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Serious Infection Rates among Children with Systemic Lupus Erythematosus Enrolled in Medicaid

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Abstract

Objective—To investigate the nationwide prevalence and incidence of serious infections among children with systemic lupus erythematosus (SLE) enrolled in Medicaid, the U.S. health insurance program for low-income patients.

Methods—From Medicaid claims (2000–2006) we identified children 5 to <18 years old with SLE (≥3 ICD-9 codes of 710.0, each >30 days apart) and lupus nephritis (LN; ≥2 ICD-9 codes for kidney disease on/after SLE codes). From hospital discharge diagnoses, we identified infection subtypes (bacterial, fungal, viral). We calculated incidence rates (IR) per 100 person-years (PY), mortality rates, and hazard ratios adjusted for sociodemographic factors, medications, and preventive care.

Results—Among 3,500 children with SLE identified, 1,053 serious infections occurred over 10,108 person-years; the IR was 10.42/100 PY (95% CI 9.80, 11.07) among all those with SLE and 17.65/100 PY (95% CI 16.29, 19.09) among those with LN. Bacterial infections were most common (87%; of which 39% were bacterial pneumonias). In adjusted models, African Americans and Native Americans had higher rates of infections compared with white children, and those with comorbidities or receiving corticosteroids had higher infection rates than those without. Males had lower rates of serious infections compared to females. The 30-day post-discharge mortality rate was 4.4%.

Conclusions—Overall, hospitalized infections were very common in children with SLE, with bacterial pneumonia being the most common infection. Highest infection risks were among

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The authors have no disclosures or conflicts of interest to declare.

African and Native American children, those with LN, comorbidities, and those taking corticosteroids.

Keywords

systemic lupus erythematosus; pediatric rheumatology; infection; complications

Background

Infections are commonly reported among individuals with systemic lupus erythematosus (SLE)(1–5). The observed increased risk of infection has been attributed to both SLE itself and the use of immunosuppressant therapies(1, 6, 7). It has been noted that those with lupus nephritis (LN) may be at higher risk of infection compared to those SLE patients without LN(1, 3, 8–10). Our prior work has demonstrated that infections were very common and associated with high mortality among adults with SLE enrolled in Medicaid in the U.S. between 2000–2006, and that infection was the second most common cause of death among children with LN-associated end-stage renal disease (ESRD) in the U. S., 1995–2006 (3, 11).

The majority of reports to date have come from single academic centers, with few estimates of a nationwide prevalence and incidence of serious infections among children with SLE. While there have been prior studies utilizing national registries that have reported infectious risk among children with juvenile arthritis (12), to our knowledge, there have been no such reports among children with SLE. Our goal was to investigate the U.S. prevalence, incidence, and mortality rates for serious infections, as well as adjusted hazard ratios comparing demographic subsets, among children with SLE, with or without LN, enrolled in Medicaid, the U.S. nationwide public insurance for low income individuals and families

Methods

Study Population and Case Identification

The Medicaid Analytic eXtract (MAX) data system contains demographic information and all billing claims for Medicaid enrollees from 47 states and the District of Columbia. We included children enrolled in Medicaid for six or more months between January 1, 2000 and December 31, 2006.

SLE and LN case identification

We identified all children with SLE (≥3 International Classification of Diseases, ninth revision (ICD-9) codes of 710.0, each at least 30 days apart), aged 5 to <18 years at the date of meeting the above criteria for SLE. As per our previously reported algorithm, among those with SLE, we identified children with LN (≥2 ICD-9 codes for kidney disease on or after SLE codes from a physician claim or a hospital discharge diagnosis) (13, 14). The date children met these criteria for SLE or LN was considered the index date. We also required a baseline, six month enrollment period. In the event that the index date fell prior to accumulation of the required six months of enrollment to establish baseline covariates, the next subsequent SLE claim was used as the index date.

