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Burden of Influenza-related Hospitalizations among Children with Sickle Cell Disease

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Abstract

Objective—Children with sickle cell disease (SCD) are considered a high-risk population for complications from influenza infection, despite minimal published data characterizing the burden of influenza in this population. Our objectives were to: 1) estimate the rate of influenza-related hospitalizations (IRH) among children with SCD, 2) compare this rate to rates for children with cystic fibrosis (CF) and with neither SCD nor CF, and 3) explore mechanisms underlying these potentially preventable hospitalizations.

Methods—We analyzed hospitalizations from 4 states (California, Florida, Maryland, New York) across 2 influenza seasons (2003/4 and 2004/5) from the Healthcare Cost and Utilization Project State Inpatient Databases. We included hospitalizations with a discharge diagnosis code for influenza in a child less than 18 years of age. Using census data and disease prevalence estimates to calculate denominators, we compared rates of IRH among children with SCD, CF, and neither.

Results—There were 7,896 pediatric influenza-related hospitalizations during the 2 influenza seasons. Of these, 159 (2.0%) included a co-occurring diagnosis of SCD. Annual rates of IRH were 112 and 2.0 per 10,000 children with and without SCD, respectively, across both seasons. Children with SCD were hospitalized with influenza at 56 times the rate of children without SCD (95% CI: 48–65). Children with SCD had approximately double the risk of IRH compared to children with CF (RR = 2.1 [1.5 – 2.9]). IRH among children with SCD were not longer, more costly or more severe than IRH among children without SCD, were rarely nosocomial, and co-occurred with a diagnosis of asthma in 14% of cases.

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Conclusions—Influenza-related hospitalizations are substantially more common among children with SCD than those without, supporting the potential importance of vigorous influenza vaccination efforts targeting children with SCD.

Keywords

Sickle cell disease; influenza; surveillance; hospitalization

Introduction

Influenza is a morbid infection in children resulting in thousands of hospitalizations annually.^{1–11} Compared with healthy children, those with certain chronic medical conditions are believed to be at increased risk for influenza-related morbidity and mortality.^{2, 4, 7, 11–15} These high-risk conditions include pulmonary, cardiac, neurologic, metabolic, immunologic, hematologic, and other disorders.¹⁶ Among these chronic conditions, the most is known about the interaction between influenza and asthma, the condition with the greatest prevalence.¹³ In contrast, the burden of influenza-related morbidity among children with sickle cell disease (SCD), the most frequent disease detected on newborn screening,¹⁷ is largely unknown.

SCD comprises a family of prevalent and highly morbid genetic disorders. Children with SCD are at increased risk for invasive bacterial infections by encapsulated organisms, due in part to reduced splenic function associated with SCD.^{18–20} In addition, children with SCD may be at increased risk for complications from influenza, though few published data support this contention. The postulated risk associated with influenza infection could be secondary to increased susceptibility of individuals with SCD to invasive bacterial infections,²¹ an associated increased frequency of acute chest syndrome, an increased prevalence of asthma among children with SCD,^{22–24} or other factors. Based on these concerns, children with SCD have been designated a high-risk target population for influenza vaccination by the Centers for Disease Control and Prevention (CDC) since the 1970s.^{16, 25}

Using hospital discharge data for 4 states across 2 influenza seasons, our primary objectives were to: 1) estimate the rate of influenza-related hospitalizations (IRH) among children with SCD and the subset with homozygous hemoglobin S (i.e., sickle cell anemia (SCA)); 2) compare these rates to those for children without SCD and for children with cystic fibrosis (CF), another CDC-identified high-risk group;¹⁶ and 3) use the epidemiology of IRH among children with SCD to begin to explore mechanisms underlying these potentially preventable hospitalizations.

