Age-Stratified Risk of Critical Illness in Young Children Presenting to the Emergency Department with Suspected Influenza

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Objective To investigate the risk of critical illness by age group among young children without a chronic condition presenting to the emergency department (ED) with suspected influenza.

Study design Retrospective study of patients aged <2 years presenting to the ED with suspected influenza (defined by diagnostic codes for influenza or influenza-like illness) from 2009 to 2017 in 49 hospitals in the Pediatric Health Information System. Patients with chronic conditions were excluded. The main clinical outcomes were intensive care unit (ICU) admission, ventilatory support, vasopressor administration, and mortality, which were compared independently by age group (<3 months, 3 to <6 months, 6 to <12 months, and 12 to <24 months). To compare outcomes by age, we estimated the prevalence of each outcome by age group after fitting logistic regression models to control for demographic differences between groups.

Results A total of 55 986 children were studied. Overall admission and ICU admission rates were 20% and 2%, respectively. After adjustment for demographic variables, infants aged <3 months had higher rates of ICU admission (2.7%; 95% CI, 2.0%-3.3%; $P < .001$ compared with other age groups) and ventilatory support (2.5%; 95% CI, 1.9%-3.2%; $P < .001$ compared with other age groups); however, there were no differences in vasopressor administration. The overall case fatality rate was low (0.007%) and thus could not be compared across age groups.

Conclusions Infants aged <3 months with suspected influenza are at greatest risk for critical illness. Although critical illness is uncommon, these findings should be incorporated into acute management decisions, including the need for specified outpatient follow-up or hospitalization, and public health efforts should focus on prevention and disease-modifying interventions in this high-risk population. *(J Pediatr 2019;215:132-8)*.

Young children aged <2 years are at increased risk for morbidity and mortality associated with influenza.[1-5] Although most previously healthy children with influenza have an uncomplicated course, acute care clinicians make real-time management decisions regarding the potential risk of severe illness in children with suspected influenza, often without test results. In addition, for children who are not hospitalized, the progression of disease and subsequent revisits often influence management decisions made during the index visit. An improved understanding of which children are at increased risk for potential progression to critical illness would aid these decisions in patients presenting with suspected or confirmed influenza.

Intuitively, young infants are at greatest risk for severe complications; however, 2 previous small studies of infants and young children with influenza concluded that younger infants are more likely to be hospitalized but have similar clinical outcomes as older infants, particularly if previously healthy.[6,7] Theoretically, young infants may have increased protection from maternal antibodies transferred transplacentally or via breastfeeding despite a less-developed immune system.[8,9]

We aimed to investigate the risk of critical illness (defined as intensive care unit [ICU] admission, ventilatory support, vasopressor administration, and/or mortality) and other important age-stratified outcomes among young children aged <2 years without a chronic condition who were diagnosed with suspected influenza (influenza or influenza-like illness [ILI]) in the emergency department (ED). Based on the limited literature indicating similar outcomes among the youngest infants, we sought to evaluate the risk of critical illness by age in a large pediatric cohort.

BIPAP	Bilevel positive airway pressure
CPAP	Continuous positive airway pressure
ED	Emergency department
HFNC	High-flow nasal cannula
ICU	Intensive care unit
ICD	*International Classification of Diseases*
ILI	Influenza-like illness
PHIS	Pediatric Health Information System

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Methods

Data for this study were obtained from the Pediatric Health Information System (PHIS), an administrative database that contains inpatient, ED, ambulatory surgery, and observation encounter-level data from US tertiary care pediatric hospitals. These hospitals are affiliated with the Children's Hospital Association (Lenexa, Kansas). Data quality and reliability are assured through a joint effort between the Children's Hospital Association and participating hospitals. Portions of the data submission and data quality processes for the PHIS database are managed by Truven Health Analytics (Ann Arbor, Michigan). For the purposes of external benchmarking, participating hospitals provide discharge or encounter data including demographic information, diagnoses, and procedures. Nearly all these hospitals also submit resource utilization data (eg, pharmaceutical, imaging, laboratory) into the PHIS. Data are deidentified at the time of submission and are subjected to a number of reliability and validity checks before being included in the database. For this study, data from 49 hospitals with complete demographic and billing information during the study period were eligible for inclusion in the analysis.