Serious infection outcome definition

Serious infections were defined as those requiring hospitalization, and were identified from discharge diagnosis ICD-9 codes beginning the day following the index date. We did not restrict to those admissions where infection was listed as the primary discharge diagnosis, in order to capture all infections requiring hospitalization. Infections occurring after the age of 18 years were censored. These admissions were grouped into subtypes of infection including bacterial (bacteremia, cellulitis, pneumonia, pyelonephritis, osteomyelitis, septic arthritis endocarditis), fungal (aspergillosis, cryptococcosis, histoplasmosis, pneumocystosis), viral (herpes zoster, cytomegalovirus, varicella zoster, influenza) and mycobacterial infections (tuberculosis, atypical mycobacteria). A prior study observed that ICD-9 codes from hospital discharge diagnosis codes were a good surrogate for chart review, with positive predictive values (PPV) of 80% for bacterial and 76% for opportunistic infections, excluding systemic candidiasis(15). Hence we excluded systemic candidiasis from our fungal infection outcome definition, as well as excluding meningitis and encephalitis due to challenges in distinguishing infectious causes from those due to SLE itself.

Covariates

For the children identified as having SLE and LN, we defined demographic characteristics including age, sex, self-reported race and ethnicity, region of residence in the U.S., and socioeconomic stratus (SES) group (high, low delineated by median threshold score), derived from a previously developed area-level (zip code) US census-based composite score(16). We collected comorbidity, medication and preventive care-related covariates during the 6 months prior to and including the first SLE claim (baseline period). Comorbidity burden was calculated using a SLE-specific risk adjustment index, previously developed and validated in adults with SLE and shown to be a better predictor of inpatient mortality among SLE patients than the Charlson comorbidity index (17). In addition to the chronic medical conditions captured by the Charlson index(18), the SLE-specific risk adjustment index includes autoimmune hemolytic anemia, thrombocytopenia, pericarditis, pleuritis, seizures and psychosis (17). We categorized children with SLE and LN into baseline medication users for hydroxychloroquine (HCQ), corticosteroids (CS) (prednisone, methylprednisolone, dexamethasone, hydrocortisone, prednisolone and cortisone; baseline users are those on a minimum of 20mg/day of prednisone) and immunosuppressants (IS) (mycophenolate mofetil, mycophenolic acid, oral or intravenous cyclophosphamide, azathioprine, cyclosporine, or tacrolimus). We also identified those children who received *Pneumocystis jirovecii* pneumonia (PCP) prophylaxis from dispensings for trimethoprim-sulfamethoxazole, atovaquone, dapsone or pentamidine. We assessed other preventive care using CPT codes for influenza or pneumococcal vaccines.

Statistical Analysis

Among the population of children who met our definitions of SLE and/or LN between 2000–2006, subjects contributed person time starting when subjects met the definitions for SLE or LN. From that day forward, we calculated the number of serious infections requiring hospitalization to yield prevalence and incidence rates (IR) per 100 person-years (PY), overall and by infection subtype and stratified by covariates sex, age and race/ethnicity. IRs

and incidence rate ratios (IRRs) and the corresponding 95% confidence intervals (CI) were calculated using Poisson regression models, overall and stratified by socio-demographic factors. We also calculated the proportion of children with SLE and LN who were free of infection during the period of observation, and those who had 1, 2 or 3 or more infections. Hazard ratios for the time to first serious infection during follow-up were calculated using Cox regression models, adjusted for age, race/ethnicity, region of residence, year of enrollment, baseline HCQ, CS and IS medication use, and baseline preventive care (PCP prophylaxis, influenza and pneumococcal vaccination). We tested the proportional hazards assumption in all of our Cox models by testing interactions of dependent covariates of interest with the log of time. There was no evidence for violations of our proportionality assumptions in our models (19).

We examined mortality rates among those with serious infections, during and within 30 days of hospitalization (or the earlier of their final Medicaid enrollment date or the end of follow-up in our database).

All analyses were conducted in SAS, version 9.4 (Cary, NC). Data were obtained from the Center for Medicare and Medicaid Services (CMS) through an approved data use agreement. Cell counts of 10 or fewer individuals were suppressed due to Federal reporting requirements. Institutional review board approval was obtained for all aspects of this study.