Methods

Data source

The Healthcare Cost and Utilization Project (HCUP) State Inpatient Databases (SID) result from a federal-state-industry partnership sponsored by the Agency for Healthcare Research and Quality (AHRQ). The SID capture all hospitalizations in 39 participating states, translated into a uniform format to facilitate state-by-state and longitudinal comparisons and analyses.²⁶ SID from each state contain a core set of more than 100 clinical and nonclinical variables included in hospital discharge abstracts on all hospitalized patients, regardless of payer. We analyzed data from 4 SID: California, New York, Maryland, and Florida. Together, these 4 states comprised 25% of the non-Latino African American pediatric population during the study years.²⁷

Denominator estimates

We used US census data²⁷ to estimate the total population of children ages 0 to 17 years in the study states, as well as racial/ethnic subsets. For each influenza season, we averaged the US Census population estimate from the 2 involved years (e.g., for 2003/4 influenza season, estimates represent averages of 2003 and 2004 population data). Finally, we used the prevalence of SCD, SCA, and CF in non-Latino African Americans, non-Latino whites, and Latinos^{28–30} to estimate the population of children with each condition in each state.

Influenza seasons

We analyzed 2 consecutive influenza seasons, defined as July 1, 2003 to June 30, 2004 (2003/4 season) and July 1, 2004 to June 30, 2005 (2004/5 season). We could not define influenza seasons more precisely, because 2 states (MD, FL) provided only the calendar quarter and year in which the hospital discharge occurred. We selected these 2 influenza seasons because they involved some of the most recent HCUP SID data available and there was variability between the 2 seasons across a variety of attributes (Appendix 1). In particular, the 2003/4 season involved a drift variant as the predominant circulating strain, resulting in a suboptimal match with the vaccine used that season and high levels of influenza morbidity. In addition, vaccination recommendations were broadened in 2004/5, a season which was complicated by an unrelated shortage of influenza vaccine supply.

Case definition

We analyzed hospitalizations that 1) ended between July 1, 2003 and June 30, 2005, 2) involved a child less than 18 years of age, and 3) included an International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) discharge diagnosis code for influenza (Appendix 2). In the 4 states under study, the number of possible discharge diagnoses associated with each hospitalization ranged from 10 (Florida) to 25 (California). To maintain consistency across states, we limited our analyses to the first 10 listed discharge diagnoses. We followed a similar process when analyzing procedure codes. We stratified influenza-related hospitalizations (IRH) by whether or not they co-occurred with a diagnosis code for SCD, SCA, or CF (Appendix 2). Similar to other researchers, our SCA codes were intended to select only hospitalizations occurring among children with homozygous hemoglobin S;³¹ our SCD codes were intended to select hospitalizations occurring among children with any sickling hemoglobinopathy, including SCA, but excluding those with sickle cell trait.

Analysis

After extracting pediatric IRH from the HCUP SID databases, we calculated hospitalization rates using population-based denominators. We then computed risk ratios and 95% confidence intervals of IRH among children with SCD and SCA versus children with CF and those with neither SCD nor CF. Next we examined diagnosis coding patterns, as well as child and hospitalization attributes, for IRH among children with and without SCD. Finally, we hypothesized that disproportionately high rates of IRH in children with SCD could result from an increased risk of nosocomial (i.e., hospital-acquired) influenza secondary to frequent admissions for complications of SCD. To test this hypothesis, we conducted a sub-analysis on data from 2 states (CA, NY), which designated whether or not each discharge diagnosis was present at the time of admission. We considered hospitalizations in which the diagnosis of influenza was present on admission to be community-acquired and those in which the diagnosis was not present on admission to be hospital-acquired. This study of publicly available, de-identified data was approved by the Johns Hopkins University School of Medicine Institutional Review Board.