All statistical analyses were performed using Stata/SE version 14.1 (StataCorp, College Station, Texas). The study was approved by the Institutional Review Board and the administrators of the PHIS database. In accordance with PHIS policies, the identities of the institutions were not reported.

Study Population, Definitions, and Assumptions

We included all children aged <2 years of age with an ED encounter between October 1, 2009, and September 30, 2017, with a diagnosis of influenza or ILI. Both influenza and ILI were chosen to define suspected influenza, because coding of influenza as the primary diagnosis is more likely to be based on laboratory testing, and in clinical practice most acute care clinicians do not rely on rapid, point-of-care influenza diagnostic testing owing to variable test performance. The unit of analysis was the ED encounter, which was classified as a case with influenza or ILI if any of the following *International Classification of Diseases* (ICD) *Ninth Revision* (ICD-9) or *Tenth Revision* (ICD-10) codes were assigned as the diagnosis from the index ED visit: 487.0, 487.1, 487.8, 488.01, 488.02, 488.09, 488.11, 488.12, 488.19, 488.81, 488.82, 488.89, J110.0, J129, J111, J112, J118.1, J118.9, J09X1, J09X2, J09X3, and J09X9 (**Table I**; available at www.jpeds.com). Diagnostic codes were used for case definitions because primary clinical and laboratory data to confirm diagnoses are not available in the PHIS. All patients with a diagnosis of influenza or ILI were included to capture associated complications when influenza or ILI might have been assigned as a secondary diagnosis. For age-stratified analysis, patients were categorized into clinically relevant age groups of <3 months, 3 to <6 months, 6 to <12 months, and 12 to <24 months. An ED revisit was defined as a subsequent ED visit within 3 days of discharge from the index visit. ED revisit rates were calculated for all revisits as well as only for revisits with an associated admission. Admission was defined by inpatient or observation codes. Children with any complex chronic conditions were excluded based on ICD-9 and ICD-10 codes defined by Feudtner et al.[10]

Outcomes

The primary outcomes based on billing codes were critical illness defined by ICU admission, ventilatory support, vasopressor administration, and/or mortality. Ventilatory support included bilevel positive airway pressure (BIPAP), continuous positive airway pressure (CPAP), high-flow nasal cannula (HFNC), endotracheal intubation, and mechanical ventilation, and vasopressors selected for analysis were dopamine, epinephrine (parenteral administration only), and norepinephrine, because these are the most commonly used vasopressors in pediatric shock. A secondary analysis was performed of patients who received ventilatory support only with BIPAP, CPAP, endotracheal intubation, or mechanical ventilation, without HFNC.

Although the primary focus was on critical illness-related outcomes, we also measured other high-level outcomes of illness severity, including hospitalization-related outcomes (ie, hospitalization rates and hospital length of stay) and ED revisit-related outcomes (ie, rates of 3-day ED revisits and 3-day ED revisits with subsequent admission). For the primary analysis of these critical illness, hospitalization-related, and ED revisit outcomes, each outcome was analyzed independently.

In addition, to further investigate rates of critical illness among children who are discharged from the index ED visit but revisit within 3 days, we performed a secondary analysis of critical illness among the subgroup of patients who were discharged from the index ED visit and had a revisit within 3 days. For this secondary analysis, a composite measure of "critical illness"—defined as any of the following during the revisit: ICU admission, ventilatory support, vasopressor administration, and mortality—was used.