Results

We identified a total of 3,500 children with SLE between January 1, 2000 and December 31, 2006, 1,297 of whom also had LN as per our algorithm. Table 1 summarizes the demographics of the study population. The majority of the population was female (84%), between the ages of 15–18 years (48%) and African American (41%). Median follow-up time was 2.6 years (Interquartile range [IQR] 1.2, 4.4 years) in the total SLE cohort and 2.4 years (IQR 1.2, 4.2 years) among those with LN. The majority received corticosteroids during the baseline period (67% of SLE and 80% of LN). We observed that only 14% of all children with SLE and 20% of children with LN received preventive care, with 3% of those with SLE and LN receiving influenza vaccinations during the 6 month baseline period, and 11% of those with SLE and 17% of those with LN received PCP prophylaxis.

Among 3,500 children with SLE, during a cumulative follow-up of over 10,100 person years, we identified a total of 1,053 serious infections among 593 children. Of those, 624 infections occurred among 326 children with LN. At least 1 infection during follow-up was identified in 17% of all children with SLE and in 25% among children with LN. The majority of those who had an infection (63% of all SLE and 56% of LN) had a single infection during their follow-up, whereas 18% of children with SLE and 21% with LN had three or more serious infections.

The majority of infections were bacterial (87%), 11% were viral, and 1.3% were fungal. Mycobacterial infections were rare, comprising less than 1% of all infections among all children with SLE. The most common bacterial infections were pneumonia (438 cases),

followed by bacteremia (274 cases) and cellulitis (272 cases). Herpes zoster was the most common viral infection with 81 documented cases.

We observed an IR of 10.4 infections per 100PY (95% CI 9.8, 11.1) among children with SLE (Table 2). Stratified incidence demonstrated higher rates of serious infections among children in early adolescence (9–12 years) compared with the youngest children (5– <9 years) (IRR 1.44, [95% CI 1.03, 2.02]), among African American and Native American children compared with white children (IRR 1.83, [95% CI, 1.51, 2.22] and IRR 1.81, [95% CI, 1.17, 2.80], respectively), and among those with higher (*versus* lower) SLE risk adjustment indices (IRR 2.21, [95% CI 1.95–2.50]). We also observed fewer infections among male compared to female SLE (IRR 0.79 [95% CI 0.66, 0.95] and LN patients (IRR 0.68 [95% CI 0.52, 0.90]) (Table 3).

Among those with LN, we observed a higher overall incidence of serious infections (IR 17.7/100PY, [95% CI 16.3, 19.1]) (Table 2) compared to those without LN (5.8/100PY, [95% CI 5.2, 6.5]). Similar to the total SLE cohort, serious infection rates among those with LN were higher among children of African American (IRR 1.71, [95% CI 1.23, 2.36]), and Hispanic (IRR 1.44, [95% CI 1.01, 2.04]) compared with white race/ethnicity, as well as among those with higher (*versus* lower) SLE comorbidity indices (IRR 1.99, [95% CI 1.66, 2.39]). We also observed more infections among those who received prophylaxis in the baseline period, compared to those who did not, both among all SLE patients (IRR 1.39, [95% CI 1.16, 1.65]) and among those with LN (IRR 1.28, [95% CI 1.02, 1.61]).

Multivariable-adjusted Cox proportional hazards models for the risk of first infection demonstrated comparable risk across categories of age, socioeconomic status, and preventive case use at baseline, among children with SLE and LN (Table 4). Lower infection risk was observed among male compared to female patients (SLE HR 0.75 [95% CI 0.59, 0.95]; LN HR 0.72 [95% CI 0.52, 0.98]). There was evidence for elevated risk of infection among African American children with SLE and those with LN (HR 1.70, [95% CI 1.32, 2.20], HR 1.86, [95% CI 1.24, 2.80], respectively) compared with white children, as well as among Native American children compared with white children with SLE (HR 1.79, [95% CI 1.02, 3.13]). Higher comorbidity indices were also associated with an increased risk of first infection among those with SLE (HR 2.01, [95% CI 1.70, 2.38]) and those with LN (HR 1.92, [95% CI 1.52, 2.43]). Among all children with SLE, baseline CS use was associated with an elevated risk of a first infection (HR 1.59, [95% CI 1.28, 1.97]). However this association was not observed among children with LN.

Among the 354 children with SLE who had hospital admissions associated with serious infections, there were 26 deaths within 30 days of the admission, yielding an overall mortality rate of 4.4%. Of these children, over half had LN and 77% received CS during the baseline period. This was higher than the observed mortality rate of 1.6% in the total cohort of 3,500 children with SLE.

