver of antibiotic utilization in hospitalized patients but we found 25% of cases lacked the cardinal clinical signs of pneumonia and antibiotics were continued for  $\geq 3$  days after all clinical signs normalized in a third of the 75% of patients who did have signs of pneumonia. These findings suggest substantial opportunities to improve antibiotic prescribing for suspected respiratory tract infections in hospitalized patients.

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### 723. Validation of a Wild-Type Influenza A/Texas-Like H3N2 Human Challenge Model with Comparison to the Validated A(H1N1)pdm09 Model

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**Background.** Healthy volunteer challenge studies provide an opportunity to better understand influenza pathogenesis and correlates of protection. The development of vaccines and therapeutics has relied on these studies as will future universal vaccine candidates. The first fully validated wild-type human infection model with A(H1N1)pdm09 was developed at the NIH Clinical Center (CC) in 2012 and this study represents the first validation of a wild-type seasonal H3N2 human infection model. The objective of this study was to characterize a wild-type Influenza A/Texas-like H3N2 challenge virus in healthy volunteers.

**Methods.** Healthy volunteers were isolated at the NIH CC for a minimum of 9 days. Subjects received a single dose of a reverse genetics, cell-based, GMP, wild-type A H3N2 virus intranasally. Dose escalation was performed from  $10^4$  to  $10^7$  TCID<sub>50</sub>. Viral shedding and clinical disease were evaluated daily, including clinician assessments and a validated patient-reported outcome tool, FLU-PRO®.

**Results.** A total of 37 subjects were challenged. Sixteen (43%) subjects had viral shedding and 27 (73%) developed influenza symptoms, with 12 subjects (32%) experiencing mild-to-moderate influenza disease (MMID) defined as symptoms and shedding. Only subjects receiving the  $10^5$  and  $10^7$  TCID<sub>50</sub> doses experienced MMID at 44% and 40%, respectively. Nose and throat symptoms were most common and peaked by Days 2–3 post-challenge. Although serum antibody responses were observed, many of these responses were limited to a significant number of subjects.

**Conclusion.** The A/Texas-like H3N2 Influenza challenge virus safely induced MMID in healthy volunteers, but was less effective than the A(H1N1)pdm09 challenge virus. This lower MMID rate of 40% was observed at the  $10^7$  TCID<sub>50</sub> dose and was driven by less detection of shedding as the incidence of symptoms was similar to A(H1N1)pdm09. The limited serum antibody responses observed demonstrate that preexisting immunity in healthy volunteers against the seasonal H3N2 lineage may limit shedding compared with the more recently emerged seasonal A(H1N1)pdm09 lineage. The successful characterization of this H3N2 model makes future studies using this model to explore viral pathogenesis or evaluate vaccines possible.

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### 724. Neurologic Complications in Hospitalized Pediatric Patients with Influenza Infection, A Multicenter Retrospective Study in Korea

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**Background.** The aim of the study was to evaluate the incidence and characteristics of influenza associated neurologic complications (IANCs) in hospitalized pediatric patients in Korea.

**Methods.** We performed retrospective review of hospitalized cases of confirmed influenza infection from October 2010 to April 2017. Patient's data were collected from three referral hospitals in different regions of the country.

**Results.** A total 2,002 laboratory confirmed influenza cases were identified. The median age was 3.3 years old (range 0.0–18.9 years) and 1,003 patients were male (54%). Influenza A was diagnosed in 1,357 cases (68%), influenza B in 624 (31%) and both influenza A and B in 21 (1%). Other combined respiratory virus infection was detected in 104 (5.2%) cases. Out of 2,002 cases, IANCs were identified in 167 cases (8.3%); influenza virus A was detected in 116 (69.4%), B in 50 (29.9%) and both A and B in one case (0.6%). Of 167 cases with IANCs, 25 patients (15%) had underlying neurologic diseases. Eleven patients (11/167, 6.5%) had combined respiratory viral infection (Rhinovirus = 5; respiratory syncytial virus = 3; coronavirus = 2; and bocavirus = 1). The most common diagnosis was a simple febrile seizure (112/167, 67.1%), followed by other seizures (26/167, 15.6%), encephalopathy/encephalitis (17/167, 10.2%), meningitis (7/167, 4.2%), meningism (4/167, 2.4%) and acute ataxia (1/167, 0.6%). In two patients with encephalitis/meningitis, one patient had influenza A and the other patient had influenza B detected by PCR in cerebrospinal fluid. Most of the patients were fully recovered (162/167, 97%) and no neurologic complication occurred in patients who had only initial manifestation of simple febrile seizure. Ten patients (10/167, 6.0%) required hospitalization in intensive care unit. Three patients (3/167, 1.8%) died of encephalopathy ( $n = 1$ ) and combined encephalopathy/myocarditis ( $n = 2$ ). Pre-existing neurologic disease was a risk factor of IANCs with an odds ratio of 3.94 (95% confidence interval 2.37 to 6.56,  $P < 0.0001$ ).