Statistical Analyses

To describe the demographic characteristics of the sample across the age groups defined above, we calculated frequencies and proportions for categorical variables and medians with IQRs for continuous variables. Our primary analysis estimated a set of logistic regression models with each outcome (eg, ICU admission) as the dependent variable and age group as the independent variable, modeled as a set of dummy variables. We also included demographic factors (ie, year, sex, race, ethnicity, primary source of payment and a variable denoting whether an influenza diagnosis was designated as the principal diagnosis) as additional covariates. A robust variance estimator was used to accommodate the correlation resulting from the clustering of patients

Table II. Demographic characteristics of patients aged <2 years diagnosed with influenza or ILI in the EDs of US pediatric tertiary care hospitals, October 2009-September 2017

Characteristics	<3 mo (N = 6823)	3 to <6 mo (N = 8048)	6 to <12 mo (N = 16 292)	12 to <24 mo (N = 24 823)	Total (N = 55 986)
Female sex, n (%)	2974 (44)	3551 (44)	7382 (45)	11 363 (46)	25 270 (45.1)
Race, n (%)					
White	3686 (54)	4014 (50)	8234 (51)	11 897 (48)	27 831 (49.7)
Black	1301 (19)	2050 (25)	4179 (26)	7076 (29)	14 606 (26.1)
Asian	154 (2)	190 (2)	344 (2)	578 (2)	1266 (2.3)
Other	1232 (18)	1260 (16)	2390 (15)	3563 (14)	8445 (15.1)
Missing	450 (7)	534 (7)	1145 (7)	1709 (7)	3838 (6.9)
Ethnicity, n (%)					
Latino	2228 (33)	2485 (31)	5064 (31)	7145 (29)	16 922 (30.2)
Not Latino	3998 (59)	4860 (60)	9783 (60)	15 395 (62)	34 036 (60.8)
Missing	597 (9)	703 (9)	1445 (9)	2283 (9)	5028 (9.0)
Insurance status, n (%)					
Private	1507 (22)	1309 (16)	2824 (17)	4953 (20)	10 593 (18.9)
Public	5003 (73)	6371 (79)	12 659 (78)	17 728 (71)	41 761 (74.6)
Other	276 (4)	294 (4)	642 (4)	1752 (7)	2964 (5.3)
Influenza principal diagnosis, n (%)*	5268 (77)	6605 (82)	13 020 (80)	19 396 (78)	44 289 (79.1)

Percentages might not sum to 100% due to rounding.
*Any of the following ICD-9 or ICD-10 codes: 487.0, 487.1, 487.8, 488.01, 488.02, 488.09, 488.11, 488.12, 488.19, 488.81, 488.82, 488.89, J110.0, J129, J111, J112, J118.1, J118.9, J09X1, J09X2, J09X3, and J09X9.

within hospitals. From these models, we derived adjusted prevalence estimates of the given outcome (ie, the predicted prevalence estimates of each outcome with the covariates fixed at their mean values) within each age group, along with the corresponding 95% CIs. By holding the covariates constant, these adjusted estimates reflect the magnitude of the outcome prevalence in a given group (and consequently the differences in that prevalence between groups) that is due to age and not to the covariates included in the model (although we cannot account for the impact of residual confounding from unmeasured factors).

To limit the number of statistical tests performed, we first performed an omnibus test of the age group dummy variables using the Wald χ^2 test. This test assesses the null hypothesis (H_o) of no differences on a given binary outcome, P (where P equals the proportion with the outcome), between the age groups (ie, H_o: $P_{<3 \text{ month group}} = P_{3 \text{ to } <6 \text{ month group}} = P_{6 \text{ to } <12 \text{ month group}} = P_{12 \text{ to } <24 \text{ month group}}$). The alternative hypothesis is "not H_o" (ie, the group proportions are not all equal). A significant omnibus test indicates evidence of at least 1 pairwise difference among the groups. If the omnibus test was significant, we performed post hoc pairwise comparisons with Bonferroni correction to determine the pattern of differences between groups. If the omnibus was not significant, no additional testing was performed. All tests were 2-tailed, and α was set at 0.05.