Discussion

Our study used nationwide data from the U.S. Medicaid program to estimate the prevalence and incidence of serious infections among children with SLE and LN. We observed high rates of serious infections among these children in general, particularly among those with LN and those of African American and Native American race/ethnicity as well as those with a higher burden of comorbidities. A striking majority of these hospitalized infections were for bacterial pneumonia and the majority of viral infections were herpes zoster.

Our rates of serious infections are comparable to those observed in several smaller studies of childhood-onset SLE. In studies of patients followed at tertiary care centers it was observed that 37 – 57% of SLE patients had at least one serious infection requiring prolonged parenteral, antimicrobial therapy and/or hospitalization over an average observation period of 5 to 7 years (4, 5), with an estimated annual incidence of 17 infections per 100 person years(5). We observed lower rates of serious fungal infections in our population compared with a prior report of invasive fungal infections affecting almost 4% of childhood onset SLE patients followed by 10 pediatric rheumatology services in Brazil (20). The difference may, in part, be due to the fact that our study excluded systemic candidiasis from the fungal infection outcome definition, whereas candidiasis accounted for 61% of the invasive fungal infection cases observed in the Brazilian study (20).

Similar to our observation of higher rates of infection among children with LN, past studies have observed kidney involvement, as well as neuropsychiatric manifestations and treatment with CS or IS, to be associated with major infections (5). In our study, more than a third of the children with serious infections had three or more such episodes, which is higher than what was reported in prior series (4). A study of children treated with cyclophosphamide for LN in Thailand, reported that fatal infections occurred in 13 of 84 patients (15%)(21). The authors observed that previous treatment with pulse methylprednisolone, kidney disease, and fungal infection, were associated with fatal infections in their population. In the U.S., a downward trend in hospitalization-related inpatient mortality among all children with SLE, has been reported by a study of the national Kids' Inpatient Database (KID) between 2000 to 2009, with a decrease from 1% to 0.6% (p-value = 0.04)(22). The 30-day mortality rate of 4.3% in our study population is in keeping with prior reports in childhood onset SLE; of note, the mortality rate included deaths that occurred both during and following hospitalizations for serious infections. In the adult SLE population, we described a 30-day mortality following hospitalized infection of 2.1% among all adults with SLE and 3.9% among those with LN(3). Similar to the present study in children, we also observed higher rates of serious infections among adult African Americans with SLE compared to whites (HR 1.14, [95% CI 1.06–1.21]), as well as Native Americans compared with whites (HR 1.40, [95% CI 1.20–1.64])(3). In contrast, the study of infections in adults, like others (23), observed increased risk of first infection among male patients compared with female patients, rather than the relative reduced risk we observed in children with SLE. This may reflect a true difference in the relationship between sex and infectious risk between children and adults with SLE, that requires replication in an independent cohort.

A study of hospitalized bacterial infection rates among children with juvenile idiopathic arthritis (JIA) enrolled in Medicaid during a comparable era (2000–2005) reported an overall incidence of 2.8 per 100 person-years (95% CI 2.5 – 3.1)(12). This estimate included children on methotrexate and tumor-necrosis factor (TNF) inhibitor therapy. We found that incidence rates of serious bacterial infections are almost four times higher among children with SLE compared to children with JIA, and over six times higher among children with LN compared to children with JIA. Strikingly, when comparing hospitalized bacterial infection rates with the pediatric control group, rates are 10-fold higher among those with SLE and nearly 18-fold higher in LN.

We observed higher rates of infections among children with SLE who had received PCP prophylaxis during the baseline period, likely representing confounding by indication, or indication bias. If Medicaid enrollment followed a prior infection, children may have received prophylaxis due to their previous history of infection, not captured by Medicaid claims from 2000–2006. We did not observe an association between infections and vaccinations, due to the low rates of influenza and pneumococcal vaccine documentation during the baseline period. Childhood vaccinations that are not billed to Medicaid, for example those covered by community centers or the state Child Health Insurance Program (SCHIP), are not captured in MAX. (http://www.cdc.gov/vaccines/programs/vfc/providers/questions/qa-medicaid.html). Pneumococcal vaccination is administered by one or two doses during childhood. Pneumococcal vaccination rates captured by MAX are further reduced by the baseline observation window of six months, in a group of prevalent SLE cases. These factors both contribute to the lower rates of pneumococcal and influenza vaccination in our cohort and limited statistical power to investigate the relationship between preventive care and serious infections.