**Conclusion.** IANCs is not rare and may cause serious outcome including death. Clinicians should be aware of the increased risk for IANCs in certain patients with neurologic diseases.

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### 725. Clinical Outcomes of Elderly Individuals Presenting with Acute Respiratory Infections

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**Background.** Elderly individuals experience increased morbidity and mortality from acute respiratory infections (ARI), which are complicated by difficulties defining etiologies of ARI and risk-stratifying patients in order to guide care. A number of scoring tools have been developed to predict illness severity and patient outcome for proven pneumonia, however less is known about the use of such metrics for all causes of ARIs.

**Methods.** We analyzed risk factors, clinical course and major outcomes of individuals  $\geq 60$  years of age presenting to the emergency department with a clinical diagnosis of ARI over a 5-year period.

**Results.** Of the enrolled individuals 40 had proven viral infection and 52 proven bacterial infections, but 184 patients with clinically adjudicated ARI (67%) remained without a proven microbial etiology despite extensive workup. Age (71.5 vs. 65.9 years,  $P < 0.001$ ) and presence of cancer and heart failure were strongly predictive of illness severe enough to require hospital admission as compared with treatment in the outpatient setting. Of those with proven etiology, individuals with bacterial infection were more likely to require hospital and ICU admission ( $P < 0.001$ ). When applied to this study, a modified PORT score was found to correlate more closely with clinical outcome measures than a modified CURB-65 ( $r$ , 0.54 vs. 0.39). Jackson symptom scores, historically used for viral illness, were found to inversely correlate with outcomes ( $r$ , -0.34) and show potential for differentiating viral and bacterial etiologies ( $P = 0.02$ ). Interestingly, a multivariate analysis showed that a novel scoring tool utilizing sex, heart rate, respiratory rate, blood pressure, BUN, glucose and presence of chronic lung disease and cancer was highly predictive of poor outcome in elderly subjects with all-cause ARI.

**Conclusion.** Elderly subjects are at increased risk for poor clinical outcomes from ARI and their clinical management remains challenging. However, modified PORT, CURB-65, Jackson symptom score, and a novel scoring tool presented herein all offer some predictive ability for all-cause ARI in elderly subjects. Such broadly applicable scoring metrics have the potential to assist in treatment and triage decisions at the point of care.

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### 726. Viral Genomic Load, Cytokine Profiles and Life-Threatening Respiratory Syncytial Virus Infection in Previously Healthy Infants

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**Background.** Data are controversial regarding the role of viral load and the host immune response in the severity of respiratory syncytial virus (RSV) infection. The objective of this study was to analyze the relationship between viral load (VL) and host cytokine responses with RSV life-threatening disease (LTD).

**Methods.** Prospective cohort study including previously healthy infants <12 months, hospitalized with a first RSV infection in 2017. Viral titers were assessed by qPCR and cytokine levels measured in nasopharyngeal aspirates obtained on admission. All patients with LTD were admitted to the intensive care unit.

**Results.** Fifty-one patients, median age 3 months (IQR 2–4), 29(56.9%) male. Eight developed LTD (1,569 LTD cases/10,000 RSV-hospitalizations/year [95% CI 702–2,859]). Antibiotic prescription was significantly higher (42.9 vs. 87.5%,  $P < 0.001$ ) and length of hospitalization significantly prolonged ( $5.2 \pm 1.9$  vs.  $16.1 \pm 12.7$  days,  $P < 0.001$ ) in infants with LTD. No differences were seen in the number of amplification cycles needed for a positive qPCR test (CT) nor in the viral titers of patients with LTD compared with those with better outcome ( $P = 0.71$ ). Figure 1. VL was not a predictor of LTD (AUC = 0.53); however, no LTD was seen with  $\leq 159,200$  copies/mL. CT/VL did not correlate with other outcomes (Figure 2). IFN- $\gamma$  levels (Th1 response) were significantly lower in infants with LTD ( $P = 0.034$ ). We detected no differences in TNF- $\alpha$  (pro-inflammatory), IL-9, IL-13 (Th2), IL-10 or IL-17 (regulatory) levels from