Results

During the study period, a total of 60 459 ED visits for influenza or ILI were identified from 49 pediatric hospitals, of which 4473 (7.4%) were excluded due to an associated complex chronic condition. The remaining 55 986 ED visits constituted the study sample. Demographics and clinical characteristics are displayed in Table II. The sample was predominantly male (55%) with a median (IQR) age of 10.7 (5.7, 16.8) months. Influenza or ILI was the principal diagnosis in 79% of encounters. Overall hospitalization rate was 20% (n = 10 960) including 1090 ICU admissions (representing 2% of patients and 10% of admissions). Within the <3-month-old age group, there were no significant differences in age (as measured in days) between patients with (median, IQR: 55, [43, 82]) and without critical illness (median, IQR: 62 [49, 78]; median difference [95% CI] = −7.0 [−21.6, 7.6]).

Comparison of Critical Illness Outcomes by Age

Rates of primary and secondary outcomes are outlined in Table III. On univariable analysis, infants aged <3 months had higher rates of ICU admission and ventilatory support when compared with all 3 older age groups (3 to <6 months, 6 to <12 months, and 12 to <24 months). Similar to the results of the univariable analysis, after adjustment for other demographic variables, infants aged <3 months had higher rates of ICU admission (2.7%; 95% CI, 2.0%-3.3%) and ventilatory support (2.5%; 95% CI, 1.9%-3.2%) compared with the 3 older age groups; however, there were no differences in vasopressor administration across the age groups. The overall case fatality rate was 0.007% (n = 4), with 2 deaths occurring in the ED and 2 occurring during hospitalization, and it could not be compared across age groups owing to the infrequent number of events. Among patients who only received ventilatory support with BIPAP, CPAP, endotracheal intubation, or mechanical ventilation (without HFNC), infants aged <3 months had higher rates of support (1.7%;

Table III. Clinical outcomes of patients aged <2 years diagnosed with influenza or ILI in the EDs of US pediatric tertiary care hospitals, October 2009-September 2017

Clinical outcomes	<3 mo (N = 6823)	3 to <6 mo (N = 8048)	6 to <12 mo (N = 16 292)	12 to <24 mo (N = 24 823)	Total (N = 55 986)	Adjusted omnibus test
ICU admission						$\chi^2_{(3)} = 57.2$; $P < .01$
Crude	261 (3.8)	151 (1.9)	269 (1.7)	409 (1.7)	1090 (1.9)	
Adjusted	2.7 (2.0-3.3)*,†,‡	1.3 (0.9-1.7)	1.1 (0.8-1.4)	1.1 (0.8-1.4)		
Vasopressors						$\chi^2_{(3)} = 4.7$; $P = .19$
Crude	30 (0.4)	21 (0.3)	44 (0.3)	60 (0.2)	155 (0.28)	
Adjusted	0.3 (0.1-0.4)	0.2 (0.1-0.3)	0.2 (0.0-0.3)	0.1 (0.1-0.2)		
Ventilatory support						$\chi^2_{(3)} = 30.9$; $P < .01$
Crude	230 (3.4)	157 (2.0)	286 (1.8)	524 (2.1)	1197 (2.1)	
Adjusted	2.5 (1.9-3.2)*,†,‡	1.5 (0.9-2.1)	1.3 (0.8-1.8)	1.5 (0.9-2.1)		
Hospitalization						$\chi^2_{(3)} = 982.8$; $P < .01$
Crude	3565 (52.3)	1566 (19.5)	2405 (14.8)	3424 (13.8)	10 960 (19.6)	
Adjusted	52.8 (48.9-56.6)*,†,‡	18.0 (15.2-20.7)†,‡	13.2 (10.8-15.6)	12.1 (10.0-14.3)		
Hospital length of stay ≥3 d						$\chi^2_{(3)} = 183.5$; $P < .01$
Crude	914 (13.4)	565 (7.0)	861 (5.3)	1067 (4.3)	3407 (6.1)	
Adjusted	11.5 (9.9-13.0)*,†,‡	5.9 (4.8-7.0)†,‡	4.3 (3.4-5.2)‡	3.4 (2.7-4.1)		
3-d revisit§						$\chi^2_{(3)} = 39.8$; $P < .01$
Crude	320 (9.8)	418 (6.5)	849 (6.1)	1174 (5.5)	2761 (4.9)	
Adjusted	9.7 (7.4-12.0)*,†,‡	6.4 (5.3-7.4)	6.0 (5.4-6.6)	5.4 (4.8-6.0)		
3-d revisit to admit§						$\chi^2_{(3)} = 56.7$; $P < .01$
Crude	141 (4.3)	97 (1.5)	174 (1.3)	251 (1.2)	663 (1.2)	
Adjusted	4.0 (2.1-5.9)*,†,‡	1.4 (1.0-1.7)	1.1 (0.9-1.4)	1.1 (0.9-1.2)		