It is difficult to distinguish whether the increased incidence of serious infections among those with SLE is attributable to SLE therapies or the disease itself. Medication use was assessed only during the baseline period to prevent inducing a spurious association between infection and medications. By examining medications at baseline only, we avoided attributing infections to medication changes that may have occurred as a result of infection (ie: reverse causation). Our limited ability to attribute infections to medication changes during follow-up, is a limitation of the study. Further studies are needed to investigate this question further.

We acknowledge some limitations of our study. Infections could not be confirmed microbiologically or histologically, but were identified from diagnosis codes in billing claims. However, the methods used for serious infection case ascertainment have been previously validated in an adult population administrative database, in which ICD-9 discharge diagnosis codes for all bacterial conditions combined had an 80% positive predictive value(15). We could also not delineate those infections that were community-acquired from those that were nosocomial; however, our choice of certain serious infections included those more likely to have been the cause of hospitalization than to be a result of the hospitalization. Our study has a number of strengths. Using national Medicaid administrative data enabled the examination of serious infection rates among one of the largest collections of children with SLE to date over seven years of Medicaid enrollment. We

calculated serious infection incidence rates across categories of age, race/ethnicity and region of the U.S., and examined sociodemographic, medication and comorbidity associations with serious infections.

We take from this study that a high burden of serious infections exists among children diagnosed with SLE and enrolled in Medicaid from 2000–2006. There were significantly higher rates of serious infections among children of African and Native American race/ethnicity compared to white children, those with LN compared to those without LN, those with higher comorbidity, and among those treated with corticosteroids. Future studies will need to address how these observed infection rates may be mediated and modified by IS use, HCQ and prophylactic measures, including vaccination and antibiotic use, and the causes of the striking racial and ethnic disparities in this complication of SLE.

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Significance and Innovations

- Children with systemic lupus erythematosus enrolled in Medicaid between 2000–2006 experienced high rates of serious infection requiring hospitalization.
- Higher infection rates occurred among those with LN compared to those without LN, African American and Native children compared to white children and those on corticosteroids compared to those not on corticosteroids. Lower risk of infection was observed among males compared to females.
- Further work is required to elucidate the role for preventative measures including vaccine and antibiotic prophylaxis.

Table 1

Baseline demographics of children with systemic lupus erythematosus and lupus nephritis enrolled in Medicaid, 2000–2006[a]

	Systemic Lupus Erythematosus (SLE) N = 3,500	Lupus Nephritis (LN) N = 1,297
Age		
5 – <9 years	202 (5.8)	62 (4.8)
9 – <12 years	490 (14.0)	186 (14.3)
12 – <15 years	1,121 (32.0)	415 (32.0)
15 – <18 years	1,687 (48.2)	634 (48.9)
Female sex	2,929 (83.7)	1,065 (82.1)
Race/Ethnicity		
White	711 (20.3)	175 (13.5)
Black or African American	1,433 (40.9)	565 (43.6)
Asian	235 (6.7)	114 (8.8)
Native American	65 (1.9)	28 (2.2)
Other	164 (4.7)	76 (5.9)
Hispanic	892 (25.5)	339 (26.1)
Region of residence		
South	1,470 (42.0)	543 (41.9)
West	823 (23.5)	315 (24.3)
Northeast	626 (17.9)	239 (18.4)
Midwest	581 (16.6)	200 (15.4)
SLE Risk Adjustment Index[b]		
Mean (SD)	1.11 (1.73)	2.56 (1.73)
Zip code level socioeconomic status[c]		
Mean (SD)	1.24 (1.74)	1.28 (1.76)
Corticosteroid use[d]	2,351 (67.2)	1,061 (81.8)
Hydroxychloroquine use[d]	1,845 (52.7)	689 (53.1)
Immunosuppressant use[d]	1,085 (31.0)	516 (39.8)
Preventive care use[d]	500 (14.3)	256 (19.7)
Prophylaxis	395 (11.3)	219 (16.9)
Influenza vaccination	98 (2.8)	42 (3.2)
Pneumococcal vaccination	29 (0.8)	—

[a] Values are the number (percentage) of enrollees unless otherwise specified.