Results

Influenza-related hospitalization counts and rates

We identified 7,896 influenza-related hospitalizations among children during the 2 influenza seasons: 5,508 in 2003/4 and 2,388 in 2004/5 (Table 1). Of these 7,896 IRH, 159 (2.0%) included a co-occurring diagnosis of SCD, of which 144 (90%) were coded as SCA. Using US Census-based denominator estimates, rates of IRH were 177, 112 and 2.0 per 10,000 children with SCA, SCD, and neither, respectively, across both seasons. Children with SCA were hospitalized with influenza at 88 times the rate of children without SCD (95% CI: 75–104). The overall IRH rate we observed in 2004/5 (1.2 IRH per 10,000 children per year) was similar to the nationwide rate for pediatric IRH reported by the CDC's Emerging Infections Program (1.3 IRH per 10,000 children per year) for that season,³² as well as other historical incidence estimates.¹⁴ Consistent with previously published data,^{8, 10, 33} the number of hospitalizations was substantially higher in 2003/4 compared with 2004/5, for both children with and without SCD.

Comparison of influenza hospitalization rates between children with SCD and CF

The population of children with SCD was 70% larger in the 4 study states than the pediatric CF population (Table 2). Across the 4 states and 2 influenza seasons, children with SCD had approximately double the risk of children with CF of being hospitalized with influenza (RR = 2.1 [1.5 – 2.9]).

Comparison of IRH with and without co-occurring SCD

Hospitalizations involving influenza and SCD were different from those involving influenza without SCD in several key attributes (Table 3). IRH co-occurring with SCD were more likely to involve older children than IRH without co-occurring SCD (mean age 5.6 years vs. 2.8 years, $P < 0.0001$). IRH with SCD were more likely to involve Medicaid-insured (64% vs. 54%, $P = 0.002$), Black (85% vs. 17%, $P < 0.001$) children from large metropolitan areas (89% vs. 71%, $P < 0.001$) than IRH without co-occurring SCD, likely reflecting the demographics of SCD. Overall few procedures were reported. While average length of stay was shorter (3.4 days vs. 4.2 days) and total charges less (\$11,924 vs. \$18,779) for IRH with SCD than those without, neither difference was statistically significant. None of the 45 deaths associated with influenza-related hospitalizations across the 2 influenza seasons were associated with a co-occurring SCD diagnosis.

Diagnosis coding patterns among IRH co-occurring with SCD

Among the total 159 IRH including a co-occurring diagnosis of SCD, influenza and SCD were the principal discharge diagnosis in 70% and 22%, respectively (data not shown). The only other principal diagnoses with more than one occurrence were fever of unknown origin, septicemia, and convulsions, which parallels coding patterns observed for IRH generally.^{6, 9} When all listed diagnosis codes were considered, the most commonly occurring diagnoses (besides influenza and SCD) were asthma (14%), fever of unknown origin (12%), and fluid and electrolyte disorders (10%). Acute chest syndrome was coded in 10 cases (6.3%). Almost one in four children (23%) admitted with influenza and SCD were coded as experiencing a pain crisis.

Severity of illness

One state (MD) reported data on whether, and for how long, each hospitalization involved care in the intensive care unit (ICU). Across both influenza seasons, 92/805 (11%) of IRH involved at least one day of ICU care. This included 2/33 (6.1%) IRH co-occurring with SCD and 90/772 (12%) IRH not co-occurring SCD, a non-significant difference ($P = 0.32$).

Among children with an ICU stay, the median length of ICU stay was 2 days for both SCD-related and non-SCD-related IRH.

Community- versus hospital-acquired influenza

In the 2 states (NY, CA) that reported whether or not each discharge diagnosis was present on admission, hospital-acquired influenza was rare (81/4,777 (1.7%) IRH without SCD; 0/66 (0%) IRH with SCD). Regardless of whether missing 'present-on-admission' influenza data were coded as missing, present on admission (i.e., community-acquired), or absent on admission (i.e., hospital-acquired), nosocomial infection rates did not exceed 4.3% in any group. Observed absolute differences in nosocomial infection rates between IRH with and without SCD, which ranged from 1.3% to 1.7% in the sensitivity analyses, were not statistically significant.