Crude values represent n (%); adjusted values represent % (95% CI) of the outcome at the mean of the following covariates: year, sex, race, ethnicity, insurance status, and influenza principal diagnosis.
*$P < .05$ vs 3 to <6-month age group.
†$P < .05$ vs 6 to <12-month age group.
‡$P < .05$ vs 12 to <24-month age group.
§Restricted to patients discharged from the ED at the index visit.

95% CI, 1.1%-2.3%) compared with the 3 older age groups (**Table IV**; available at www.jpeds.com).

Comparison of Secondary Outcomes by Age

Infants aged <3 months had higher adjusted hospitalization-related outcomes (ie, hospitalization rates and hospital length of stay) compared with the 3 older age groups (**Table III**). In addition, adjusted 3-day ED revisits and 3-day ED revisits with subsequent hospitalization were significantly higher in the <3-month age group (9.7% [95% CI, 7.4%-12.0%] and 4.0% [CI, 2.1%-5.9%], respectively) compared with older age groups.

Analyzing critical illness as a composite outcome of ICU admission, ventilatory support, vasopressor administration, and mortality among patients discharged from the index ED visit who revisited within 3 days, 3.1% had critical illness, representing 0.2% of the children discharged initially (**Table V** and **Table VI** available at www.jpeds.com). Among those patients discharged from the index visit, adjusted 3-day ED revisits with subsequent critical illness were uncommon but highest in the <3-month age group (0.3%; 95% CI, 0.1%-0.5%).

Discussion

In this study of more than 55 000 children aged <2 years presenting to the ED with suspected influenza, we found that infants aged <3 months are at greatest risk for critical illness

Table V. Critical illness at revisit among patients aged <2 years diagnosed with influenza or ILI in the EDs of US pediatric tertiary care hospitals, October 2009-September 2017

Rates of critical illness	<3 mo	3 to <6 mo	6 to <12 mo	12 to <24 mo	Total	Adjusted omnibus test
On revisit in patients with an ED revisit*	N = 320	N = 418	N = 849	N = 1174	N = 2761	
Crude, n (%)	13 (4.1)	14 (3.4)	24 (2.8)	35 (3.0)	86 (3.1)	$\chi^2_{(3)} = 1.47$; $P = .689$
Adjusted, % (95% CI)	3.6 (1.3-6.0)	3.0 (1.6-4.4)	2.5 (1.5-3.6)	2.7 (1.4-3.9)		
On revisit in all patients discharged from index ED visit	N = 3258	N = 6482	N = 13 887	N = 21 399	N = 45 026	
Crude, n (%)	13 (0.4)	14 (0.2)	24 (0.2)	35 (0.2)	86 (0.19)	$\chi^2_{(3)} = 9.78$; $P = .021$
Adjusted, % (95% CI)	0.3 (0.1-0.5)	0.2 (0.1-0.3)	0.1 (0.1-0.2)	0.1 (0.1-0.2)		

Critical illness defined as any of the following during the revisit: ICU admission, ventilatory support, vasopressor use, and mortality. Adjusted values represent the predicted prevalence estimates as percentage (95% CI) of each outcome within each age group, with the covariates (year, sex, race, ethnicity, insurance status, and influenza principal diagnosis) fixed at their mean values.
*Restricted to patients discharged from the ED at index visit who revisited within 3 days.

compared with infants and young children aged 3-24 months. Rates of ICU admission and ventilatory support were highest in young infants aged <3 months compared with older infants and children, although no differences were found in vasopressor administration. Although revisits with progression to critical illness were uncommon, rates of revisits with critical illness were highest in the youngest age group. Beyond critical illness, infants aged <3 months had the highest rates of hospitalization and 3-day revisits.