[b] SLE Risk Adjustment index (range 0– 16)(17)

[c] Socioeconomic status based on 7 zip-code level indicators from 2000 U.S. Census ((Z-scored, range −3.82 [lowest] to 6.06 [highest])(16)

[d] Medication and preventive care during the 6 month baseline period. Corticosteroids include prednisone, methylprednisolone, dexamethasone, hydrocortisone, prednisolone and cortisone; baseline corticosteroid users are those on a minimum of 20mg/day of prednisone. Immunosuppressants include mycophenolate mofetil, mycophenolic acid, oral or intravenous cyclophosphamide, azathioprine, cyclosporine, or tacrolimus.

— Cell counts of 10 or fewer individuals have been suppressed due to Federal reporting requirements.

Table 2

Incidence Rates (IR) of serious infections by infection subtype among children with systemic lupus erythematosus and lupus nephritis enrolled in Medicaid, 2000–2006

	Systemic Lupus Erythematosus Person Years (PY) = 10,108		Lupus Nephritis Person Years (PY) = 3,536	
	N events	IR per 100PY (95% CI)	N events	IR per 100PY (95% CI)
All infections	1,053	10.42 (9.80, 11.07)	624	17.65 (16.29, 19.09)
Bacterial	917	9.07 (8.49, 9.68)	535	15.13(13.88, 16.47)
Viral	116	1.15 (0.95, 1.38)	76	2.15 (1.69, 2.69)
Fungal	14	0.14 (0.08, 0.23)	—	—

Incidence rates (IR) are reported per 100 person years (PY).

— Cell counts of 10 or fewer individuals have been suppressed due to Federal reporting requirements.

Table 3

Incidence Rates (IR) and incidence rate ratios (IRR) of serious infections in children with systemic lupus erythematosus and lupus nephritis, stratified by sociodemographics, among children enrolled in Medicaid, 2000–2006

	Systemic Lupus Erythematosus (SLE) N = 3,500		Lupus Nephritis (LN) N = 1,297	
	IR	**IRR (95% CI)**	**IR**	**IRR (95% CI)**
Age				
5 – <9 years	7.9111.39	ref	15.95	ref
9 – <12 years	10.00	**1.44 (1.03, 2.02)**	19.36	1.21 (0.75, 1.96)
12 – <15 years	10.70	1.26 (0.92, 1.75)	17.03	1.07 (0.68, 1.68)
15 – <18 years	10.79	1.35 (0.99, 1.86)	17.74	1.11 (0.71, 1.73)
Sex				
Female	8.50	ref	18.69	ref
Male	6.86	**0.79 (0.66, 0.95)**	12.76	**0.68 (0.52, 0.90)**
Race/Ethnicity [a]				
White		ref	12.01	ref
African American	12.56	**1.83 (1.51, 2.22)**	20.52	**1.71 (1.23, 2.36)**
Asian	6.86	1.00 (0.73, 1.37)	11.00	0.92 (0.58, 1.45)
Native American	12.39	**1.81 (1.17, 2.80)**	17.00	1.42 (0.72, 2.77)
Hispanic	9.46	1.38 (1.11, 1.71)	17.27	**1.44 (1.01, 2.04)**
Region of residence				
NorthEast	9.47	ref	17.90	ref
South	11.09	1.17 (0.98, 1.40)	19.07	1.07 (0.84, 1.36)
West	8.77	0.93 (0.76, 1.13)	13.85	0.77 (0.58, 1.03)
MidWest	12.42	**1.31 (1.07, 1.61)**	20.19	1.13 (0.84, 1.52)
SLE Risk Adjustment Index [b]				
Low	7.11	ref	14.20	ref
High	15.68	**2.21 (1.95, 2.50)**	28.26	**1.99 (1.66, 2.39)**
Socioeconomic status [c]				
High	10.70	ref	17.29	ref
Low	10.12	0.95 (0.83, 1.07)	17.99	0.96 (0.80, 1.15)
Preventive care use [d]				
Prophylaxis	13.78	**1.39 (1.16, 1.65)**	21.62	**1.28 (1.02,1.61)**
Influenza vaccination	9.44	0.92 (0.58, 1.48)	19.28	1.07 (0.60, 1.88)
Pneumococcal vaccination	3.95	0.37 (0.11, 1.19)	—	—

Incidence rates (IR) are reported per 100 person years (PY).