Discussion

Using databases capturing all hospitalizations in 4 states across 2 influenza seasons, we found that children with SCD were hospitalized for influenza at 56 times the rate of children without SCD and twice the rate of children with CF. The disparity for the subset of children with SCA was even wider. This result is consistent with previous research demonstrating increased IRH rates among children with high-risk chronic conditions, but is the first to quantify this disparity for children with SCD. Had children with SCD had IRH rates identical to children without SCD across the 2 study years, 156 of 159 IRH among children with SCD would have been prevented in these 4 states, with an associated reduction of \$1.9 million in direct hospital charges. Associated reductions in parent work absenteeism and other indirect costs would have added to these savings.

We chose to compare IRH rates among children with SCD to those among children with CF for several reasons. Like SCD, CF is a genetic condition for which comprehensive preventive care is essential to minimize disease complications. Children with CF have a plausible mechanism by which they could be at elevated risk for complications from influenza infection (i.e., compromised pulmonary function) and are a CDC-designated high-risk group for influenza vaccine administration.¹⁶ Our finding that IRH occur at twice the rate among children with SCD compared to those with CF, therefore, is potentially concerning, particularly given that several authors have recently highlighted the disparities that exist between research and clinical care for children with CF compared to those with SCD.^{34, 35} Further research is needed to better understand the underlying determinants of these disparities in chronic disease outcomes and their potential relationships to disparities in preventive services delivery.

Our finding that IRH occur among children with SCD at substantially higher rates than among children without SCD has several possible explanations warranting further study. One possibility is that this disparity is vaccine-related. Children with SCD may receive influenza vaccination less reliably than children without SCD, and/or the vaccine may be less efficacious in children with SCD. The ACIP for the CDC has strongly and consistently recommended influenza vaccination for children with these target conditions since 1978.²⁵ Despite these recommendations, influenza vaccination among children with high risk conditions remains suboptimal, though typically better than children without high risk conditions (Appendix 1). In a recent study of adolescents with high-risk conditions, influenza vaccination rates ranged from 8.3 to 15% across 10 influenza seasons; subjects with hemoglobinopathies were as likely as children with asthma to receive influenza vaccination in adjusted models.³⁶ In one surveillance study of influenza-related hospitalizations, children with high-risk chronic conditions reported receiving influenza vaccination in that season only one-fourth of the time, though they were 3 times more likely

than healthy children to report influenza vaccination (26% vs. 9%, respectively).⁶ To counter these low rates, reminder/recall systems have shown promise in improving influenza vaccination rates among children with high-risk conditions, even during periods of vaccine shortage.³⁷⁻³⁹ It remains unclear, however, whether hematologists or primary care physicians assume primary responsibility for influenza vaccination delivery to children with SCD.

While the influenza vaccine has been shown to be immunogenic in children with SCD,^{21, 40} its effectiveness in this population compared to children without SCD is unknown. Influenza vaccination reduces influenza-related complications in healthy children.⁴¹ Evidence for the benefit of influenza vaccination in 'high risk' pediatric populations is weaker. For example, a systematic review of influenza vaccination in children with asthma was unable to demonstrate a clear benefit,⁴² and no randomized trials of influenza vaccination for children with cystic fibrosis or SCD have been conducted.⁴³ New recommendations to immunize all children against influenza¹⁶ make it extremely unlikely that such trials will be conducted in the future.

A second possibility is that influenza is a more morbid illness in children with SCD than those without. This could result through direct effects (e.g., episodes of pneumonia, acute chest syndrome,⁴⁴ or pain crises caused by influenza) or indirect effects (e.g., influenza-induced asthma exacerbations, given the probable increased prevalence of asthma in children with SCD compared to those without).²²⁻²⁴ Our finding that 1 in 7 hospitalizations for influenza among children with SCD also included a diagnosis code for asthma, a condition associated with increased IRH rates itself,^{12, 13} provides preliminary support for the latter hypothesis. Nonetheless, our findings that IRH associated with SCD were neither longer, more expensive, nor more likely to result in ICU admission or death than those not associated with SCD argues against the notion that influenza is a more morbid illness in children with SCD.