Identifying previously healthy patients in the acute care setting who are at increased risk for disease progression and potential critical illness is both important and challenging during influenza epidemics. Although young children aged <2 years are considered at high risk for influenza-associated complications,[11] much of the risk of critical illness, including mortality, is among patients with underlying medical conditions.[1,12-16] In our sample of young children without chronic conditions, the risk for critical illness was found to vary by age. Although most young healthy children with influenza have an uncomplicated clinical course, improved understanding of risk strata can aid the management decisions of patients presenting with suspected influenza.

Intuitively, young infants would be at greatest risk for critical illness from influenza, similar to respiratory syncytial virus infection.[17-19] Among children hospitalized for laboratory-confirmed influenza, including those with chronic conditions, Dawood et al[12] found that infants aged <6 months had higher rates of hospitalization compared with older children. However Bender et al,[7] in a study of 833 children aged <24 months seen in the ED with laboratory-confirmed influenza, noted that infants aged <3 months had similar rates of critical illness and shorter hospital length of stay compared with infants and young children aged 3-24 months. In another study of 73 infants aged <6 months hospitalized for laboratory-confirmed influenza, Lopez-Medina et al[6] found that critical illness was uncommon among children without underlying medical conditions (1 ICU admission, no ventilatory support or mortality). Although young infants have a less well-developed immune system and are not candidates for vaccination, passive immunity from maternal antibodies may confer added protection.[8,9] Yet in our large, multicenter sample of young children that included more than 6000 infants aged <3 months with influenza or ILI, we found that the youngest infants were at increased risk for critical illness during the index visit, and among children not initially hospitalized, young infants had significantly higher rates of both revisits and revisits with subsequent hospitalization as compared with older children. Although critical illness after initial ED discharge was uncommon, rates were highest in the youngest age group.

Progression to critical illness and mortality from influenza can occur quickly even in previously healthy children, with mortality for some children occurring at home or in the ED.[2] Of the 4 deaths in our sample, 2 occurred in the ED and 2 occurred during hospitalization. Similar to other influenza-related complications, mortality from influenza in young children is greatest in those with chronic conditions.[2] Even with the inclusion of chronic conditions, overall and age-specific case fatality rates for influenza are difficult to estimate.[20] However, based on published rates from the Centers for Disease Control and Prevention,[21] the case fatality rate for influenza was approximately 0.003% among children aged <4 years. Comparatively, in our sample of previously healthy young children aged <2 years the case fatality rate was 0.007%. In addition, our analysis included only ED and hospital mortality in PHIS centers and did not include prehospital mortality or mortality occurring within non-PHIS EDs. Given the risk of critical illness both at the index visit and on revisit, early recognition and specified close outpatient follow-up and/or observation is warranted for young infants with suspected influenza.