Bolded IRRs indicated statistically significant (p<0.05) values

[a] 4.7% of children with SLE had missing or other race reported

[b] SLE Risk Adjustment index (median value in cohort is threshold for high vs. low)(17)

[c] Socioeconomic status based on 7 zip-code level indicators from 2000 U.S. Census ((Z-scored, range −3.82 [lowest] to 6.06 [highest])(16)

[d] Preventive care during the 6 month baseline period

— Cell counts of 10 or fewer individuals have been suppressed due to Federal reporting requirements.

Table 4

Risk of first serious infection (HR) [a] in children with systemic lupus erythematosus (SLE) and lupus nephritis (LN), adjusted for sociodemographics and categories of medication use among children enrolled in Medicaid, 2000–2006

	Systemic Lupus Erythematosus (SLE) HR (95% CI)	Lupus Nephritis (LN) HR (95% CI)
Age (ref: 5 – <9 years)		
9 – <12 years	1.10 (0.73, 1.68)	0.81 (0.48, 1.37)
12 – <15 years	0.99 (0.66, 1.46)	0.79 (0.49, 1.28)
15 – <18 years	1.06 (0.72, 1.55)	0.77 (0.48, 1.24)
Sex (ref: Female)		
Male	**0.75 (0.59, 0.95)**	**0.72 (0.52, 0.98)**
Race/Ethnicity (ref: White)		
African American	**1.70 (1.32, 2.20)**	**1.86 (1.24, 2.80)**
Asian	1.02 (0.68, 1.52)	1.07 (0.61, 1.88)
Native American	**1.79 (1.02, 3.13)**	1.49 (0.64, 3.44)
Hispanic	1.23 (0.93, 1.64)	1.42 (0.92, 2.19)
Region of residence (ref: NorthEast)		
South	1.18 (0.91, 1.54)	1.12 (0.78, 1.61)
West	1.14 (0.87, 1.51)	0.99 (0.69, 1.43)
MidWest	**1.40 (1.05, 1.87)**	1.34 (0.90, 1.99)
SLE Risk Adjustment Index [b] (ref: Low)		
High	**2.01 (1.70, 2.38)**	**1.92 (1.52, 2.43)**
Zip code level socioeconomic status [c] (ref: High)		
Low	0.83 (0.68, 1.01)	0.84 (0.63, 1.11)
Medication Use [d] (ref: No use at baseline)		
Hydroxychloroquine	0.85 (0.72, 1.00)	0.96 (0.76, 1.20)
Immunosuppressants	1.06 (0.89, 1.27)	1.06 (0.84, 1.34)
Glucocorticoids	**1.59 (1.28, 1.97)**	0.83 (0.60, 1.14)
Preventive care use [d] (ref: No use at baseline)		
Pneumocystis prophylaxis	1.25 (0.99, 1.58)	1.10 (0.82, 1.47)
Influenza vaccination	1.17 (0.65, 2.08)	1.24 (0.63, 2.44)
Pneumococcal vaccination	0.42 (0.11, 1.70)	-

Bolded HRs indicated statistically significant ($p<0.05$) values

[a] Cox proportional hazard models adjusted for age, sex, race/ethnicity, region, zip code level socioeconomic status, SLE risk adjustment index, calendar year, hydroxychloroquine, corticosteroid and immunosuppressant and preventive care use never/ever.

[b] SLE Risk Adjustment index (median value in cohort is threshold for high vs. low)(17)

[c] Socioeconomic status based on 7 zip-code level indicators from 2000 U.S. Census (median value in cohort is threshold for high vs. low)(16)

[d] Medication and preventive care during the 6 month baseline period

- Cell counts of 10 or fewer individuals have been suppressed due to Federal reporting requirements.