A third possibility is that children with SCD who develop fever with influenza are more likely to be hospitalized than children with fever but without SCD, presumably to exclude the possibility of invasive bacterial disease, for which children with SCD are at elevated risk. One in 8 IRH occurring in children with SCD included the diagnosis 'fever of unknown origin', supporting this possibility. However, a substantial fraction of IRH among children with SCD occurred among children greater than 3 years of age, in whom outpatient management with antibiotics is probably more common than among younger children.⁴⁵ Our data cannot discriminate between hospitalizations for acute care versus those for evaluation and monitoring. A diagnostic testing bias may also partly explain the observed disparity in IRH, if children with SCD are more likely to receive influenza testing when hospitalized compared to children without SCD. It is likely that a combination of all of the above factors explains the wide disparity observed in rates of IRH between children with and without SCD and further study will be needed to untangle the relative contributions of each. Nonetheless, the potential of influenza vaccination in children with SCD to decrease influenza infection and subsequent health care utilization is clear.

A fourth possibility is that children with SCD have increased exposure to the risk of nosocomial influenza infection due to frequent hospitalizations for other SCD-related complications (e.g., pain crises). Precise pediatric nosocomial influenza rates are unknown, as most data originate from outbreak investigations, but surveillance studies suggest that nosocomial transmission of influenza in hospital settings is fairly common.^{46, 47} Nonetheless, our data from 2 states providing "present on admission" data for influenza diagnoses argue strongly against this hypothesis as an explanation for the elevated rates of IRH observed among children with SCD.

Our study has several limitations. We depended on discharge diagnosis coding to identify IRH. A recent surveillance study conducted influenza testing for all children less than 5 years of age hospitalized with acute respiratory tract infections or fever in 3 counties. At the time of discharge, only 28% of hospitalizations in which the surveillance testing was ultimately influenza positive received a discharge diagnosis of “influenza”. This was due, in large part, to low rates of provider-initiated testing for influenza as part of standard clinical care, suggesting that the true burden of IRH is greater than that indicated by discharge diagnosis codes.⁶ Another recent study of laboratory-confirmed, IRH found that the sensitivity for influenza ICD-9-CM codes was 65%.⁴⁸ This latter study analyzed only provider-initiated testing and more closely reflects real-world clinical practice. Nonetheless, we have no reason to believe that undercoding of influenza was different across children with and without SCD. In addition, we suspect that SCD is more likely to be undercoded than overcoded. If so, the observed disparity in influenza-related hospitalization rates between children with and without SCD likely underestimates the true disparity, since a subset of IRH occurring among children with SCD would be misclassified as having occurred in children without SCD.

Conclusion

Influenza-related hospitalizations are substantially more common among children with SCD than those without, supporting the potential importance of vigorous influenza vaccination efforts targeting children with SCD. Future research should measure influenza vaccination rates and predictors of influenza vaccine receipt among children with SCD, as well as attempt to correlate receipt of influenza vaccine with reductions in influenza-related health care utilization and morbidity.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Abbreviations

ACIP	Advisory Committee on Immunization Practices
AHRQ	Agency for Healthcare Research and Quality
CA	California
CDC	Centers for Disease Control and Prevention
CF	cystic fibrosis
FL	Florida
HCUP	Healthcare Cost and Utilization Project
IRH	influenza-related hospitalization
MD	Maryland
NY	New York
SCA	sickle cell anemia
SCD	sickle cell disease
SID	State Inpatient Database

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Table 1
Influenza-related Hospitalizations (IRH) in Children with & without Sickle Cell Disease