This study has several important limitations. First, we based our investigation on a large administrative database that inherently does not allow patient-level review for clinical characteristics or illness severity, and we were unable to adequately adjust for illness severity, beyond the outcomes that we examined. There may have been treatment bias associated with younger infants and the primary outcomes of ICU admission and ventilatory support, given that some infants may be treated more conservatively due to their age. However, among patients who received ventilatory support only with BIPAP, CPAP, endotracheal intubation, or mechanical ventilation (without HFNC), infants aged <3 months had higher rates of support compared with the 3 older age groups. In addition, we used a composite outcome of ventilatory support that included HFNC, CPAP, BIPAP, and mechanical ventilation, and it is possible that there may have been age-related variability in the type of ventilatory support administered to children of different ages. However, these high-level outcomes are at least reflective of the fact that these patients may be at greater risk for decompensation due to some measure of their clinical severity, irrespective of the type of support administered. Previous work has suggested that principal diagnosis codes can be used to identify patients with influenza[22,23]; however, this likely underestimates the number of patients with a diagnosis of influenza, because many pediatric hospitals do not routinely test every patient. Given this, patients with a diagnosis of both influenza or ILI were included. This inclusion criteria potentially resulted in the inclusion of sicker patients with influenza, because patients with milder ILI may have been coded with other more generic symptom codes, such as fever or viral syndrome. The clinical progression of influenza is likely different than that of other respiratory viruses, and given the nature of the data, we were unable to evaluate for laboratory-confirmed viruses including influenza, viral coinfections, or maternal vaccination for influenza that might affect frequency of critical illness, which may help explain the differences from previous studies of patients with laboratory-confirmed influenza. However, the use of the combined diagnoses of influenza and ILI in our sample likely captures our target population of patients with suspected influenza, given that acute care clinicians often manage patients without laboratory testing, especially during epidemics. Although the outcome of ICU admission by itself may have variable determinants by site, in these large tertiary pediatric hospitals, it is likely a reasonable reflection of clinically relevant critical illness.

For generalizability, we aimed to identify a relatively healthy population of young children presenting with suspected influenza, and although we excluded patients with complex chronic conditions, we were unable to exclude all possible comorbidities that could influence the development of critical illness. Clinically relevant categorical age groups, rather than age as a continuous predictor for critical illness, were chosen a priori to mirror previous febrile infant literature, because clinicians often view decision making for young infants based on these previously defined age groups. Although these categorical age groups do not likely reflect meaningful adjustments to risk in individual patients, within the age group of young infants aged <3 months, median age was similar in infants with critical illness and those without critical illness. We were unable to perform age-stratified analysis of mortality as an outcome given the rarity of mortality even in the large sample. Furthermore, our sample represents children at major US pediatric hospitals, and the results might not be generalizable to other settings. Because patients are tracked longitudinally at a single institution, we do not know whether patients presented to a different institution for follow-up.

Infants aged <3 months with suspected influenza (defined as influenza or ILI) are at greater risk not only for ventilatory support and ICU admission, but also for hospitalization, ED revisits, and prolonged hospital length of stay compared with older infants and young children. This age-stratified risk in young children with suspected influenza should be considered in acute management decisions, including the need for specified outpatient follow-up or hospitalization. Although uncommon, given the increased risk of critical illness in this population, future research should focus on better understanding of risk stratification, evaluation, management, clinical pathway development, and vaccination strategies. Furthermore, public health efforts should focus on prevention and disease-modifying interventions in this high-risk population. ■

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Data Statement

Data sharing statement available at www.jpeds.com.

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Table I. ICD-9 and ICD-10 codes assigned as a diagnosis from the index ED visits

ICD-9 code	Description	ICD-10 code	Description
4870	Influenza with Pneumonia	J1100	Influenza Due to Unidentified Influenza Virus with Unspecified Type of Pneumonia
		J129	Viral Pneumonia, Unspecified
4871	Influenza with Other Respiratory Manifestations	J111	Influenza Due to Unidentified Influenza Virus with Other Respiratory Manifestations
4878	Influenza with Other Manifestations	J112	Influenza Due to Unidentified Influenza Virus with Gastrointestinal Manifestations
		J1181	Influenza Due to Unidentified Influenza Virus with Encephalopathy
		J1189	Influenza Due to Unidentified Influenza Virus with Other Manifestations
48801	Influenza Due to Identified Avian Influenza Virus with Pneumonia	J09X1	Influenza Due to Identified Novel Influenza A Virus with Pneumonia
48802	Influenza Due to Identified Avian Influenza Virus with Other Respiratory Manifestations	J09X2	Influenza Due to Identified Novel Influenza A Virus with Other Respiratory Manifestations
48809	Influenza Due to Identified Avian Influenza Virus with Other Manifestations	J09X3	Influenza Due to Identified Novel Influenza A Virus with Gastrointestinal Manifestations
		J09X9	Influenza Due to Identified Novel Influenza A Virus with Other Manifestations
48811	Influenza Due to Identified 2009 H1N1 Influenza Virus with Pneumonia	J09X1	Influenza Due to Identified Novel Influenza A Virus with Pneumonia
48812	Influenza Due to Identified 2009 H1N1 Influenza Virus with Other Respiratory Manifestations	J09X2	Influenza Due to Identified Novel Influenza A Virus with Other Respiratory Manifestations
48819	Influenza Due to Identified 2009 H1N1 Influenza Virus with Other Manifestations	J09X3	Influenza Due to Identified Novel Influenza A Virus with Gastrointestinal Manifestations
		J09X9	Influenza Due to Identified Novel Influenza A Virus with Other Manifestations
48881	Influenza Due to Identified Novel Influenza A Virus with Pneumonia	J09X1	Influenza Due to Identified Novel Influenza A Virus with Pneumonia
48882	Influenza Due to Identified Novel Influenza A Virus with Other Respiratory Manifestations	J09X2	Influenza Due to Identified Novel Influenza A Virus with Other Respiratory Manifestations
48889	Influenza Due to Identified Novel Influenza A Virus with Other Manifestations	J09X3	Influenza Due to Identified Novel Influenza A Virus with Gastrointestinal Manifestations
		J09X9	Influenza Due to Identified Novel Influenza A Virus with Other Manifestations

Table IV. Ventilatory support without HFNC in patients aged <2 years diagnosed with influenza or ILI in the EDs of US pediatric tertiary care hospitals, October 2009-September 2017

Ventilatory support (without HFNC)	<3 mo (N = 6823)	3 to <6 mo (N = 8048)	6 to <12 mo (N = 16 292)	12 to <24 mo (N = 24 823)	Total (N = 55 986)	Adjusted omnibus test
Crude, n (%)	178 (2.6)	106 (1.3)	160 (1.0)	219 (0.9)	663 (1.2)	$\chi^2_{(3)} = 74.6$; *P* <.01
Adjusted, % (95% CI)	1.7 (1.1-2.3)[*,†,‡]	0.9 (0.4-1.3)[†,‡]	0.6 (0.3-1.0)	0.5 (0.2-0.9)		

Adjusted values represent percentage (95% CI) of the outcome at the mean of the following covariates: year, sex, race, ethnicity, insurance status, and influenza principal diagnosis.
**P* <.05 vs 3 to <6-month age group.
†*P* <.05 vs 6 to <12-month age group.
‡*P* <.05 vs 12 to <24-month age group.

Table VI. Rates of critical illness outcomes (ie, ICU admission, ventilatory support, and vasopressor administration) at revisit among patients aged <2 years diagnosed with influenza or ILI in the EDs of US pediatric tertiary care hospitals, October 2009-September 2017

Critical illness outcomes on revisit	<3 mo	3 to <6 mo	6 to <12 mo	12 to <24 mo	Total
In patients with an ED revisit, n (%)*	N = 320	N = 418	N = 849	N = 1174	N = 2761
ICU admission	8 (2.5)	8 (1.9)	15 (1.8)	22 (1.9)	53 (1.9)
Ventilatory support	8 (2.5)	8 (1.9)	14 (1.7)	26 (2.2)	56 (2.0)
Vasopressor administration	3 (0.9)	4 (0.9)	5 (0.6)	4 (0.3)	16 (0.6)
In all patients discharged from index ED visit, n (%)	N = 3258	N = 6482	N = 13 887	N = 21 399	N = 45 026
ICU admission	8 (0.3)	8 (0.1)	15 (0.1)	22 (0.1)	53 (0.1)
Ventilatory support	8 (0.3)	8 (0.1)	14 (0.1)	26 (0.1)	56 (0.1)
Vasopressor administration	3 (0.1)	4 (0.5)	5 (0.0)	4 (0.0)	16 (0.0)

Age-stratified analysis of mortality as a critical illness outcome could not be performed given the total number of patients (n = 4).
*Restricted to patients discharged from the ED at index visit who revisited within 3 days.