	2003/4 Influenza Season					2004/5 Influenza Season					Total	Grand Total
	CA	NY	FL	MD	Total	CA	NY	FL	MD	Total		
Denominator: population estimates												
Children ages 0-17 years	9,424,619	4,584,164	3,858,138	1,376,760	19,243,680	9,429,095	4,542,046	3,933,606	1,376,479	19,281,225	19,281,225	38,524,905
Children without SCD	9,422,859	4,582,043	3,856,049	1,375,627	19,236,578	9,427,366	4,539,957	3,931,485	1,375,345	19,274,153	19,274,153	38,510,731
Children with SCD ^a	1,760	2,121	2,089	1,133	7,102	1,728	2,089	2,121	1,134	7,072	7,072	14,174
Children with SCA ^b	1,029	1,210	1,191	643	4,072	1,011	1,192	1,209	643	4,056	4,056	8,128
Numerator: IRH counts (rates)^c												
Total IRH	2,231 (2.4)	1,417 (3.1)	1,319 (3.4)	541 (3.9)	5,508 (2.9)	509 (0.5)	838 (1.8)	777 (2.0)	264 (1.9)	2,388 (1.2)	2,388 (1.2)	7,896 (2.0)
IRH without SCD	2,214 (2.3)	1,385 (3.0)	1,285 (3.3)	517 (3.8)	5,401 (2.8)	509 (0.5)	818 (1.8)	754 (1.9)	255 (1.9)	2,336 (1.2)	2,336 (1.2)	7,737 (2.0)
IRH with SCD	17 (97)	32 (151)	34 (163)	24 (212)	107 (151)	-d (0)	20 (96)	23 (108)	-d (79)	52 (74)	52 (74)	159 (112)
IRH with SCA ^e	14 (136)	26 (215)	32 (269)	24 (374)	96 (236)	-d (0)	18 (151)	22 (182)	-d (124)	48 (118)	48 (118)	144 (177)
IRH risk ratio, SCD / non-SCD [95% CI]	41 [26 – 66]	50 [35 – 71]	49 [35 – 68]	56 [38 – 84]	54 [44 – 65]	0	53 [34 – 83]	57 [37 – 85]	43 [22 – 83]	61 [46 – 80]	61 [46 – 80]	56 [48 – 65]
IRH risk ratio, SCA / non-SCD	58 [34 – 98]	71 [48 – 104]	81 [57 – 114]	99 [66 – 148]	84 [69 – 102]	0	84 [53 – 133]	95 [62 – 144]	67 [33 – 135]	98 [73 – 130]	98 [73 – 130]	88 [75 – 104]

^aPrevalence of sickle cell disease (SCD) estimated at 1 in 396 non-Latino African Americans + 1 in 122,988 non-Latino whites + 1 in 36,497 Latinos.

^bPrevalence of sickle cell anemia (SCA) estimated at 1 in 700 non-Latino African Americans + 1 in 158,127 non-Latino whites + 1 in 45,622 Latinos. Children with SCA comprise a subset of children with sickle cell disease.

^cRates are IRH per 10,000 children per year.

^dThe AHRQ HCUP Data Use Agreement precludes reporting of cell counts when cells comprise 10 or fewer hospitalizations.

^eIRH among children with SCA comprise a subset of IRH among children with SCD.

Table 2

Influenza-related Hospitalizations (IRH) in Children with Sickle Cell Disease, Cystic Fibrosis, or Neither

	Influenza Season		Total
	2003/4	2004/5	
Denominator: population estimates			
Children ages 0–17 years	19,243,681	19,281,226	38,524,907
Children with neither SCD nor CF	19,232,412	19,270,016	38,502,427
Children with SCD ^a	7,102	7,072	14,174
Children with CF ^b	4,167	4,139	8,306
Numerator: IRH counts (rates)^c			
Total IRH	5,508 (2.9)	2,388 (1.2)	7,896 (2.0)
IRH with neither SCD nor CF	5,373 (2.8)	2,319 (1.2)	7,692 (2.0)
IRH with SCD	107 (151)	52 (74)	159 (112)
IRH with CF	28 (67)	17 (41)	45 (54)
IRH risk ratio, SCD / CF [95% CI]	2.2 [1.5 – 3.4]	1.8 [1.0 – 3.1]	2.1 [1.5 – 2.9]

^aPrevalence of sickle cell disease (SCD) estimated at 1 in 396 non-Latino African Americans + 1 in 122,988 non-Latino whites + 1 in 36,497 Latinos.

^bPrevalence of cystic fibrosis (CF) estimated at 1 in 15,000 non-Latino African Americans + 1 in 2,500 non-Latino whites + 1 in 10,000 Latinos.

^cRates are IRH per 10,000 children per year.

Table 3

Influenza-related Hospitalizations in Children with and without Sickle Cell Disease

	IRH without SCD (N=7,737)	IRH with SCD (N=159)	P-value
Child attributes			
Mean age ± SD (years)	2.8 ± 4.3	5.6 ± 5.6	<0.0001
<1 year (N(%))	3,279 (42)	24 (15)	
1 year	1,143 (15)	27 (17)	
2 years	1,028 (13)	23 (14)	
3–5 years	917 (12)	21 (13)	
>5 years	1,370 (18)	64 (40)	<0.0001
Female (N(%))	3,290 (43)	81 (51)	0.03
Race (N(%))			
White	2,852 (37)	– <i>a</i> (1.9)	
Black	1,303 (17)	135 (85)	
Hispanic	2,276 (29)	– <i>a</i> (5.7)	
Asian / Pacific Islander	296 (3.8)	– <i>a</i> (0)	
Native American	25 (0.32)	– <i>a</i> (0)	
Other / Missing	985 (13)	12 (7.5)	<0.001
Urban / rural residence (N(%))			
Large metro (≥1,000,000 residents)	5,517 (71)	141 (89)	
Small metro (<1,000,000 residents)	1,799 (23)	17 (11)	
Micropolitan area	226 (2.9)	– <i>a</i> (0)	
Other / missing	195 (2.5)	– <i>a</i> (0.63)	<0.001
Hospitalization attributes			
Admission source (N(%))			
Emergency department	4,718 (61)	120 (75)	
Ambulatory (non-ED)	2,435 (31)	36 (23)	
Other hospital	576 (7.4)	– <i>a</i> (1.9)	
[Missing]	– <i>a</i> (0.10)	– <i>a</i> (0)	0.001
Procedures reported (N(%))			
Mechanical ventilation	336 (4.3)	– <i>a</i> (0)	0.007
Respiratory medication administered by nebulizer	432 (5.6)	– <i>a</i> (0.63)	0.007
Other oxygen enrichment	205 (2.6)	– <i>a</i> (1.3)	0.28
Transfusion	143 (1.8)	20 (13)	<0.001
Injection of antibiotics	450 (5.8)	– <i>a</i> (5.7)	0.93
Lumbar puncture	1,046 (14)	– <i>a</i> (1.3)	<0.001
Mean length of stay	4.2 days	3.4 days	0.27
Mean total charges	\$18,779	\$11,924	0.11
Primary expected payer (N(%))			

	IRH without SCD (N=7,737)	IRH with SCD (N=159)	P-value
Medicaid	4,198 (54)	101 (64)	
Private insurance	2,872 (37)	38 (24)	
Other	677 (8.6)	20 (13)	0.002
Deaths (N(%))	45 (0.58)	– ^a (0)	0.34

^aThe AHRQ HCUP Data Use Agreement precludes reporting of cell counts when cells comprise 10 or fewer hospitalizations.

Table 4

Comparison of hospital- vs. community-acquired influenza infections in hospitalizations with and without co-occurring diagnoses of sickle cell anemia^a

	Influenza-related hospitalizations ^b			P-value
	Without SCD	With SCD		
Influenza diagnosis present on admission?^c (N(%))				
Yes (community-acquired)	4,777 (98)	66 (100)		0.29
No (hospital-acquired)	81 (1.7)	0 (0)		

^aData limited to 2 states (CA, NY) reporting whether discharge diagnoses were present on admission.

^b61 hospitalizations included more than 1 influenza discharge diagnosis code (2 influenza codes: N=60; 3 influenza codes: N=1). For these 61 hospitalizations, the first-listed influenza diagnosis was assessed as present or absent on admission.

^cExcludes hospitalizations for which the relevant 'present on admission' variable is missing.